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Heart failure prognosis and the options to improve

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The impact of anthropometric measures of obesity on heart failure outcomes in Asia

C Chanchal Chandramouli[1]; WT Tay[1]; THK Teng[1]; XY Jin[1]; S Asali[1]; J Tromp[1]; JJL Yap[1]; MR Macdonald[2]; AM Richards[3]; LH Ling[3]; I Anand[4]; CSP Lam[1]
[1]National Heart Centre Singapore, National Heart Research Institute Singapore, Singapore, Singapore; *[2]Changi General Hospital, Singapore, Singapore*; *[3]Cardiovascular Research Institute, Singapore, Singapore, Singapore*; *[4]Veterans Affairs Medical Center, Minneapolis, United States of America*

On behalf of: ASIAN-HF Investigators
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Background: The inverse association between obesity, traditionally classified by body mass index (BMI), and mortality among patients with heart failure (HF) is well-reported in Western nations but confined to a few small single-centre studies across Asia. Given the reservations against using BMI to measure obesity and the predisposition of Asian patients to a lean HF phenotype we assessed whether this obesity paradox exists in this region when different anthropometric measures are used.
Purpose: To examine a) the associations of BMI with clinical characteristics (b) the relationships of BMI, waist circumference (WC) and waist-to-height ratio to outcomes among Asian patients with HF.
Methods: Using the prospective multinational Asian Sudden Cardiac Death in HF (ASIAN-HF) Registry, the relationship between BMI (WHO-recommended Asian cut-offs: < 18.5, 18.5-23.0, 23.0-27.5, = 27.5 kg/m^2 for underweight, normal, overweight and obese respectively) with clinical characteristics and outcomes was assessed. In a subset of patients with available measurements of WC, the associations of BMI, WC, waist-to-height ratio with 1-year all-cause mortality and composite outcomes (HF hospitalisation or 1-year mortality) were examined.
Results: Among 5954 subjects (mean age 61.7years, 26.3% women) 6.1, 30.3, 37.5 and 26.2% were underweight, normal, overweight and obese respectively. Positive correlations were observed between increasing BMI and blood pressure, WC, prevalence of hypertension, diabetes, myocardial infarction, and peripheral oedema (p-trend < 0.001).
A linear inverse trend in crude all-cause mortality at 1-year was observed across BMI subgroups (16.5%, 11.5%, 9.5%, 6.9%, p < 0.001), with the lowest rates in the obese category. Compared to obese patients, underweight patients had the highest hazards of 1-year all-cause mortality (adjusted hazards ratio [aHR] = 2.38; 95% CI 1.64-3.44) and composite outcomes (aHR = 1.53; 95 CI 1.16-2.00), followed by patients in normal and overweight categories.
Among subjects with available WC measures (n = 2051), every 1kg/m^2 increase in BMI was associated with reduced crude and adjusted risk of mortality (5% and 8% respectively, p < 0.003). WC and waist-to-height ratio did not affect the crude hazards of death. Interestingly, BMI (per 1kg/m^2) and waist-to-height ratio (per 0.1 increment) was respectively associated with 6% lower and 55% higher adjusted risk of composite outcomes (p < 0.01).
Conclusion: Among Asian patients with HF, those with high BMI had more prevalent comorbidities yet better outcomes, compared to low BMI. This obesity paradox was observed, only when obesity was defined by BMI and not WC or waist-to-height ratio. A direct correlation was observed between central obesity and poor composite outcomes in HF. These findings carry implications for the clinical application of anthropometric parameters in risk stratification of patients with HF.

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S2PLIT Score: a simple risk score predicting post-discharge 1-year mortality in patients with acutely decompensated heart failure

JA Josip Andjelo Borovac[1]; K Novak[2]; J Bozic[1]; D Glavas[2]
[1]University of Split School of Medicine, Department of Pathophysiology, Split, Croatia; *[2]University Hospital of Split, Division of Cardiology, Department of Internal Medicine, Split, Croatia*

Background: The acutely decompensated heart failure (ADHF) is a condition associated with poor outcomes, especially during the first year after hospitalization.
Purpose: To assess the performance of the S2PLIT scoring model in predicting a 1-year all-cause mortality in ADHF patients.
Methods: Clinical and laboratory data of 340 patients admitted for ADHF at a single-center ICCU were retrospectively examined. Variables that were significantly associated with 1-year mortality in multivariate regression analysis adjusted for age, sex, NYHA class, post-discharge medications, and comorbidities were included in the risk stratification model. Hosmer-Lemeshow test and C-statistic were used to determine the validity and predictive power of the model. Kaplan-Meier survival analysis was used to assess survival among risk groups.
Results: The average age of the studied population was 74 ± 9.8 years and 50.6% were women. Seventy-eight patients (22.9%) were NYHA II, 162 (47.8%) were NYHA III while 100 patients (29.5%) belonged to NYHA IV functional class. The average left-ventricular ejection fraction (LVEF) was 42.2 ± 9.5% while average systolic blood pressure (SBP) was 137.4 ± 27.4 mm Hg. Serum creatinine, uric acid, and sodium levels averaged 142.3 ± 96.2 μmol/L, 489 ± 172.9 μmol/L, and 138.2 ± 4.4 mmol/L, respectively. Significant independent predictors for 1-year all-cause mortality in our sample were LVEF, SBP, prior history of ADHF hospitalization(s) and serum creatinine, uric acid, and sodium levels. According to calculated S2PLIT score (Table 1), 153, 78 and 109 patients were stratified into a low-, intermediate- and high-risk groups with the observed mortality rates of 9.8% (15/153), 33.3% (26/78) and 91.7% (100/109), respectively. The obtained area under the curve (AUC) for the proposed score model was 0.900 (95% CI 0.864-0.937, SE 0.019, p < 0.001) (Figure 1A) with clear separation among respective risk groups in terms of cumulative survival (Figure 1B).
Conclusions: The S2PLIT scoring model performed well and demonstrated high predictive power for all-cause mortality in ADHF patients during the 1-year period following discharge.

Table 1

Variable collected at admission	Points
Left-ventricular ejection fraction ≤ 45%	1
Serum creatinine of 125-160 μmol/L (1 point) or > 160 μmol/L (2 points)	1 OR 2
Serum sodium ≤ 135 mmol/L	1
Serum uric acid > 440 μmol/L	1
Systolic blood pressure < 130 mm Hg	1
History of prior hospitalization(s) due to exacerbation of the heart failure	1

Clinical and laboratory parameters incorporated into the S2PLIT score.

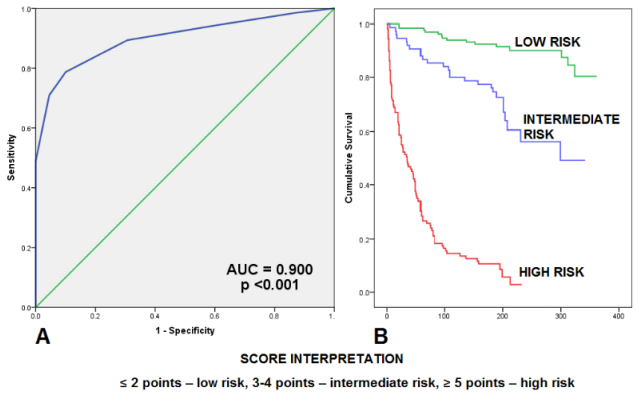

Figure 1

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Increased all-cause mortality in newly diagnosed patients with heart failure between 2006 and 2012: a retrospective, population-based study in Sweden

K Lindmark[1]; K Boman[2]; M Olofsson[2]; S Bruce Wirta[3]; CC Proenca[4]; A Levine[5]; A Castelo-Branco[5]; J Stalhammar[6]; G Wikstrom[7]

[1]Umea University Hospital, Department of Public Health and Clinical Medicine and Heart Centre, Umea, Sweden; [2]Research Unit, Medicine Geriatric, Skellefteå County Hospital, Department of Public Health and Clinical Medicine, Umea, Sweden; [3]Novartis Sweden AB, Stockholm, Sweden; [4]Wellmera AG, Basel, Switzerland; [5]IQVIA, Solna, Sweden; [6]Uppsala University, Department of Public Health and Caring Sciences, Family Medicine and Preventive Medicine, Uppsala, Sweden; [7]Uppsala University, Institute for Medical Sciences, Uppsala, Sweden

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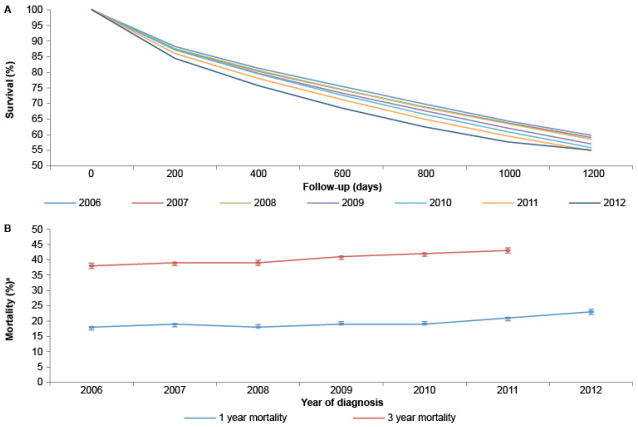
Background and Purpose: Recent analyses have shown decreasing incidence and increasing prevalence of heart failure (HF) in Sweden over time, suggesting a slowly changing composition of patients' characteristics. Factors influencing these trends in patient characteristics and mortality were studied in newly diagnosed patients.

Methods: Patients with HF were identified using secondary care data from the National Patient Register (NPR) linked via unique identifiers to data from the Cause of Death Register. Patients aged = 18 years with = 2 diagnoses of HF between 2006 and 2012, and an International Statistical Classification of Diseases and Related Health Problems, Tenth Edition (ICD-10) diagnostic code of I50 (inclusive of all granular codes), I42.0, I42.6, I42.7, I42.9, I11.0, I13.0 or I13.2 in any position were included. Date of first diagnosis was the index date. ICD-10 codes also identified comorbidities occurring in the 5 years before index. A 10-year look-back was used to exclude prevalent HF cases. Hazard ratios (HRs; adjusted for age, sex and year of diagnosis) and 95% confidence intervals (CIs) for all-cause mortality were estimated using a Cox proportional hazards model at 1 year post-index for years 2006-2012.

Results: Overall 141 607 patients were identified as newly diagnosed with HF in the NPR during 2006-2012 (median age: 80 years; 47% women; 80% first diagnosed in an inpatient setting). Patients' mean age was constant at 77 years, their Charlson comorbidity index increased significantly from 1.4 to 1.6 (P < 0.0001) and the proportion of patients with a previous myocardial infarction decreased significantly from 14% to 12% (P < 0.0001) during the study period. One-year all-cause mortality (95% CI) increased from 18% (17%, 18%) in 2006 to 23% (22%, 24%) in 2012; similar trends were seen for 3-year mortality (Figure). The risk of all-cause mortality 1 year post-index increased from 2006 to 2012 (HR [95% CI] relative to 2006: 2007, 1.06 [1.01, 1.10]; 2008, 1.04 [1.00, 1.08]; 2009, 1.07 [1.02, 1.11]; 2010, 1.08 [1.03, 1.13]; 2011, 1.18 [1.13, 1.23]; and 2012, 1.34 [1.29, 1.40]); this was significant (P < 0.0001) for the year 2007 and years 2009-2012 versus 2006.

Conclusions: These results suggest a shift in the clinical profile and HF aetiology of newly diagnosed patients with HF over time. The increasing comorbidity burden might explain the increasing mortality over time in patients with newly onset HF, and indicates the need for intense evaluation and care of these patients.

Figure. A) Survival and B) 1 and 3 year mortality over 3 years post-index in newly diagnosed patients with HF by year of diagnosis



*3 year mortality in patients diagnosed in 2012 is unavailable because NPR data collection ended in 2014, therefore none of these patients have 3 full years of follow-up on which to calculate 3 year mortality.

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One year follow-up of heart failure patients: role of the new tnm-like classification

P Paolo Severino[1]; M Alfarano[1]; M Pucci[1]; M Straito[1]; E Pagliaroli[1]; I Ferrari[1]; S Calcagno[1]; D Alunni Fegatelli[2]; S Sciomer[1]; AR Vestri[2]; M Mancone[1]; F Fedele[1]

[1]Sapienza University of Rome, Department of Cardiovascular, Respiratory, Nephrology, Anesthesiology and Geriatric Sciences, Sapien, Rome, Italy; [2]Sapienza University of Rome, Department of Public Health and Infectious Diseases, Rome, Italy

Introduction: NYHA is the most used classification for heart failure (HF), but it does not include some clinical features. We proposed a new staging system for HF, named HLM (JACC 2014;20;63(19):1959-60), which refers to heart damage (H), lung involvement (L), and malfunction (M) of peripheral organs analogous to the TNM classification used in oncology. Each parameter is allocated in four levels of severity (H1-H4, L0-L3, M0-M3).

Purpose: The aim of our study is to validate HLM as nosology for HF patients, comparing it with the classic NYHA to achieve the most accurate prognosis of these patients, in terms of rehospitalization for MACCE and mortality at 6 and 12 months follow up.

Methods: We enrolled 1064 consecutive patients with the diagnosis of, or at risk for, HF. According to HLM classification, all parameters for heart, lungs and peripheral organs function were collected and each patient was classified according to NYHA and HLM. At 6 and 12 months patients were followed up.

Results: At 6 and 12 months follow-up, comparing to NYHA, HLM showed a greater area under the ROC curve (AUC) for rehospitalization as well as for cardiac death. MACCE and cardiac death rates have been assessed for each combination of H, L and M parameters. At 1 year follow up, comparing to NYHA, each stage of HLM identifies different risk profile ranging from the initial stage of H1L0M0 with a probability of 5.25% (95% CI 3.53-7.72) of MACCE and a probability of 0.60% (95% CI 0.25-1.43) of cardiac death up to the end stage H4L3M3 that showed a probability of 67.05% (95% CI 56.67-76.0) of MACCE and a probability 35.36% (95% CI 23.37-49.53) of cardiac death. On the other hand, at 1 year follow up NYHA classes recognizes a "narrower" window of probability of events, ranging from a probability of 2.11 (95% CI 0.53 - 8.03) of MACCE and a probability of 9.47 (95% CI 5.00 - 17.21) of cardiac death for patients in class I, up to a probability of 34.54% (95% CI 28.18-41.49) of MACCE and a probability of 11.34% (95% CI 7.58-16.62) of cardiac death for subject in class IV.

Conclusions: According to these preliminary data, HLM nosology seems to be more accurate than NYHA classification to stratify risk of rehospitalization for MACCE and of cardiac death in HF patients, since the area under the ROC curve is greater for HLM in terms of rehospitalization and mortality. Moreover, within any NYHA class, HLM classification is able to better determine the prognosis at 1 year, because it evaluates both heart, lung, renal, hepatic, cerebral and hematopoietic involvement. This means that a wider and systemic approach should be used in HF patients, changing the "cardiocentric" methodology of NYHA.

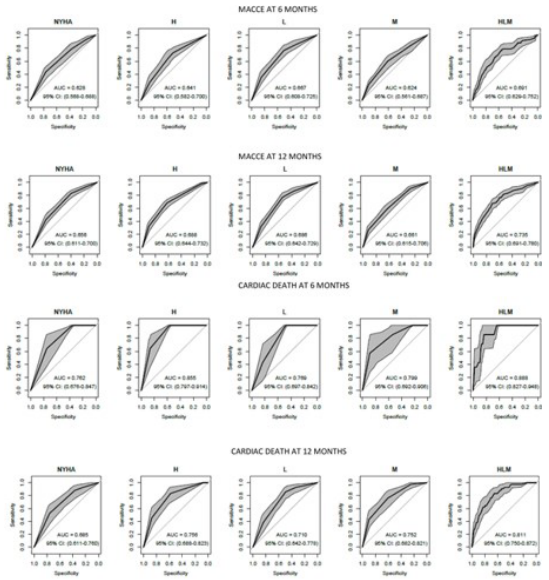

Figure 1 : ROC curve for NYHA and for HLM regarding cardiac death and major adverse cardiovascular and cerebrovascular events (MACCE) at 6 and 12 months follow up.

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Sacubitril/valsartan initiation among renin-angiotensin aldosterone system inhibitor-naive heart failure patients with reduced ejection fraction

AF Mohanty[1]; EB Levitan[2]; JA Dodson[3]; T He[1]; PA Russo[4]; AP Bress[5]
[1]*University of Utah, Internal Medicine, Salt Lake City, United States of America*; [2]*University of Alabama Birmingham, Epidemiology, Birmingham, United States of America*; [3]*New York University School of Medicine, Medicine, New York, United States of America*; [4]*Novartis Pharmaceuticals Corporation, East Hanover, United States of America*; [5]*University of Utah, Population Health Sciences, Salt Lake City, United States of America*

Funding Acknowledgements: Novartis Pharmaceuticals Corporation

Background/Introduction: The 2016 ESC Guideline on the Diagnosis and Treatment of Acute and Chronic Heart Failure endorsed sacubitril/valsartan (S/V) as class I-B treatment for heart failure with reduced ejection fraction(HFrEF) based on the PARADIGM-HF trial. Data on characteristics of S/V initiators and S/V adherence among renin-angiotensin aldosterone system inhibitor (RAASi)-naï ve patients treated in the community are limited.

Purpose: Determine associated baseline patient and healthcare facility characteristics and medication adherence of S/V vs angiotensin converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB) in RAASi-naïve HFrEF patients.

Methods: Retrospective cohort study of U.S. Veterans Affairs (VA) data including HFrEF (= 1 record of left ventricular ejection fraction (LVEF) = 40%) patients with = 1 in/outpatient visit for HF within 1-year pre-index (baseline period) treated with S/V, ACEI, or ARB from July 2015-June 2017. The index date was first S/V pharmacy fill and if none, first ACEI or ARB fill. RAASi-naïve defined as no S/V, ACEI, or ARB fills during the baseline period. Poisson regression models with robust errors were used to compare baseline characteristics and 4-month medication adherence (i.e. follow-up fills, proportion of days covered [PDC], and discontinuation) for S/V vs ACEI or ARB. Medication adherence comparisons were adjusted for baseline characteristics using matching weights.

Results: Among RAASi-naïve HFrEF Veterans (N = 10,743), most (97.5%) were male and 371 (3.5%) had an S/V pharmacy fill and 10,372 (96.5%) had an ACEI or ARB fill on the index date. Mean (standard deviation) baseline age, estimated glomerular filtration rate, and LVEF in S/V vs ACEI or ARB initiators were 73.6 (10.7) vs 70.3 (11.4) years, 61.3 (19.1) vs 66.4 (25.2) mL/min/1.73 m2, and 27.9% (8.3%) vs 34.4% (12.0%), respectively. History of ischemic cardiomyopathy was associated with S/V vs ACEI or ARB initiation. Veterans with lower systolic blood pressure, history of stroke, hypertension, myocardial infarction, or a visit with a Cardiologist on the index date were less likely to initiate S/V. In Veterans with a 30 day-supply index fill (N = 251 S/V and N = 3,101 ACEI or ARB) the adjusted risk ratio for 4-month PDC >80% was 0.78, 95% (confidence interval: 0.66-0.93) for S/V vs ACEI or ARB. Follow-up fills and discontinuation were similar for S/V vs ACEI or ARB. Adherence was similar for S/V vs ACEI or ARB among Veterans with a 90 day-supply.

Conclusions: In a large, integrated healthcare system, 3.5% RAASi-naïve HFrEF patients initiated S/V during the first 2-years post U.S. FDA approval. Overall, our findings suggest that S/V adherence is similar to ACEI or ARB in community-treated RAASi-naïve HFrEF patients. The low numbers of S/V initiation may reflect a lag in formulary availability; S/V was added to the VA Formulary in October 2016. The reasons for lack of guideline-directed S/V initiation needs further elucidation.

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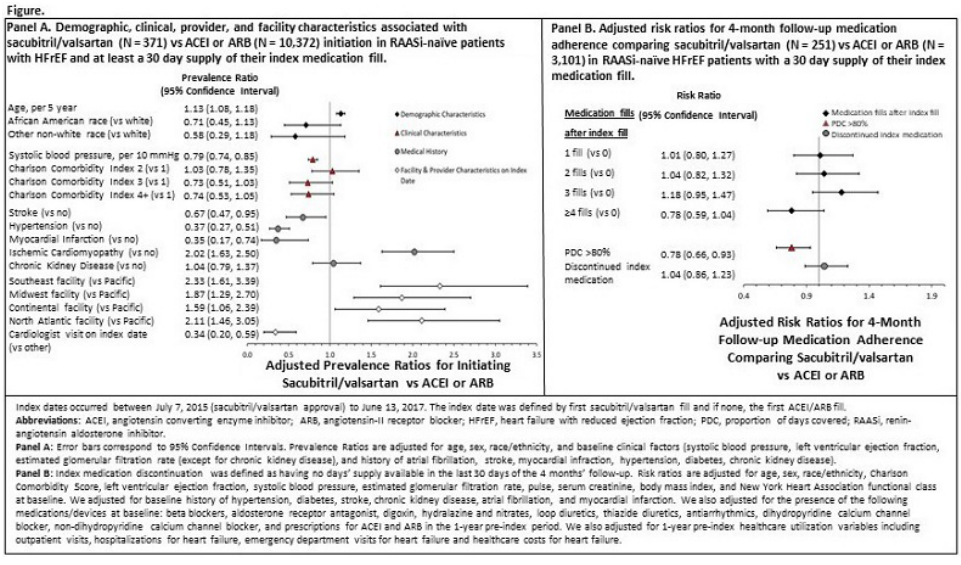
High-dose loop diuretics are associated with adverse clinical outcomes in outpatients with chronic heart failure and mid-range and preserved ejection fraction: observations from the ESC Heart Failure

C Chris Kapelios[1]; C Laroche[2]; MG Crespo-Leiro[3]; M Piepoli[4]; A Coats[5]; SD Anker[6]; G Filippatos[7]; A Maggioni[8]; P Seferovic[9]; G Rosano[10]; A Mebazaa[11]; M Lainscak[12]; A Hoes[13]; F Ruschitzka[14]; LH Lund[15]
[1]*Laiko University General Hospital, Athens, Greece*; [2]*European Society of Cardiology, Sophia-Antipolis, France*; [3]*University Hospital Complex A Coruña, A Coruña, Spain*; [4]*Guglielmo da Saliceto Hospital, Piacenza, Italy*; [5]*University of Warwick, Coventry, United Kingdom*; [6]*Charite University Hospital, Berlin, Germany*; [7]*Attikon University Hospital, Athens, Greece*; [8]*ANMCO Foundation For Your Heart, Florence, Italy*; [9]*University of Belgrade, Belgrade, Serbia*; [10]*San Raffaele Hospital of Milan (IRCCS), Milan, Italy*; [11]*University Paris Diderot , Paris, France*; [12]*General Hopsital Celje, Celje, Slovenia*; [13]*University Medical Center Utrecht, Utrecht, Netherlands*; [14]*University Heart Center, Zurich, Switzerland*; [15]*Karolinska University Hospital, Stockholm, Sweden*

Figure.



Index dates occurred between July 7, 2015 (sacubitril/valsartan approval) to June 13, 2017. The index date was defined by first sacubitril/valsartan fill and if none, the first ACEI/ARB fill.
Abbreviations: ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin-II receptor blocker; HFrEF, heart failure with reduced ejection fraction; PDC, proportion of days covered; RAASi, renin-angiotensin aldosterone inhibitor.
Panel A: Error bars correspond to 95% Confidence Intervals. Prevalence Ratios are adjusted for age, sex, race/ethnicity, and baseline clinical factors (systolic blood pressure, left ventricular ejection fraction, estimated glomerular filtration rate (except for chronic kidney disease), and history of atrial fibrillation, stroke, myocardial infraction, hypertension, diabetes, chronic kidney disease).
Panel B: Index medication discontinuation was defined as having no days' supply available in the last 30 days of the 4 months' follow-up. Risk ratios are adjusted for age, sex, race/ethnicity, charlson comorbidity Score, left ventricular ejection fraction, systolic blood pressure, estimated glomerular filtration rate, pulse, serum creatinine, body mass index, and New York Heart Association functional class at baseline. We adjusted for baseline history of hypertension, diabetes, stroke, chronic kidney disease, atrial fibrillation, and myocardial infarction. We also adjusted for the presence of the following medications/devices at baseline: beta blockers, aldosterone receptor antagonist, digoxin, hydralazine and nitrates, loop diuretics, thiazide diuretics, antiarrhythmics, dihydropyridine calcium channel blocker, non-dihydropyridine calcium channel blocker, and prescriptions for ACEI and ARB in the 1-year pre-index period. We also adjusted for 1-year pre-index healthcare utilization variables including outpatient visits, hospitalizations for heart failure, emergency department visits for heart failure and healthcare costs for heart failure.

Figure

Introduction: High doses of loop diuretics (HDLD) have been associated with adverse outcomes in patients with chronic heart failure (CHF) and reduced ejection fraction (HFrEF). However, there are no studies to date in patients with heart failure with mid-range (HFmrEF) and preserved ejection fraction (HFpEF). We investigated whether HDLD are associated with adverse outcomes in patient with HF stratified by EF.
Methods: Of 9,749 outpatients we included the 8,130 (83.4%) CHF patients who continued diuretics after the index outpatient visit. Loop diuretics were converted to furosemide equivalents based on: 1 mg bumetanide = 20 mg torsemide = 40mg furosemide. Patients were divided based on median dose into low-dose (= 40 mg) and high-dose (< 40 mg). The association between dose and a) the composite endpoint of all-cause mortality or HF hospitalization and b) worsening renal function (WRF) at 1-year follow-up were examined, using Cox models. All covariates that were significant in the univariate analyses (P < 0.10) and those with known associations with disease severity (body mass index, history of chronic kidney disease and diabetes, systolic blood pressure, clinical stability, etc.) were entered in the final model. Clinical stability was defined as NYHA class I-II, no history of HF hospitalization during the past 6 months and absence of signs of congestion or hypoperfusion. WRF was defined as increase in serum creatinine = 0.3 mg/dl (= 26.5 μmol/L) at 12-month follow-up compared to index visit.
Results: Mean age was 66 ± 13 years, 71% men. Mean left ventricular ejection fraction was 37 ± 14% (62% HFrEF, 19% HFmrEF, 19% HFpEF). HDLD was independently associated with the composite endpoint in patients with HFrEF (adjusted HR: 1.51; 95% CI: 1.31-1.73, P < 0.001), HFmrEF (adjusted HR: 1.63; 95% CI: 1.40-2.39, P < 0.001) and HFpEF (adjusted HR: 1.84; 95% CI: 1.41-2.42, P < 0.001) at 1-year follow-up. Importantly, HDLD was also independently associated with an increased risk for WRF during 1-year follow-up in patients with HFmrEF (adjusted HR: 2.04; 95% CI: 1.33-3.12, P < 0.001) and HFpEF (adjusted HR: 2.00; 95% CI: 1.35-2.96, P < 0.001), but not in patients with HFrEF (adjusted HR: 1.19; 95% CI: 0.96-1.47, P = 0.121).
Conclusions: Use of HDLD was associated with worse outcomes, not only in HFrEF, as previously reported, but also in HFmrEF and HFpEF patients. This risk, which is proportionally higher in two latter sub-groups, seems to be paralleled by an increased risk for WRF, potentially pinpointing an underlying mechanism of the observed excess in morbidity/mortality.

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Lung ultrasound may reduce heart failure hospitalizations: preliminary results from the LUS-HF trial.

M Rivas-Lasarte[1]; A Maestro Benedicto[1]; J Fernandez Martinez[1]; J Alvarez-Garcia[1]; E Sole Gonzalez[1]; L Lopez Lopez[1]; S Mirabet[1]; A Sionis[1]; E Roig Minguell[1]; J Cinca Cuscullola[1]
[1]Hospital de la Santa Creu i Sant Pau, Cardiology Department, Barcelona, Spain

On behalf of: LUS-HF investigators
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Background: Pulmonary congestion is expressed in the form of B-lines detected by lung ultrasound (LUS), which has proven to be a potent prognostic predictor of hospitalization and mortality in HF. However, it is still unknown if a treatment strategy guided by LUS in HF patients may improve outcomes.

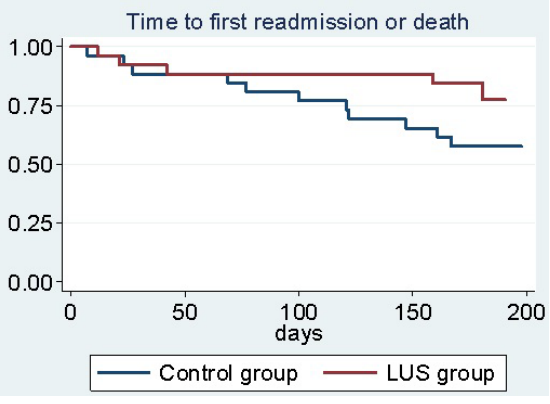

Figure. Kaplan Meier curves for first r

Purpose: The objective of our study is to analyze whether a treatment guided by LUS in patients with HF reduces the combined endpoint of readmission for HF worsening or death in a 6-month follow-up.
Methods: LUS-HF (NCT02959372 at ClinicalTrials.gov) is a randomized, single center, simple blind clinical trial that enrolls patients older than 18 years who have been hospitalized for HF. The exclusion criteria are life expectancy less than 6 months or severe lung disease. Eligible patients are randomized into either the "LUS group" or the "control group". The follow-up consists of visits in the HF clinic at periods of 15 days, 1, 3, and 6 months after discharge. Both groups are examined with LUS, but the result of the test is only provided to the treating physician in the "LUS group".
Results: Clinical characteristics of the first 52 patients included are summarized in the table. The primary endpoint occurred in the 42.3% of the "control group" versus 19.2% of the "LUS group" (log-rank test 0.077, figure).
Conclusions: According to the preliminary results of the LUS-HF trial, LUS guided treatment may reduce readmissions in HF patients.

Table. Clinical characteristics of LUS-H

	Control group (n = 26)	LUS group (n = 26)	P value
Age (years), × (DE)	69.8(13)	69.8(13)	0.98
Male, n (%)	20(77)	21(81)	0.73
HFrEF, n (%)	16 (62)	15(58)	0.54
HFmrEF, n (%)	4 (15)	7 (27)	
HFpEF, n (%)	6 (23)	4 (15)	
Diabetes, n (%)	13 (50)	11 (42)	0.58
Renal insufficiency*, n (%)	13 (50)	10 (38)	0.40
NT-proBNP **(ng/L), x (DE)	3511 (3595)	3523 (4872)	0.99
Number of B lines**, x (DE)	5.0 (4.3)	5.4 (4.4)	0.70
Readmissions	10 (38.5)	5 (19.2)	0.13
Death	1 (3.9)	2(7.7)	0.55

*Creatinine clearance < 60ml/kg/1.73m2. ** The day of dischargeLUS: lung ultrasound; HF heart failure; rEF: reduced ejection fraction (< 40%); mrEF: mild reduced ejection fraction (40-49); pEF: preserved ejection fraction

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Hemodynamic evaluation as a tool for patient selection for percutaneous mitral valve repair

AJ Rieth[1]; MJ Richter[2]; E Gerhardt[1]; U Fischer-Rasokat[1]; C Liebetrau[1]; C Hamm[2]; C Walther[1]
[1]Kerckhoff Heart Center, Bad Nauheim, Germany; *[2]Justus-Liebig University of Giessen, Giessen, Germany*

Background: Percutaneous mitral valve repair (PMVR) has become a standard therapy for patients with moderate to severe mitral regurgitation (MR) and high surgical risk. Grading of MR severity by echocardiography alone may be inadequate for selection of patients. In particular, the presence of concomitant left ventricular heart failure can obscure the clinical significance of MR. In patients undergoing evaluation for PMVR, exercise hemodynamic parameters reflecting MR severity are widely unknown. Hemodynamic measurements at rest and during exercise may help to identify patients with MR who could benefit from PMVR. The objective of the present study was to explore the impact of pre-procedural hemodynamics on the benefit from PMVR.
Methods: Between Dec. 2009 and Feb. 2017, 211 patients with symptomatic MR underwent PMVR in our center. Out of these, 51 patients undergoing PMVR (CardioBand® n = 2, MitraClip® n = 49) had exercise hemodynamics taken prior to PMVR, which resulted in a reduction of MR = 1 grade in all patients. For this study, patients' benefit from PMVR was defined as sustained MR reduction = 1 grade at follow up, combined with improved (if NYHA III/IV before) or stable (if NYHA II before) symptoms.
Results: Patients had a median age of 78 years (IQR 74-83), 35,3% of the patients were female, and 72,5% presented with symptoms according to NYHA class III. 56,9% of the patients had an ejection fraction (EF) <40%. The median NT-proBNP serum level was 3131 pg/ml (IQR 1307-8250), and echocardiography revealed that 43.1% had severe MR and 56.9% moderate MR. Mean follow-up time was 7 months. The pre-specified primary outcome of benefit from PMVR was met by 30 patients (58.8%).
Compared with patients without benefit, these 30 patients had a higher V-wave in the pulmonary artery wedge pressure (PAWP) tracing at rest (p = 0.019) and a larger increase (?) in cardiac output (CO) during exercise (p = 0.036) prior to PMVR.
Prediction of improvement at follow up in univariate regression analysis was significant for PAWP V-wave, ?CO and ?PAWP/?CO (slope). Adjusted for EF, MR severity and PAWP V-wave, the PAWP/CO-slope remained an independent predictor of successful PMVR with an OR of 3.29 (95% CI 1.18-9.17, p = 0.023). ROC analysis

identified a cutoff 14.4 mmHg/l/min for the slope with an AUC of 0.67 (p = 0.08 95% CI 0.47-0.88, sensitivity 77%, specificity 73,1%).
Conclusions: In our cohort of high-risk patients with indication for PMVR, preprocedural hemodynamic parameters were associated with a sustained benefit after the procedure. A low PAWP V-wave, a low ?CO and a high PAWP/CO-slope were associated with negative outcomes. The latter two parameters are suggestive of a too advanced stage of heart failure for successful intervention, whereas the first implies a relation to MR severity. Future studies are warranted to refine the use of hemodynamic criteria as a complement to echocardiography to identify patients who may benefit from PMVR.

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Outcomes up to 2 years from the multicenter CE trial of transcatheter mitral valve annuloplasty in patients with functional mitral regurgitation

K-H Karl-Heinz Kuck[1]; F Maisano[2]; S Baldus[3]; A Colombo[4]; O Alfieri[4]; J Juliard[5]; A Vahanian[5]; G Nickenig[6]; R Von Bardeleben[7]; J Van Der Heyden[8]; J Hausleiter[9]; A Kerner[10]; C Tamburino[11]
[1]Asklepios Clinic St. Georg, Cardiology, Hamburg, Germany; [2]University Hospital Zurich, Zurich, Switzerland; [3]Cologne University Hospital - Heart Center, Cologne, Germany; [4]San Raffaele Hospital of Milan (IRCCS), Milan, Italy; [5]Hospital Bichat-Claude Bernard, Paris, France; [6]University Hospital Bonn, Bonn, Germany; [7]University Medical Center of Mainz, Mainz, Germany; [8]St Antonius Hospital, Nieuwegein, Netherlands; [9]Ludwig-Maximilians University, Munich, Germany; [10]Rambam Health Care Campus, Haifa, Israel; [11]Ferrarotto Hospital, Catania, Italy

Funding Acknowledgements: Edwards Lifesciences

Background : The Edwards Cardioband™ Mitral Valve Reconstruction System is a CE-mark approved transcatheter implant delivered via a transseptal approach.
Purpose : The aim of this multicenter study was to evaluate the feasibility, safety and outcomes of the Edwards Cardioband™ Mitral System in the treatment of patients with secondary mitral regurgitation (MR). We report outcomes up to 2 years of patients who underwent the Cardioband Mitral System procedure which led to the CE approval of the device.
Methods : Between February 2013 and June 2016, 61 patients at high surgical risk with clinically significant secondary MR were enrolled at 11 European sites. All patients were screened by a heart team using echocardiography and cardiac CT. All echocardiography follow up assessments were performed by an independent core lab.
Results: Mean patient age was 72 ± 7 years, 44 were males (72%). Mean EuroSCORE II was 7.1%. At baseline, 52 patients (85%) were in New York Heart Association (NYHA) functional class III or IV, with a mean left ventricular ejection fraction of 33 ± 11%. The implant success rate was 98% and the device success rate 78%. After implant size adjustment, an average 28% septolateral annular reduction was observed (from 37 ± 4 mm to 26 ± 4 mm; p <0.01). At one-month follow-up, two patients had died from non-device related causes, and 87% of patients had MR = 2+. At one-year follow-up, available for 39 patients, an average 31% annular reduction was observed (from 36 ± 4 mm to 25 ± 4 mm; p <0.01), and 95% of patients demonstrated MR = 2+. Two-year follow-up is currently available for 20 patients. An average 28% annular reduction was observed (from 36 ± 4 mm to 26 ± 4 mm; p <0.0001), and 95% of patients demonstrated MR = 2+. Of the 20 patients, 89% were in NYHA class I or II. In addition, Minnesota Living with Heart Failure Questionnaire scores improved significantly by an average of 16 points (p = 0.0019).
Conclusions: : Transcatheter mitral valve repair using the Cardioband Mitral System provides clinically significant annular reduction and MR grade reduction. The favorable clinical and hemodynamic results of this customized annular reduction procedure are maintained out to two years. This novel therapy demonstrates sustained effectiveness for patients with functional mitral regurgitation while leaving options open for future interventions.

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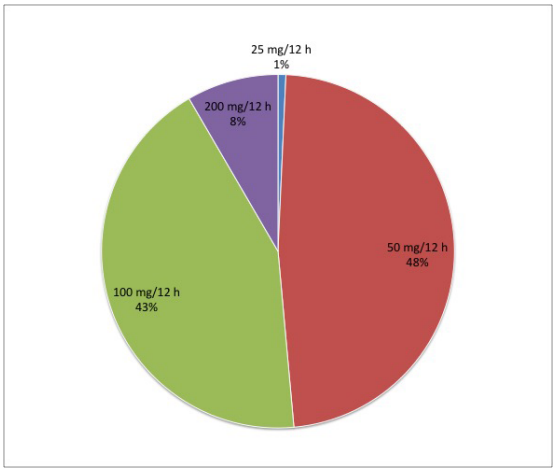
The clinical profile of a non-selected population treated with sacubitril/valsartan is different from PARADIGM-HF trial

L Lourdes Vicent Alaminos[1]; A Esteban Fernandez[2]; M Gomez Bueno[3]; J De Juan[4]; P Diez Villanueva[5]; A M Iniesta[6]; A Ayesta[1]; H Gonzalez Saldivar[1]; A Rojas[5]; R Bover Freire[2]; D Iglesias[7]; M Garcia Aguado[8]; JA Perea Egido[9]; M Martinez-Selles[1]
[1]University Hospital Gregorio Maranon, Cardiology, Madrid, Spain; [2]Hospital Clinic San Carlos, Madrid, Spain; [3]University Hospital Puerta de Hierro Majadahonda, Madrid, Spain; [4]University Hospital 12 de Octubre, Madrid, Spain; [5]University Hospital De La Princesa, Madrid, Spain; [6]University Hospital La Paz, Madrid, Spain; [7]University Hospital Infanta Sofia, Madrid, Spain; [8]Hospital de Mostoles, Madrid, Spain; [9]University Hospital of Getafe, Getafe, Spain

Introduction: Sacubitril/valsartan (SV) is a new milestone therapy in heart failure with reduced ejection fraction.
Purpose: Our aim is to describe the characteristics of the patients receiving SV in daily clinical practice.
Methods: Prospective registry in 10 hospitals including all patients who started SV in everyday clinical practice: SUMA (Sacubitril/valsartan Usado en Madrid Ambulatoriamente - sacubitril/valsartan used in Madrid in outpatients). We performed a comparative analysis with the data from the PARADIGM-HF trial.
Results: From October 2016 to March 2017, 427 patients started treatment with SV. The mean age was 68.1 ± 12.4 years and 30.5% were women (22.0% in PARADIGM-HF, p <0.001). Comparing the data from SUMA with those of PARADIGM-HF, baseline treatment was different, with a lower ratio of angiotensin converting enzyme inhibitors/angiotensin II receptor blockers (2.7 Vs. 3.5, p <0.001), and a higher proportion of patients with implantable cardioverter defibrillator (53.8 vs. 15%, p <0.001), and cardiac resynchronization therapy (25.8% vs. 5%, p <0.001). Treatment with mineralocorticoids receptor antagonists was more frequent (76.7% vs. 60.0%, p <0.001) and the use of beta-blockers was similar (94.6% vs. 93.0%, p = 0.43). We observed a lower left ventricular ejection fraction (28.8 ± 6.9% vs. 29.6 ± 6.1%, p = 0.008), more patients in functional class III-IV (30.4 vs. 24.8, P = 0.015), higher levels of Nt pro-BNP (3421 [interquartile range: 904 - 4161] vs. 1631 [interquartile range: 885 - 3154] pg/mL) and worse renal function (creatinine level 1.3 ± 0.7 vs. 1.1 ± 0.3 mg/dL, p <0.001). SV starting doses are resumed in the figure.
Conclusions: In real life patients receiving SV have a higher risk profile than in the pivotal trial, with lower left ventricular ejection fraction, poorer functional class, higher levels of natriuretic peptides, and worse renal function.

	SUMA (N = 427)	PARADIGM-HF (N = 8442)	P
Age (years)	68.1±12.4	63.8±11.5	<0.001
Female sex	131 (30.5%)	1857 (22%)	<0.001
Medical history - Ischemic heart disease - LVEF (%)	227 (53%) 28.8±6.9	5065 (59.9%) 29.6±6.1	0.005 0.008
Creatinine (mg/dL)	1.26±0.7	1.13±0.3	<0.001
Nt Pro BNP (pg/mL) median (IQR)	3421 (904 - 4161)	1631 (885 - 3154)	<0.001
Functional class I II III IV	5 (1.2%) 293 (68.5%) 116 (27.1%) 14 (3.3%)	422 (5.1) 5909 (70.2%) 2026 (24.0%) 68 (0.8%)	<0.001

Comparison of the baseline characteristics in the SUMA registry and in the PARADIGMHF trial.



SV starting doses

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Cervicothoracic tens attenuates sympathetic cardiac overdrive in heart failure patients

ACL Antonio Claudio Lucas Nobrega[1]; MO Campos[1]; SM Miranda[1]; T Bessa[1]; CT Mesquista[1]; IA Fernandes[1]
[1]Fluminense Federal University, Department of Physiology and Pharmacology , Niteroi, Brazil

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Background: The cardiac sympathetic overdrive provides inotropic support to the failing heart. However, as myocardial insult evolves, this compensatory response impairs contractile function and constitutes an independent mortality predictor and a primary target in the treatment of heart failure (HF). We then propose cervicothoracic transcutaneous electrical nerve stimulation (TENS) as a non-pharmacological therapy to attenuate cardiac sympathetic overdrive in patients with HF. Objectives: To test whether short-term use of TENS decreases cardiac sympathetic activity in HF.
Methods: In this prospective, randomized double blind controlled crossover trial, 8 HF patients (7 men, 60 ± 5 yrs., NYHA II–III, left ventricle ejection fraction 33 ± 2%) were randomly assigned to either an in-home cervicothoracic TENS (30 min twice a day with 80 Hz frequency and pulse duration of 150μs) or a control intervention (SHAM) for 14 consecutive days. Following a 60-day washout phase, patients crossed over and underwent the opposite condition. Arterial pressure (AP), heart rate (HR), heart-to-mediastinum ratios (HMR) and washout rate (WR), indexes of sympathetic innervation density and activity from planar 123I-metaiodobenzylguanidine (123I-MIBG) myocardial scintigraphy images respectively, were quantified at the beginning and end of each condition.
Results: HMR and AP did not change throughout the study. TENS, but not SHAM, promoted a significant reduction in the WR (TENS -11 ± 11 vs. STHI + 9 ± 22%, p = 0.01) and HR (TENS -3 ± 3 vs. STHI + 3 ± 5 beats/min, p = 0.01).
Conclusion: These findings indicate that short-term cervicothoracic TENS therapy attenuates cardiac sympathetic overdrive in patients with HF with no impact on myocardial innervation density.

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Gender differences in low-flow, low-gradient aortic stenosis

P E Philipp Emanuel Bartko[1]; MA Clavel[2]; A Dahou[2]; R Capoulade[3]; H Baumgartner[4]; I Lang[1]; G Mundigler[1]; J Bergler-Klein[1]; J Rodes-Cabau[2]; P Pibarot[2]; J Mascherbauer[1]
[1]Medical University of Vienna, Department of Internal Medicine II, Division of Cardiology, Vienna, Austria; *[2]Quebec Heart and Lung Institute, Quebec, Canada*; *[3]Massachusetts General Hospital, Institute for Heart, Vascular and Stroke Care, Boston, United States of America*; *[4]University Medical Center, Münster, Germany*

On behalf of: TOPAS Investigators

Background: Prior research is limited with regards to sex related differences in patients with Low-Flow, Low-Gradient Aortic Stenosis (LFAS). The present TOPAS sub-study sought to investigate gender related effects on anthropomorphic data, clinical presentation and outcome in patients with LFAS.
Methods: 342 Patients (263 male and 79 female) with LFAS (valve area = 1.2 cm^2, left ventricular (LV) ejection fraction (EF) = 40%, mean gradient = 40 mmHg) were prospectively enrolled. Anthropomorphic data, clinical history and symptomatic status were assessed. Dobutamine stress echocardiography was used to assess contractile reserve and stenosis severity.
Results: Size, weight and body surface area (BSA) were smaller in women than men (p <0.001, Table 1). Although women reported similar symptomatic status at study entry (p = 0.515, Table 1) females had significantly worse 6-minute walk test (6MWT) performance and a lower duke activity status index (DASI) score (both p <0.01). Echocardiography at rest revealed larger LV end-diastolic (EDD) index at rest (p = 0.028) despite similar effective orifice area (EOA) index (p = 0.995) and mean gradients (MG) (p = 0.608). At peak stress women had similar stroke volume index and ejection fraction (p = 0.776 and p = 0.242) but a larger EOA index compared to men (0.047) (Table 1).
During 4 year follow up 132 Patients died. 193 (56%; 152male and 41female) patients underwent valve intervention and 149 (44%; 111male, 38female) patients were managed medically. Kaplan-Meier and Univariate Cox regression analysis revealed a higher overall mortality in women compared to men (HR1.533, 95%CI 1.047 - 2.244, p = 0.028), Figure 1A. Sub-analysis according to treatment groups revealed that this was solely due to a higher mortality of women in the valve intervention group (HR 2.378, 95%CI 1.347 - 4.198, p = 0.003, Figure 1B) while no difference in overall survival was found between men and women in medically treated patients (HR 1.004 95% CI 0.598 - 1.685, p = 0.989, Figure 1C). In the intervention group, female gender remained independently associated with outcome even after correcting for age, BSA, stenosis severity and ejection fraction at peak stress (HR 2.672, 95%CI 1.069-6.680, p = 0.036).
Conclusion: In patients with LFAS women report similar symptoms but are at an advanced stage of the disease as assessed by more objective tests like the 6MWT and DASI. Similar stenosis severity at rest and even larger EOA at peak stress but larger LV dimensions and worse exercise capacity indicate a more pronounced impact of the valvular lesion on female hearts and a more advanced disease stage that might not be reversible and result in worse outcome after valve intervention.

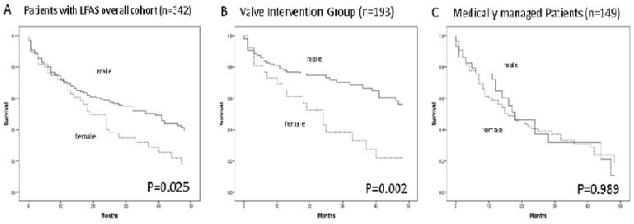

Figure 1

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Patients with severe aortic valve stenosis and concomitant atrial fibrillation have an adverse clinical and hemodynamic profile

MT Micha Maeder[1]; L Weber[1]; P Ammann[1]; D Altmann[1]; R Brenner[1]; NF Ehl[1]; M Buser[1]; PK Haager[1]; H Rickli[1]
[1]Cantonal Hospital St. Gallen, St. Gallen, Switzerland

Background: In patients with aortic stenosis (AS) undergoing aortic valve replacement (AVR), the presence of atrial fibrillation (AF) is associated with increased long-term mortality. However, little is known about the detailed clinical and hemodynamic profile of patients with AS and concomitant AF. In the present study, we compared the clinical, non-invasive and invasive hemodynamic characteristics in patients with severe AS with and without AF.
Methods: We studied 486 patients (age 74 ± 10 years, 58% male) with severe AS [indexed aortic valve area (iAVA) 0.41 ± 0.13 cm2/m2, left ventricular ejection fraction (LVEF) 58 ± 12%] undergoing a detailed pre-AVR assessment including right heart catheterization. Fifty patients were in AF, and 436 patients were in sinus rhythm (SR) at the time of the assessment. All patients subsequently underwent surgical (n = 350) or transcatheter (n = 136) AVR. The median follow-up was 3.7 (interquartile range, 2.6-5.2) years.
Results: Patients with AF were older (80 ± 6 vs. 73 ± 10 years) and had higher heart rate (80 ± 19 vs. 68 ± 11 bpm) and B-type natriuretic peptide [median (interquartile range 444 (223-787) vs. 166 (67-367) ng/l] and lower estimated glomerular filtration rate (65 ± 24 vs. 75 ± 29 ml/min/1.73 m2) than patients in SR (p < 0.05 for all comparisons). Despite similar iAVA (0.41 ± 0.11 0.41 ± 0.12 cm2/m2) patients with AF had lower LVEF (51 ± 13 vs. 58 ± 12%), larger left atrial size (left atrial area: 32 ± 9 vs. 24 ± 6 cm2), and worse right ventricular function (tricuspid annular plane systolic excursion: 17 ± 4 vs. 22 ± 5 mm) than patients in SR (p < 0.05 for all comparisons). Patients with AF had higher mean pulmonary artery pressure (34 ± 13 vs. 24 ± 9 mmHg), mean pulmonary artery wedge pressure (22 ± 8 vs. 15 ± 7 mmHg), and pulmonary vascular resistance (2.8 ± 1.9 vs. 2.0 ± 1.3 Wood units) and lower cardiac index (2.0 ± 0.5 s. 2.5 ± 0.6 l/min/m2) and stroke volume index (26 ± 9 vs. 37 ± 10 ml/m2) than patients with SR. Although the number of AF patients was relatively small, there was a strong trend toward higher long-term mortality in AF compared to SR patient (log rank p = 0.05).
Conclusions: Patients with severe AS and concomitant AF represent a particularly sick subgroup of AS patients with worse biventricular function and an adverse hemodynamic profile with unfavorable outcome after AVR compared to SR patients. Thus, further studies are required to investigate the interaction between AF and valve disease with a view to develop novel treatment strategies beyond AVR for these patients.

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Six-month outcomes from the transcatheter tricuspid valve repair multicentre TRI-REPAIR trial

A Azeem Latib[1]; G Nickenig[2]; RS Von Bardeleben[3]; J Hausleiter[4]; U Schafer[5]; KH Kuck[6]; S Baldus[7]; JM Juliard[8]; A Vahanian[8]; F Maisano[9]
[1]San Raffaele Hospital (IRCCS), Milan, Italy; *[2]University Hospital Bonn, Bonn, Germany*; *[3]University Medical Center of Mainz, Mainz, Germany*; *[4]University Hospital of Munich, Munich, Germany*; *[5]University Heart Center Hamburg, Hamburg, Germany*; *[6]Asklepios Clinic St. Georg, Hamburg, Germany*; *[7]Heart Center University of Köln, Koln, Germany*; *[8]Hospital Bichat-Claude Bernard, Paris, France*; *[9]University Hospital Zurich, Zurich, Switzerland*

Background: The Edwards Cardioband™ Valve Reconstruction System enables transcatheter repair to address patients with mitral or tricuspid regurgitation. The safety and performance in the treatment of functional mitral regurgitation have been validated in the CE mark trial.

Purpose: to report up to 6 months follow-up results from the first 30 patients included in the study designed to assess safety, feasibility and efficacy in the treatment of functional tricuspid regurgitation (FTR).
Methods: Between October 2016 and July 2017, thirty patients with severe symptomatic FTR were enrolled among 9 participating sites in Europe. All patients were screened by the heart teams of the local sites and underwent thorough pre-procedural echocardiography and cardiac computed tomography evaluation. Echocardiographic data were assessed by an independent core lab.
Results: Mean patient age was 75.2 years, 73.3% were females, 23.3% had ischemic heart disease and the mean EuroSCORE II was 4.1%. At baseline, 83.3% of patients were in NYHA functional class III-IV and LVEF was 57.5%. Successful access, deployment and positioning was achieved in 100% of the patients. There were two deaths at one month follow-up. Implant size adjustment resulted in an average reduction of septolateral tricuspid annular diameter of 16.5% (4.43 ± 0.44cm to 3.7 ± 0.45cm; $p < 0.01$) at discharge.
Thirty-day follow-up is available for 28 patients. 82.2% of patients were in NYHA class I-II. Echocardiography compared to baseline showed reduction in PISA EROA of 51% (from 0.79 ± 0.5 cm2 to 0.39 ± 0.3 cm2, $p < 0.001$) and a 28% reduction in mean vena contracta (from 1.25 ± 0.4 cm to 0.9 ± 0.4 cm, $p < 0.001$).
Six month follow-up is currently available for 22 patients. 85.7% of patients were in NYHA class I-II. Compared to baseline, there was a significant improvement in 6 minute walk test from 278.4 m to 327.4 m, ($p < 0.05$), and a decrease in the occurrence of peripheral edema from 76% to 48% ($p = 0.06$). Echocardiography showed significant reduction in PISA EROA of 48% (from 0.73 ± 0.5 cm2 to 0.38 ± 0.2 cm2, $p < 0.05$) and a 27% reduction in mean vena contracta (from 1.1 ± 0.3 cm to 0.8 ± 0.3 cm, $p < 0.001$).
Conclusions: Outcomes up to 6-months suggest feasibility and safety of transcatheter tricuspid repair with the Cardioband Tricuspid System in patients with symptomatic TR. Significant annular reduction and reduction of tricuspid regurgitation was observed despite treating a large proportion of patients with "torrential" TR at baseline. The study is ongoing and further follow-up data are warranted to validate the initial promising results.

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Predictors of rehospitalization after percutaneous edge-to-edge mitral valve repair by MitraClip implantation

M Mirjam Kessler[1]; J Seeger[1]; J Woehrle[1]; W Rottbauer[1]; S Markovic[1]
[1]*University of Ulm, Department of Internal Medicine II, Ulm, Germany*

Background: In patients with prohibitive surgical risk due to concomitant comorbidities such as heart failure, transcatheter edge-to-edge mitral valve repair by MitraClip (Abbott, Abbott Park, IL, USA) implantation for severe, symptomatic mitral regurgitation (MR) has proven to relieve symptoms of MR and improve quality of life and to reduce the rate of heart failure rehospitalization.
Purpose: Rehospitalization for heart failure decompensation occurs frequently after MitraClip implantation, negatively impacting on quality of life. We aimed here to determine predictors of heart failure rehospitalization in a 1-year follow-up.
Results: 355 patients received implantation of MitraClip for severe MR at our centre. Within the 1-year follow-up period, 18.3% ($n = 65$) were readmitted to hospital for heart failure decompensation at an average of 116 days (median 76 days, interquartile range 42-153 days) after MitraClip implantation. These patients had higher levels of Troponin T (106.8 ± 321.1 vs. 43.1 ± 51.7 ng/l, $p= 0.006$), higher levels of creatinine (145.5 ± 51.0 vs. 127.3 ± 71.1 µmol/l, $p = 0.05$), a higher logistic EuroSCORE (10.5 ± 8.3 vs. 8.3 ± 7.9, $p = 0.046$) and a reduced left ventricular ejection fraction (36.6 ± 17.6% vs. 45.5 ± 17.3%, $p < 0.001$) compared to patients that were not hospitalized for heart failure within the 1-year follow-up. The etiology of mitral regurgitation was mainly functional in the rehospitalization group (73.0% vs. 49.1%, $p < 0.001$). In the 3-year follow-up, patients readmitted for heart failure decompensation after MitraClip implantation had a 2.2-fold increased risk for mortality and 3.0-fold increased risk for cardiovascular mortality. Multivariate Cox proportional-hazard regression analysis identified left ventricular ejection fraction ($p= 0.020$), Troponin T ($p= 0.003$) and NYHA class ($p= 0.020$) as independent predictors for rehospitalization within 1 year after MitraClip implantation.
Conclusion: After percutaneous edge-to-edge mitral valve repair by MitraClip implantation, rate of rehospitalization due to heart failure decompensation was 18.3% during 1-year follow up. Patients readmitted for heart failure decompensation after MitraClip implantation had a 2.2-fold increased risk for mortality and 3.0-fold increased risk for cardiovascular mortality within 3 years after MitraClip procedure in comparison to patients not requiring rehospitalization. Baseline left ventricular ejection fraction, Troponin T and NYHA functional class are independent predictors for heart failure rehospitalization within 1 year after MitraClip implantation.

Moderated Posters - Diagnosis and biomarkers

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Pulsatile hemodynamics in heart failure with reduced ejection fraction - role of forward wave amplitude

T Thomas Weber[1]; P Pecnik[1]; B Hametner[2]; S Wassertheurer[2]; R Binder[1]
[1]*Klinikum Wels-Grieskirchen, Wels, Austria*; [2]*AIT-Austrian Institute of Technology, Vienna, Austria*

Background: The blood pressure (BP) curve can be separated into a forward wave and a backward wave. The forward wave results from the interaction between cardiac ejection and elastic properties of the large arteries. Whereas brachial BP has no role for risk stratification in HFrEF, the the prognostic value of more advanced BP components is currently unknown.
Purpose: We aimed to clarify the determinants and prognostic value of the forward wave amplitude (Pf) in HFrEF.
Methods: We determined Pf, using radial tonometry, a transfer function and dedicated algorithms for wave separation analysis, in 81 patients (mean age 61 years, 90% men) with HFrEF (mean EF 28%, mean nt-proBNP 3851 pg/ml), and followed them for 4.1 years. Patients were divided into quartiles (Qu), according to Pf. Main outcome was all-cause mortality.
Results: As compared to Qu2+3, patients in Qu1 had lower BP, larger left atria and ventricles, lower EF, shorter ejection duration, and higher nt-proBNPs. The predominant etiology was dilated cardiomyopathy.
As compared to Qu2+3, patients in Qu4 were older, more often had hypertension and a prior myocardial infarction, had higher nt-pro-BNP, higher blood pressures, a longer ejection duration, and a higher pulse wave velocity.
In survival analysis, brachial SBP (p = 0.68) and DBP (p = 0.44) did not predict mortality.
In contrast, Pf was significantly (p = 0.029, log-rank test) related to outcome in a u-shaped fashion: 38.9, 22.5, and 56.5% of the patients died during follow-up in Qu1, Qu2+3, and Qu4, respectively. HR Qu1 vs Qu2+3 was 3.0 (95% CI 1.1-8.5); HR Qu4 vs Qu2+3 was 3.7 (95% CI 1.5 - 9.0) - Figure.
In a multivariate Cox proportional hazards model predicting all-cause mortality, Qu4 (HR 3.32 (95% CI 1.31-8.40), p = 0.01), log nt-proBNP (HR 2.72 (95% CI 1.19-6.20), p = 0.018), the presence of ischemic cardiomyopathy (HR 2.43 (95% CI 1.12-5.25), p = 0.025) and, of borderline significance, Qu1 (HR 2.63 (95% CI 0.90-7.70), p = 0.08), were the independent predictors, whereas age, gender, EF, SBP and DBP were not.
Conclusion: Lower as well as higher Pf is associated with impaired survival in HFrEF. In the first case, the lower Pf is the expression of a very poor cardiac function. In the latter case, the higher Pf suggests increased pulsatile afterload. Both conditions can be detrimental.

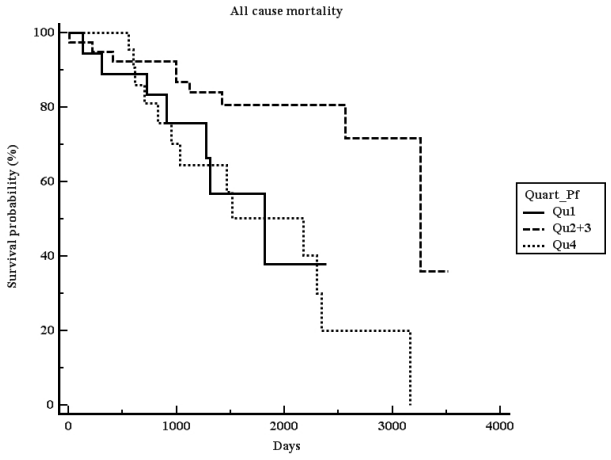

Figure: Quartiles of Pf and survival

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Prognostic relevance of right ventricle global longitudinal strain in heart failure with preserved ejection fraction.

C Clotilde Roy[1]; A Slimani[1]; C De Meester[1]; M Amzulescu[1]; A Pasquet[1]; D Vancraeynest[1]; C Beauloye[1]; J-L Vanoverschelde[1]; B Gerber[1]; A-C Pouleur[1]
[1]*Cliniques Saint-Luc UCL, Cardiology, Brussels, Belgium*

Background: Right ventricle (RV) strain has emerged as an accurate and sensitive tool for RV function assessment and is a powerful predictor of survival in heart failure with reduced ejection fraction. The impact of RV strain in HFpEF is unknown.
Purpose: We sought to analyze RV strain and its prognostic value in HFpEF patients.
Methods: Between January 2015 and June 2017, we prospectively enrolled 94 consecutive patients with HFpEF (78 ± 9 years, 71% women) and 30 age and sex matched volunteers (75 ± 6 years, 60% women). All patients underwent complete 2D echo in sinus rhythm. A RV-focused four-chamber view was analyzed by 2D speckle tracking to evaluate the global longitudinal strain of RV (RV-GLS). Patients were followed up for all-cause mortality.
Results: In HFpEF patients, mean RV-GLS and TAPSE were significantly lower than controls (-23.0 ± 4.9% vs -26.3 ± 3.9%; p = 0.002 and 20 ± 5mm vs 24 ± 4mm; p < 0.001 respectively), as opposed to RV FAC (44 ± 7% vs 46 ± 7%, p = 0.22. Table). Intra observer reproducibility for RV-GLS was high (ICC 0.83 in controls and 0.89 in HFpEF). Multiple regression analysis showed that TAPSE (beta=-0.37[-0.54- -0.19], p < 0.001), RV/RA gradient (beta = 0.14[0.06- 0.22], p = 0.001) and indexed LV end-diastolic volume LV EDVi (beta = 0.12 [0.02-0.23], p = 0.025) were associated with RV strain. During a mean follow-up of 21 ± 7months, 17 patients (18%) died. In univariate analysis, RV-GLS was significantly associated with outcome (HR= 1.13 [1.03-1.24], p = 0.005). Multivariate Cox analysis identified GFR (HR= 0.97 [0.95-0.99], p = 0.040), hemoglobin (HR= 0.64 [0.47-0.87], p = 0.005) and LV EDVi (HR = 1.02 [1.00-1.04], p = 0.013) as independent predictors of prognosis ($?^2$model= 28.50). Adding RV-GLS to this preliminary model (HR = 1.10 [1.00-1.21], p = 0.050) improves $?^2$model to 34.3, demonstrating the predictive value of RV-GLS for mortality in HFpEF patients.
Conclusions: In HFpEF, RV-GLS is associated with a poorer prognosis with higher rate of mortality and added significant information compared to usual clinical and imaging variables.

	Controls (n = 30)	HFpEF (n = 94)	P value
Indexed LV end-diastolic volume (ml)	62±10	67±17	0.10
LVEF (%)	65±5	63±7	0.13
LV GLS (%)	-21.0±2.5	-17.2±3.0	<0.001
RV/RA gradient (mmHg)	19±6	33±11	<0.001
RV FAC (%)	46±7	44±7	0.22
TAPSE (mm)	24±4	20±5	<0.001
RV GLS (%)	-26.3±3.9	-23.0±4.9	0.002

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The opioid system and pathophysiology of heart failure and renal dysfunction

J E Lisa Emmens[1]; JM Ter Maaten[1]; J Struck[2]; A Bergmann[2]; K Damman[1]; AA Voors[1]
[1]*University Medical Center Groningen, Cardiology, Groningen, Netherlands*; [2]*Sphingotec, Hennigsdorf, Germany*

Funding Acknowledgements: BIOSTAT-CHF was funded by the European Commission [FP7-242209-BIOSTAT-CHF; EudraCT 2010-020808-29].

Background: Proenkephalin (PENK) is a stable surrogate marker for enkephalins, endogenous opioid peptides, which exert important cardiovascular effects by decreasing myocardial contractility, blood pressure, and heart rate, and renal

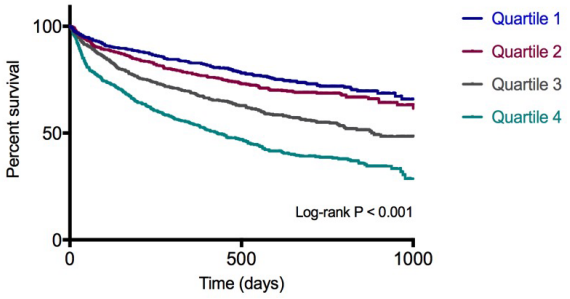
effects by increasing renal blood flow and urinary output. In heart failure (HF), PENK has been associated with renal function, heart failure severity, and clinical outcome. Yet it has only been studied to a limited extent and its exact biomarker position, additive value, and underlying pathophysiological mechanisms in HF require further investigation.

Purpose: We aim to thoroughly determine the biomarker position of PENK in HF by investigating the relationship between PENK and a wide variety of clinical variables, biomarkers, and clinical outcome.

Methods: In a large multicentre clinical cohort (BIOSTAT-CHF) consisting of 2,180 chronic HF patients, the relationship between PENK and clinical variables, biomarkers, and two clinical endpoints (mortality and a composite endpoint of death or HF hospitalisation) was established utilising several modern statistical approaches to achieve meticulous positioning.

Results: Median PENK was 86.2 (63.7 - 120.2) pmol/L. Higher levels of PENK were, among others, associated with higher age, lower systolic and diastolic blood pressure, higher BNP and NT-proBNP, higher creatinine, lower eGFR, higher NGAL, higher renin, and higher urea (all P = 0.001). The strongest predictors of log PENK were log creatinine, female sex, log NT-proBNP, log NGAL, and age (R^2 = 0.549). Using a correlation heatmap and hierarchical cluster analysis, PENK strongly clustered with renal markers such as NGAL, urea, and creatinine. PENK was a strong predictor of WRF, even after adjustment for log creatinine (OR 3.42 (2.35 - 4.96), P < 0.001). Higher levels of PENK were independently associated with an increased risk of mortality and the composite endpoint, even after correction for risk models developed for this cohort and log creatinine (HR 1.47 (1.22 - 1.78), P < 0.001 for mortality, HR 1.19 (1.01 - 1.40), P < 0.034 for the composite endpoint).

Conclusions: PENK is a novel biomarker in HF reflecting more severe heart failure, renal dysfunction, and worsening renal function beyond creatinine and therefore provides new insights into the pathophysiological role the opioid system might play in HF.



KM curve PENK for combined endpoint

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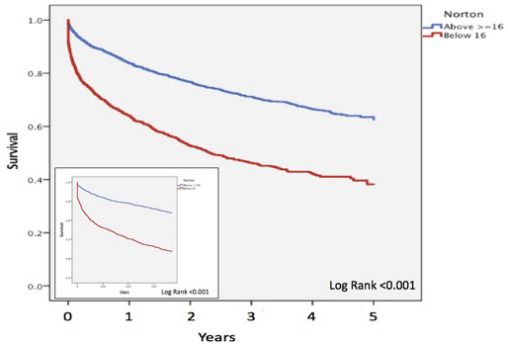
Norton admission scale as a prognostic factor among acute heart failure patients

I Israel Mazin[1]; R Klempfner[1]; I Goldenberg[1]; E Shaviv[1]; Y Peled[1]; E Massalha[1]; N Shlomo[1]; S Natanzon[1]
[1]*Chaim Sheba Medical Center, Tel Hashomer, Israel*

Background: The Norton scale scoring system was created in 1962 assessing the frailty hospitalized patients, and is still being used nowadays by nurses evaluating patients at hospital admission. Accordingly, this scale may be an important predictor of outcome following hospitalization We hypothesized that a low Norton score is an independent predictor of long-term mortality among hospitalized acute heart failure patients.



Kaplan-Meir survival analysis

Methods: of the present study population comprised 4388 acute heart failure patients presenting to Sheba medical center between the years 2008-2016, and were followed-up for long-term mortality and HF hospitalization following discharge cohort was divided according to the Norton score, low score (<16) and high score (> = 16). Multivariate Cox proportional hazards regression modeling was used to assess the independent association between Norton score and long-term mortality.

Results: Patients with low score (n = 1611 [37%]) were older, had higher prevalence of co-morbidities such as hypertension, COPD, anemia, CVA and renal failure compared to high score (n = 3323) (p <0.05 for each). Kaplan-Meir survival analysis (Figure) showed that at 1-year of follow-up mortality rates were significantly higher among patients with a low Norton score (34%) as compared with those with a high score (15%; p <0.001 for the overall difference during follow-up). After adjustment for confounders and comorbidities, multivariate analysis showed that a low Norton score was associated with >2-fold increased risk of all-cause mortality at 1 and 5 years of follow-up following hospitalization (p <0.001 for both). The association between Norton and mortality was consistent in both the HFrEF and HFpEF subgroups (p-value for interaction < 0.10).

Conclusion: Our findings, from a large cohort of hospitalized heart failure patients, show that the Norton score at admission is powerful independent predictor of long-term mortality. These data suggest that the scale should be added as an important risk stratification parameter in this high-risk population.

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Baseline B-type natriuretic peptide is the strongest predictor of transition to stage C heart failure in an at-risk population; Results from the STOP-HF prevention programme

S Mcclelland[1]; L Healy[1]; R Murphy[1]; S Zhou[1]; J Gallagher[2]; C Watson[3]; M Ledwidge[1]; K Mcdonald[1]
[1]*St. Vincent's University Hospital Healthcare Group, Dublin, Ireland*; [2]*University College Dublin, School of Medicine, Dublin, Ireland*; [3]*Queen's University of Belfast, Belfast, United Kingdom*

Background: Heart Failure (HF) is a global epidemic with multiple prevalent risk factors, resulting in a large at-risk population. Within this population, prevention programmes must be targeted to those at highest risk of HF development. However, the incidence of HF within a prevention service remains unknown, as does the phenotype of those at-risk patients most likely to develop HF.

Purpose: This study aimed to determine the incidence of stage C HF in an asymptomatic population with risk factors (stage A) and/or structural/functional cardiac abnormalities (stage B) in the STOP-HF prevention programme (Ledwidge et. al., 2013), and, within this population, to characterise the phenotype of patients most likely to progress to stage C (symptomatic) HF.

Methods: 2,037 patients in the STOP-HF service were characterised as stage A or stage B HF. Baseline echocardiographic parameters, BNP, blood pressure, weight and renal function, among other indices, were compared between the cohort that progressed to stage C and the population that did not.

Results: 86 patients developed Stage C HF during a median follow up of 4.8 years (overall incidence of 4.2%) with an incidence rate of 8.3 per 1000 patient years.

Strong clinical univariate predictors of progression-risk included older age (69.5 ± 8.9 vs 63.4 ± 10.6 years, p < 0.001), male gender (59.3 vs 44.9%, p = 0.012), higher body mass index (BMI) (29.8 vs 28.3, p < 0.001), higher BNP (134.6 ± 183.6 vs 39.6 ± 66pg/ml, p < 0.001) and higher creatinine (95.7 ± 34.7 vs 84.6 ± 21.3umol/L, p = 0.01) at baseline. Echocardiographic features included lower baseline EF (57.8 ± 13.9 vs 66.1 ± 7.8%, p < 0.001), higher left atrial volume index (40.6 ± 14.1 vs 28 ± 9.6, p < 0.001), left ventricular mass index (118.1 ± 27.2 vs 95 ± 46.7, p < 0.001), E/E' ratio (10.5 ± 4.1 vs 8.1 ± 3.1, p < 0.001) and left atrial diameter (44 ± 5.9 vs37.2 ± 5.7mm, p < 0.001) in patients who subsequently transitioned to stage C. The prevalence of diabetes (47.7 vs33.5%, p = 0.01), peripheral vascular disease (PVD) (9.3% vs 2.3%, p < 0.001), valvular heart disease (VHD) (4.7 vs 0.82%, p = 0.003), atrial fibrillation (17.4 vs 4%, p < 0.001) and prior myocardial infarction (36 vs 7.2%, p < 0.001) were significantly higher at baseline in patients who subsequently transitioned to stage C than in those that did not.

Multivariate analysis identified baseline BMI, BNP, reduced EF, VHD and PVD as independent predictors of the development of stage C HF. Baseline BNP level was the strongest predictor of transition to Stage C, with a value of 60.3pg/ml determined as the optimal level by which to differentiate high- and low-risk patients.

Conclusions: The incidence rate of stage C HF in the STOP-HF prevention programme is 8.3 per 1000 patient years. Among a number of independent predictors identified, the strongest indicator of transition risk is baseline BNP. These findings support the use of BNP measurement to more tightly define HF risk in an asymptomatic at-risk population.

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Echocardiographic Killip Classification

A Milwidsky[1]; D Greidinger[2]; Y Topilsky[1]
[1]Tel Aviv Sourasky Medical Center, cardiollogy, Tel Aviv, Israel; *[2]Tel Aviv University, Sackler Faculty of Medicine, Tel Aviv, Israel*

Background: The Killip classification is a well-recognized clinical assessment tool for heart failure in patients presenting with acute coronary syndromes. We hypothesized that an echocardiographic correlate of this classification, using diastolic grade and stroke volume index (SVI) as indicators of pulmonary congestion and systemic perfusion respectively, could be a useful risk stratification tool among all patients.
Methods: We included all consecutive patients in sinus rhythm evaluated by our research echo technicians and reviewed by a single senior cardiologist in Tel-Aviv Medical Center between 01/2013 to 12/2015. Echocardiographic killip (eKillip) class was defined according to diastolic grade and SVI, with levels above 35ml/m2 considered normal. Patients with a normal filling pressure (normal diastolic function or impaired relaxation) and normal SVI were defined as eKillip class-1. Patients with pseudo-normal or restrictive diastolic patterns and a normal SVI were ascribed to eKillip class-2 or 3, respectively. Those with pseudo-normal or restrictive diastolic patterns and a sub-normal SVI were defined as eKillip class-4.
Results: The study population comprised 571 patients, mean age was 65 ± 18 and 303(53%) were males. Three hundred and eighty-nine (68%) patients were at eKillip class-1, and 113 (20%), 26(5%) and 43(8%) were ascribed to eKillip classes 2, 3 and 4 respectively. In a univariate logistic regression model, e-Killip class was highly associated with all-cause mortality ($p < 0.001$). In a multivariate binary logistic regression model adjusted to age, gender, renal function, multiple cardio-vascular co-morbidities and malignancy, increasing eKillip class remained associated with all-cause mortality ($p = 0.02$). Compared to patients with eKillip class-1, those at classes 2-4 had 68%, 281% and 385% higher mortality rates, respectively (95% CI 0.80-3.50, 1.00-7.88 and 1.58-9.37, with $p = 0.17$, 0.05 and < 0.01, respectively).
Conclusion: Echocardiographic Killip class defined by combination of diastolic grade and SVI among all patients undergoing echocardiography in a tertiary hospital, was significantly associated with all-cause mortality.

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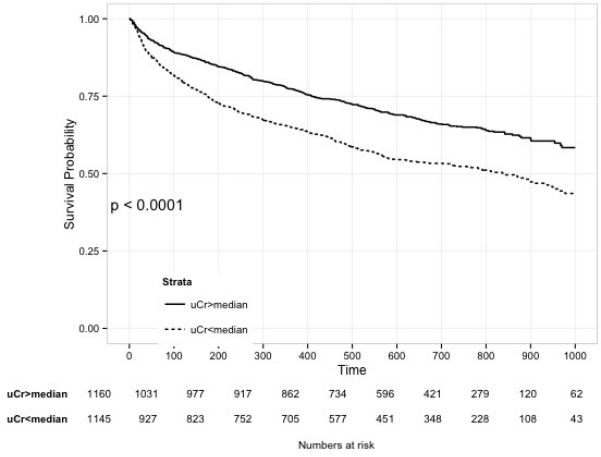
Urinary creatinine is a marker of body composition and muscle wasting in patients with worsening heart failure

J M Jozine Ter Maaten[1]; KW Streng[1]; K Damman[1]; AA Voors[1]
[1]University Medical Center Groningen, Groningen, Netherlands

Background: Muscle wasting and unintentional weight loss has been associated with more advanced disease and poor outcome in patients with heart failure. Timely identifying muscle wasting is very difficult, yet urinary creatinine might be an easy obtainable marker to assess this.



Kaplan Meier urinary creatinine

Purpose: This study aimed to identify the value of urinary creatinine in acute and worsening heart failure patients and be the first to evaluate its association with changes in body composition.
Methods: We measured spot urinary creatinine at baseline in 2,313 patients enrolled in the BIOlogy Study to Tailored Treatment in Chronic HF (BIOSTAT-CHF) trial. The association between urinary creatinine and outcome was evaluated by Cox regression analysis adjusted for potential confounders.
Results: Median spot urinary creatinine was 5.2 [2.7-9.6] mmol/L, and lower urinary creatinine was associated with older age, lower height and weight, worse renal function, and more severe heart failure. The risk of weight loss after 9 months was significantly greater in patients with lower spot urinary creatinine (OR: 1.24 [1.01-1.25] per log decrease, $P = 0.029$).
In multivariable cox regression analysis, lower spot urinary creatinine was associated with an increased risk of the combined endpoint of all-cause mortality or heart failure hospitalization (1.22 [1.14-1.30] per log decrease, $P < 0.001$), and all-cause mortality (1.27 [1.17-1.37] per log decrease, $P < 0.001$). The association remained significant after correction for body dimensions and renal function.
Conclusions: This study is the first to show that lower spot urinary creatinine is associated with smaller body dimensions, renal dysfunction and more severe heart failure in patients with acute and worsening heart failure. Additionally, lower spot urinary creatinine is associated with an increased risk of weight loss and could therefore be a novel, easy obtainable marker to assess (risk of) muscle wasting in heart failure patients.

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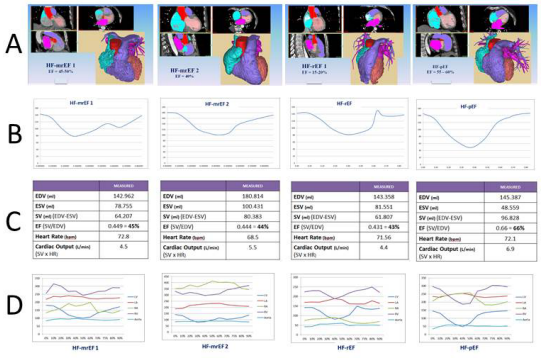
3-Dimensional analysis of the haemodynamics of heart failure (HF) in mid-range- (HF-mrEF), reduced- (HF-rEF) and preserved- (HF-pEF) ejection fraction classification patients

H O' Grady[1]; H Zafar[2]; K Mostafa[3]; L Morris[1]; F Sharif[2]
[1]Galway Mayo Institute of Technology GMIT, Galway, Ireland; *[2]National University of Ireland, Cardiovascular Research Centre (CVRC), Galway, Ireland*; *[3]Galway University Hospital, Department of Cardiology, Galway, Ireland*

Background / Introduction: Heart Failure (HF) is a complex condition which may be accompanied by considerable alterations in ventricular volume depending on the particular phenotype. Analysis of 3-dimensional volume changes of the heart chambers over the cardiac cycle can provide a more global insight into HF dynamics than consideration of Ejection Fraction (EF%) alone.
Purpose: This study investigated the haemodynamics of Heart Failure using analysis of 3-dimensional volumes in patients with Heart Failure with Mid-Range- (HF-mrEF), Reduced- (HF-rEF) and Preserved- (HF-pEF) Ejection Fraction.
Methods: Cardiac-gated CT scans for 11 stages (0-90%) of the cardiac cycle were segmented using specialised software into 4 chambers and aorta. 3-dimensional models of Left Atrium (LA), Right Atrium (RA), Left Ventricle (LV) and Right Ventricle (RV) and aorta were reconstructed and exported for analysis. 3-dimensional volumes for all chambers were calculated and recorded. Cardiac cycle timings and Heart Rate (bpm) were determined from CT scan data. 3-d volumes were plotted against timings and maximum and minimum volumes measured for all chambers. LV End-Systolic Volume (ESV) and End-Diastolic Volume (EDV) of the LV were determined and clinical indices of Stroke Volume (SV), Ejection Fraction (EF %), and Cardiac Output (CO) were calculated from the results. All variables were determined for each of the 4 cases of HF EF% classification.
Results: 3-dimensional models for HF-mrEF (2), HF-rEF and HF-pEF cases were created (IMAGE A).
Values for 3-dimensional volumes for 11 stages of the cardiac cycle were tabulated and plotted against exact timings for each cycle stage (0-90%) (IMAGE B).
Values for LV volumes and clinical indices were tabulated and compared to those recorded clinically (IMAGE C).
Values for 3-dimensional volumes for 4 chambers and aorta for 11 stages of the cardiac cycle were tabulated and plotted (IMAGE D).
Conclusion(s): This study showed that the 3-dimensional analysis of volumetric changes across the cardiac cycle can provide important information regarding the haemodynamics of different classifications of Heart Failure. Further work is planned to expand this research for application in determination of clinically relevant indices representing global HF dynamics.



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Changes in energy consumption during exercise and fatigue symptoms: a new marker of cardiac functional reserve in LVAD patients.

S Boschi[1]; M Masetti[1]; A Loforte[1]; M Bellettini[1]; E Pilato[1]; S Martin-Suarez[1]; G Marinelli[1]; F Grigioni[1]; L Potena[1]

[1]University Hospital Policlinic S. Orsola-Malpighi, Heart Failure and Heart Transplant Program, Bologna, Italy

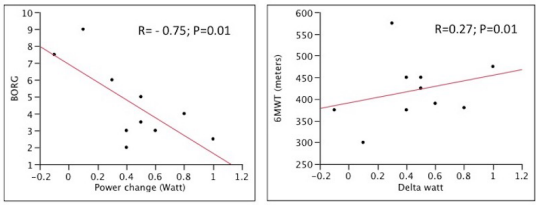
Introduction: Left ventricular assist device (LVAD) therapy may allow significant improvement of survival and quality of life in patients with advanced heart failure, in the context of a bridge to transplant or destination strategy. Tolerance to exertion is a key factor driving the perception of quality of life in these patients, and it depends upon the tailored optimization of LVAD support to cardiocirculatory function.

Objective: In this study we analyzed the variability of LVAD energy consumption and estimated flow in a group of patients undergoing six-minutes walking test (6MWT) to investigate how LVAD function may adapt to the physiological changes occurring during exercise.

Methods: We considered for inclusion all consecutive patients with Heartware LVAD presenting at our outpatient clinic for routine follow-up between May and November 2017 and with at least 2 months distance from implant. We excluded patients who had not completed rehabilitation, and with extracardiac reasons impairing ability to walk. Watt, estimated flow, and heart rate were measured before and after 6MWT. Distance walked and Borg scale represented outcome measures.

Results: Ten patients fulfilled inclusion criteria (age52 $\pm$ 14, 20 $\pm$ 18 months after implant, 2592 $\pm$ 60 rpm). Average distance walked was 420 $\pm$ 74 m, and Borg scale was 4.6 $\pm$ 2.3. Energy consumption (3.74 $\pm$ 0.41 to 4.19 $\pm$ 0.46 watt; $P < 0.01$), and estimated flow (4.17 $\pm$ 0.86 vs. 5.02 $\pm$ 0.75 l/min; $P < 0.01$) significantly increased after exercise. LVAD parameters did not predict distance walked, but changes in energy consumption and estimated flow correlated with Borg scale after exercise ($R=-0.72$; $P = 0.02$; see Figure).

Conclusions: In this pilot study we found that increase in energy consumption of LVAD during exercise is associated with lower grade of dyspnea reported by the Borg scale, but not with the distance walked. Because the function of Heartware device is highly dependent on pre-load conditions, we hypothesize that our observation reflects the ability of the LVAD to improve function in patients with left ventricle functional reserve. Further data are needed to confirm whether energy consumption variability during exercise could become a good marker to aim at in the rpm regulations and overall therapy management, to improve exercise tolerance in LVAD patients.



Clinical Case Corner 1 - Stories of women and of their broken hearts

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An unusual case of aborted sudden cardiac death in a young woman: which is the culprit?

M Mapelli[1]; E Conte[1]; A Dello Russo[1]; G Vettor[1]; A Baggiano[1]; M Muratori[1]; L Fusini[1]; D Andreini[1]; G Pontone[1]; M Pepi[1]; PG Agostoni[1]
[1]*Cardiology Center Monzino IRCCS, Milan, Italy*

Background: Anomalous origin of a coronary artery (AAOCA) carries an associated risk of Sudden Cardiac Death (SCD) with interarterial anomalous left or right coronary artery course (ALCA and ARCA respectively). Myocarditis, especially with extensive fibrosis at MRI is also a risk factor for SCD in young population. Increasing use of cardiac imaging techniques is enhancing myocarditis and AAOCA diagnosis, previously completely skipped.
Clinical case: We present a 23y/o woman without any relevant previous disease (except for BMI 15 Kg/m2) resuscitated by a relative from SCD while she was sleeping (5 DC shocks due to ventricular fibrillation, VF), followed by uneventful course and full recover. A cardiac CT scan showed an ARCA with interarterial course (between aorta and pulmonary artery) and moderate narrowing of RCA lumen at rest (Fig.1) and she was referred at our hospital for surgical coronary artery re-implantation, asymptomatic with no further arrhythmias. Blood sample showed normal CBC, Troponin, C-reactive protein values. A cardiac MRI showed a picture consistent with a previous, subclinical, myocarditis with diffuse myocardial fibrosis (non-ischemic pattern) and mild reduction in ejection fraction (Fig.1). A right side myocardial biopsy failed to take a pathological sample due to epicardial fibrosis distribution. Both cardiac tissue PCR and serum antibodies were negative for common myocarditis viruses. Patient underwent an electrophysiological study without induced arrhythmias. A Subcutaneous Defibrillator (S-ICD) was implanted and she was discharged with no complications.
Discussion: In this peculiar case 2 diagnosis could be responsible for the aborted SCD. A recent review on AAOCA underlines the importance of ischemia in patients with ARCA where, particularly without proximal vessel narrowing, a conservative approach may be reasonable. In this woman affected both by AAOCA and myocardial fibrosis the culprit disease is debatable, but in absence of recurring events, signs of ischemia and imaging criteria for malignant pattern (acute take-off, slit-like, severe compression), eventual surgery was postpone and she was protected with a S-ICD (SCD secondary prevention). Furthermore the occurrence of VF at rest is less typical for AAOCA, mostly occurring during exercise. At 6 months she is asymptomatic without clinical events.
Conclusions: We present a case of an aborted SCD with 2 possible culprit diagnosis in which multimodality imaging is fundamental in case management and clinical decisions.

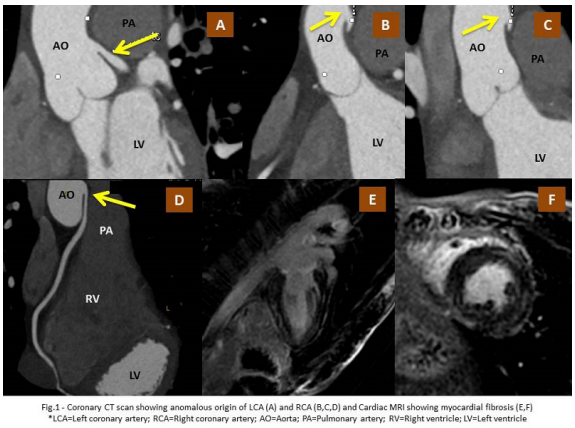

Fig.1 - Coronary CT scan showing anomalous origin of LCA (A) and RCA (B,C,D) and Cardiac MRI showing myocardial fibrosis (E,F)
*LCA=Left coronary artery; RCA=Right coronary artery; AO=Aorta; PA=Pulmonary artery; RV=Right ventricle; LV=Left ventricle

Fig.1

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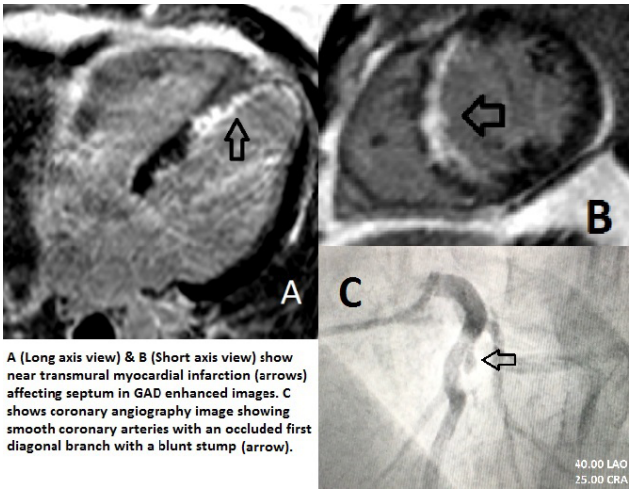
Presumed post-partum cardiomyopathy? beware of the confounder of pregnancy

CWJ Cheuk Wing Jonathan Lee[1]; A Khand[1]; R Sankaranarayanan[1]; P Kanagala[1]
[1]*Aintree University Hospital, Cardiology, Liverpool, United Kingdom*

Pregnancy is a complex process in which physiology changes significantly. The stress of pregnancy can unmask underlying heart disease or cause post-partum cardiomyopathy.
A 33 year old lady, 3 months post-partum, presented to the emergency department with 12 weeks history of breathlessness, orthopnoea, paroxysmal nocturnal dyspnoea and associated upper abdominal discomfort. She denied having any chest pain. On examination, blood pressure was 112/71 mmHg and heart rate was 90 beats per minute. There was peripheral pitting oedema, soft systolic murmur at the apex, an elevated jugular venous pressure and diminished air entry at the lung bases.



A (Long axis view) & B (Short axis view) show near transmural myocardial infarction (arrows) affecting septum in GAD enhanced images. C shows coronary angiography image showing smooth coronary arteries with an occluded first diagonal branch with a blunt stump (arrow).

GAD enhanced MRI and angiography image

Blood tests reviewed mild normocytic anaemia (Haemoglobin 109g/L) and mild transaminitis (alanine aminotransferase 143). D dimer was strongly positive. Arterial blood gas showed type 1 respiratory failure. Electrocardiogram revealed poor R wave progression from v1-v4 with accompanying 1-3mm deep T wave inversions and deep q waves (7-12mm). Chest X ray revealed raised cardiothoracic ratio with accompanying pulmonary congestion and minor blunting of the costophrenic angles consistent with small pleural effusions. CT pulmonary angiogram excluded pulmonary embolism. Echocardiogram revealed significant enlargement of all 4 cardiac chambers with severe biventricular systolic dysfunction consistent with a diagnosis of peri-partum cardiomyopathy. The patient was managed with diuretics, ACE inhibitor (subsequently switched to sacubitril/ valsartan), beta blocker and spironolactone. Follow up was arranged in the outpatient setting.
At approximately 2 year follow up, she remained symptomatic (NYHA class III). A cardiac MRI was arranged. This revealed a dilated left ventricle with moderate left ventricular systolic dysfunction. On late enhancement imaging there was extensive, near transmural infarction of the mid to distal septum involving the apex, consistent with a full-thickness proximal left anterior descending territory infarct. Coronary angiography revealed smooth coronaries except an occluded first diagonal branch with a blunt stump. There was ectasia and mild irregularity of the mid LAD at the origin of the first diagonal branch. The appearances were strongly suggestive of SCAD (spontaneous coronary artery dissection). On further questioning, patient revealed episodes of chest pain towards later stage of pregnancy.

Conclusions: and implications for clinical practice
1. Spontaneous coronary artery dissection is a known risk in pregnancy
2. Electrocardiography and troponin sampling at the time of chest pain with early access to coronary angiography and revascularisation could have ameliorated the extent of myocyte necrosis
3. Cardiac MRI provides unrivalled tissue characterisation and should be considered for all patients in heart failure post-partum
4. SCAD with infarction and other pathologies should be considered and actively sought before committing to a diagnosis of post-partum cardiomyopathy

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Severe acute dyspnea in asthmatic patient due to secondary Takotsubo syndrome and cardiogenic shock

D Danijel Crncic[1]; D Rajtman[1]; LM Hodoscek[1]; D Kovac[1]; S Horvat[1]; UB Ferko[1]; SV Rauter[1]; J Tepes[1]; I Nikolajevic[1]; M Lainscak[1]
[1]General Hospital Murska Sobota, Department of Internal Medicine, Murska Sobota, Slovenia

Introduction: Takotsubo syndrome is an acute and usually reversible heart failure syndrome. Described triggers include asthma exacerbation but we are not aware of any reports with typical and inverted Takotsubo syndrome in a single individual.
Description: A 63-year old woman with a recent episode of primary inverted Takotsubo syndrome (3 months ago, coronary angiography without any lesions, circumferential basal hipokinesia) and history of asthma presented with severe acute dyspnea that started at 3am during sleep. After repeated rescue salbutamol inhaler dyspnea did not resolve so she was reffered to Emergency room. There was no recent history of fever, cough or chest pain. On examination she was in respiratory distress with tachypnoea (22/min), oxygen saturation on room air of 78%, peak expiratory flow of 160 L/min (steady state values of 400 L/min), used accesory respiratory muscles, and had prolonged expiratory phase with wheezing. Her blood pressure was 116/76 mmHg, chest X-ray showed lung hyperinflation and electrocardiogram (ECG) was unremarkable except sinus tachycardia. Initial management included oxygen (31% Venturi mask), intravenous methyl-prednisone and fenoterol/ipratropium inhalation. High sensitivity troponin I was 100 ng/l (reference < 15.6 ng/l), NT-proBNP was 204 ng/l, and arterial blood gas analysis showed severe combined metabolic and respiratory acidosis with pH 7.16 and elevated lactate of 3.0 mmol/l. Patient deteriorated despite supportive therapy: her blood pressure dropped to 95/55 mmHg and she presented with cardiogenic shock. Emergency transthoracic echocardiograpy showed typical apical balooning and severely depressed left ventricular ejection fraction of 30%. She was transferred to intensive care unit and was treated with levosimendan, dobutamine and furosemide. In ECG, ST segment elevation with inverted T waves in inferior, anterior and lateral leads developed but she denied any chest pain. Troponin and NT-proBNP peaked at 6057 ng/l, and 8186 ng/l, respectively. In view of recent coronary angiography we did not repeat the invasive diagnostics. After supportive measures, she recovered completely and was discharged with normal levels of cardiac biomarkers and at steady state pulmonary function tests. Echocardiography 2 weaks after discharge showed normal left ventricular ejection fraction of 65 % with no segmental wall motions abnormalities.
Conclusion: We presented a case of secondary Takotsubo syndrome with cardiogenic shock triggered by severe asthma exacerbation in a patient with history of inverted Takotsubo syndrome. In clinical practice, differentiation of dyspnea cause in patients with asthma is challenging but crucial for trigger identification and appropriate management. This case emphasizes the importance of cardiac assessment including FoCUS ultrasound and cardiac biomarkers in patients who remain symptomatic despite appropriate obstructive pulmonary disease therapy.

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Pregnancy after cardiac transplantation: maternal and fetal outcomes in a Portuguese tertiary hospital

S Sara Nunes[1]; P Araujo[2]; AP Machado[3]; S Amorim[4]; N Montenegro[3]
[1]Hospital Center of Tras-os-Montes and Alto Douro, Obstetrics & Gynecology, Vila Real, Portugal; *[2]Sao Joao Hospital, Cardiology, Porto, Portugal*; *[3]Sao Joao Hospital, Obstetrics & Gynecology, Porto, Portugal*; *[4]Sao Joao Hospital, Cardiothoracic Surgery, Porto, Portugal*

Background: The number of pregnancies after maternal cardiac transplantation is increasing since the first report in 1988. According to current literature, cardiac function of the transplanted heart is generally adequate to pregnancy's needs, albeit the risk of hypertension and preeclampsia. Beyond these, which are associated with preterm birth and fetal growth restriction, fetal outcomes are also dependent of the maternal medication used during pregnancy.
Purpose: To evaluate maternal and fetal outcomes of pregnant women with previous cardiac transplantation.
Methods: We evaluated the clinical data of pregnant women diagnosed with previous cardiac disease, followed between 2007 and 2017, in a Portuguese tertiary hospital. From 313 pregnant women with cardiac disease, there were two with previous cardiac transplantation. Clinical information was collected from Obscare® and SClínico® databases.
Results: The first case occurred in 2008, in a 32-years-old nulliparous woman, transplanted 6 years before due to a familial dilated cardiomyopathy. The unplanned pregnancy was diagnosed at 8 weeks' gestation. By then, she was treated with cyclosporine, prednisolone, diltiazem, aspirin, lisinopril, as well as magnesium and iron supplements. Lisinopril was discontinued, but all remaining medication was maintained throughout pregnancy. This was uneventful until 35 weeks, when an increased blood pressure (systolic >140 and diastolic >90 mmHg) associated with proteinuria (2+ in test strip) was found. Patient was hospitalized with a suspected preeclampsia that was not confirmed. An elective c-section was performed at 37 weeks and a healthy male was born with 2530gr. Uterine atony during surgery was controlled with oxytocin and B-Lynch suture. Maternal echocardiography revealed a preserved biventricular function during the entire pregnancy. The second case occurred in a 28-years-old woman also transplanted due a familial dilated cardiomyopathy in 2010. She presented several rejection episodes until 2015 when she had a diagnosis of a 4 weeks' pregnancy. At that time, her medication regimen included trimethoprim/sulfamethoxazole, azathioprine, tacrolimus and furosemide. Furosemide was suspended and supplementation with magnesium was started. Cardiac function remained normal throughout all pregnancy period (left ventricular ejection fraction of 67%). She already had a healthy son from an uneventful pregnancy previous to cardiac transplantation. There were no complications during this second pregnancy and labor occurred spontaneously at 37 weeks. An urgent c-section was required because of non-reassuring fetal heart rate. A healthy female was born with 2800gr.
Conclusions: Despite the growing better outcomes presented by cardiac transplanted pregnant women, obstetrical and cardiac monitoring of these pregnancies remain a challenge. Multidisciplinary teams are crucial to deal with this particular clinical situation and improve the wellbeing of both mother and fetus.

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A rare presentation of heart failure

A De Marvao[1]; S Hadjiphilippou[2]; A Escudier[2]; J Arnold[2]; M Sweeney[2]; C Roufosse[3]; M Pickering[4]; C Plymen[2]
[1]Imperial College London, MRC London Institute of Medical Sciences, London, United Kingdom; *[2]Imperial College Healthcare NHS Trust, Department of Cardiology, London, United Kingdom*; *[3]Imperial College Healthcare NHS Trust, Department of Histopathology, London, United Kingdom*; *[4]Imperial College Healthcare NHS Trust, Centre for Complement and Inflammation Research, Division of Immunology and Inflammation, London, United Kingdom*

A previously well 38-year-old female presented in December 2016 with abdominal pain radiating to her back. Non-contrast CT excluded renal calculi but demonstrated abnormal appearances of the renal parenchyma bilaterally. Subsequent contrast CT and MR imaging revealed widespread aortic thrombus extending into both renal arteries with bilateral renal infarction. Vasculitic and thrombophilia screen was positive for lupus anticoagulant and the patient was started on warfarin for presumed antiphospholid syndrome.
A month later she reported arthralgia. Autoimmune testing demonstrated positive antinuclear and anti-Ku antibodies. She was commenced on hydroxychloroquine. Subsequently she developed increasing breathlessness, peripheral and pulmonary oedema. Echocardiogram revealed severe biventricular systolic dysfunction (left ventricular (LV) ejection fraction ~ 15%) so prognostic medical therapy for heart failure was initiated and she was referred on to our centre. Ongoing deterioration prompted immunosuppression with mycophenolate mofetil and cyclophosphamide.
Cardiac MRI demonstrated LV hypertrophy and severely impaired biventricular systolic function. Late gadolinium enhancement pattern was unusual, with intense LV circumferential and subendocardial fibrosis with predominant nodular septal enhancement. There was patchy enhancement of the RV septum and both atria (Fig 1A and 1B). Differential included sarcoid, amyloid, vasculitis and connective tissue disease.
Renal and myocardial biopsies showed, respectively, glomerular and interstitial deposition of amorphous, congo red-positive amyloid (Fig 1C) with characteristic yellow-green appearance under polarised light (Fig 1D). Immunochemistry staining of the amyloid deposits was positive for lambda light chains, confirming diagnosis of AL amyloid.
One year following initial presentation, the patient was started on Bortezomib chemotherapy and falling lambda light chain levels indicated response to therapy. However she continued to deteriorate and was transferred to a heart transplant centre for biventricular assist device implantation. She died soon after due to pulmonary haemorrhage.
Cardiac amyloid is a rare cause of systolic heart failure in young patients and prognosis is guarded. We show that classical cardiac imaging findings are not always present. Diagnosis of amyloidosis can only be confirmed by tissue biopsy and this should be pursued early if amyloidosis is suspected.

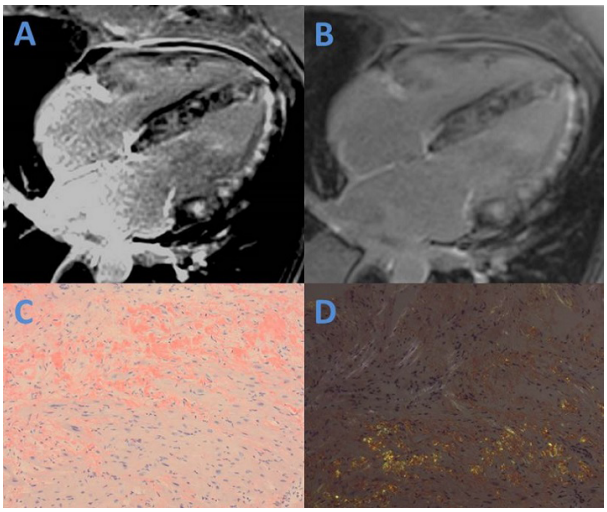

Figure 1

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Breastfeeding woman with severely depressed left ventricular systolic function

D Diogo Bras[1]; RA Guerreiro[1]; K Congo[1]; J Pais[1]; M Carrington[1]; P Semedo[1]; J Aguiar[1]

[1]Hospital Espirito Santo de Evora, Cardiology, Evora, Portugal

Introduction: Heart failure (HF) related morbidity in pregnancy comprise a substantial part of maternal morbidity. The most common cause of HF in late pregnancy and postpartum without any underlying cause, is peripartum cardiomyopathy (PPCM). However, other causes of peripartum HF should be bore in mind.

CLINICAL CASE: A 22-year-old female, with smoking habits and overweight, breastfeeding her child (aged 5 months) and with a past history of not studied seizures, went to the hospital after an episode of syncope.

A few minutes after an intense discussion with her partner, the patient started a malaise, followed by syncope and masseter myoclonias and abnormal limb movements, for approximately 20 minutes. Sphincter incontinence or tongue bite were not present. Soon after, she completely recovered her consciousness and had no symptoms.

Her heart rate at admission was 105 bpm and blood pressure was 109/74 mmHg. The auscultation was normal and she denied chest pain.

An ECG was performed, revealing a discrete ST-segment elevation (<0.5 mm) in II, III, aVF and V2 to V6. The blood test revealed a maximum troponin I of 1.92 ng/mL (cut-off >0.1) and NT-proBNP 3300 pg/mL. An echocardiogram was performed, showing mid-apical dilation of the left ventricle, with hypokinesis of the middle and apical segments of all walls, resulting in a poor systolic function (Left ventricle ejection fraction (LVEF) 29%). After admission in Intensive Cardiac Care Unit, she underwent coronary angiography that revealed no significant lesions. The ventriculography, however, showed an apical ballooning ventricle.

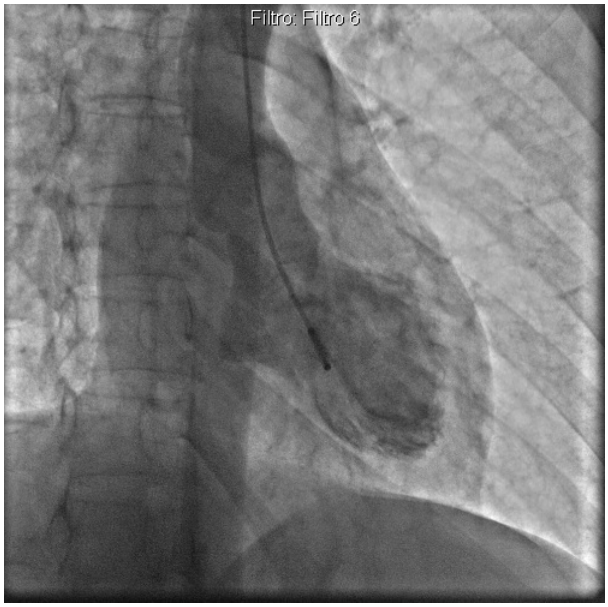
The most likely diagnostic hypothesis at the moment were MINOCA, myocarditis, PPCM and Takotsubo syndrome. Treatment with bromocriptine, carvedilol, captopril and spironolactone was initiated.

Within a few days, the systolic function and segmental abnormalities markedly improved, as shown in the revaluation echocardiogram performed 6 days after admission (LVEF 39%).

A cardiac magnetic resonance was also performed (7 days after admission), revealing a normal systolic function (LVEF 55%) with no segmental wall motion abnormalities and absence of late myocardial enhancement, making unlikely the hypothesis of MINOCA or myocarditis sequelae.

She was discharged with beta-blocking therapy and referred to cardiology and neurology appointments.

Discussion: After detailed investigation, Takotsubo syndrome was the most likely diagnosis. The patient clearly had an emotional stress event and the maximum troponin did not correlate with the extension of affected myocardium. Also, she had rapid recovery of the systolic function and wall motion abdnormalities and absence of late myocardial enhancement. However, Takotsubo syndrome is an uncommon condition in reproductive women. Particularly, in this case of a breastfeeding woman, the high prolactin levels and decreased oestrogen levels could be implicated, as oestrogens protect the myocardium of catecholamine toxicity.



Ventriculography

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Pregnant woman with high-output heart failure related to Parkes Weber syndrome

R Mourilhe Rocha[1]; J Prezioso[1]; BB Harboe[1]; WL Agrizzi[1]; FAR Medeiros[1]; IC Furtado[1]; BR Wasjbrot[1]; DXB Setta[1]; FN Albuquerque[1]; MI Bittencourt[1]; R Esporcatte[1]; DC Albuquerque[1]

[1]State University of Rio de Janeiro (UERJ), Rio de Janeiro, Brazil

Introduction: Parkes Weber's syndrome is a rare congenital condition characterized by a large amount of vascular abnormalities. The major signs and symptoms include capillary malformation on the skin, bone and soft tissue hypertrophy of the affected limb and multiple arteriovenous fistulas that can potentially lead to heart failure. There may also be pain in the affected limb and a size difference between limbs. Some cases of this syndrome result from mutations in the RASA1 gene and are inherited in an autosomal dominant. Physical examination is sufficient to make a diagnosis, but diagnostic imaging, including computed tomography (CT) angiography, is necessary to confirm it, to assess the extent and severity of the disease.

Case report: a first trimester pregnancy female (17 weeks), 31 years old daughter of consanguineous parents, with congenital scoliosis and glaucoma, was hospitalized after severe abdominal pain radiating to the right flank, associated with syncope. Physical examination revealed syndromic facies, marked cutaneo pallor, asymmetric bilateral lower limbs edema higher on the right side. Regular heart rhythm, with systolic murmur in tricuspid focus (3+/6+). P2 > A2 and HR = 130bpm. Digestive endoscopy showed severe peptic esophagitis with signs of recent bleeding. Echocardiography revealed severe tricuspid insufficiency with pulmonary hypertension (PASP = 76mmHg), with preserved systolic function, with increase in cardiac index (6.5L/min/m2). Venous Doppler of lower limbs and chest angiotomography confirmed the association of pulmonary thromboembolism, starting treatment with enoxaparin. Angiotomography of lower limbs showed complete deviation of large vessels, internal iliac artery fistulas with right common iliac vein, femoral vein thrombus on the same side with total occlusion of the lumen.

Patient progresses with blood dyscrasia, metabolic acidosis and acute renal failure due to renal tubular acidosis, requiring hemodialysis. At this time, it was decided for interrupting gestation (19 weeks) due to the high risk of maternal death. After the abortion, the patient developed clinical improvement and recovery of renal function as well as hemodynamic profile. Follow-up echocardiogram showing reduction of cardiac output, PASP = 40mmHg, and receiving hospital discharge, with conservative treatment of arteriovenous fistulas, using bisoprolol, furosemide and warfarin.

Conclusion: gestation is a clinical condition that naturally increases the patients' volemia and in association with a rare disease like Parkes Weber's syndrome, markedly got worse the high-output heart failure. Treatment should be individualized according to the age and clinical characteristics of each patient and depends on the presence and severity of the symptoms. The goal is to prevent disease progression and heart failure. Although conservative treatment can be considered,

surgery continues to play an important role in improving the quality of life of these patients.

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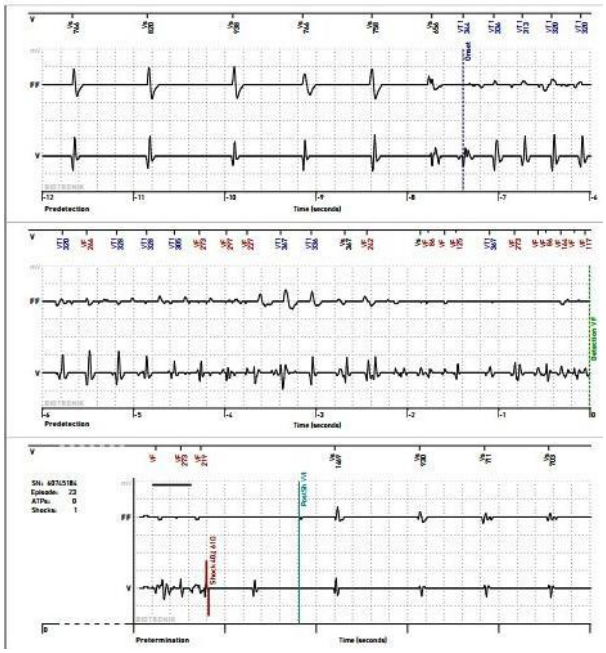
Pregnancy in long QT syndrome and implanted cardioverter-defibrillator for secondary prevention

S Garkina[1]; R Tatarsky[1]; T Lubimtzeva[1]; S Gureev[1]; V Lebedeva[1]; E Mikhaylov[1]; D Lebedev[1]

[1]Almazov National Medical Research Centre, Saint-Petersburg, Russian Federation

Background: The long QT syndrome (LQTS) is associated with high risk of ventricular tachyarrhythmias mainly triggered by adrenergic activation whereas the annual rate of sudden cardiac death (SCD) is estimated up to 5% for patients with LQTS and syncope. Specialized guidelines on treatment of pregnant women with inherited arrhythmias and implanted devices are lacking and patients are usually recommended to avoid pregnancy.



VF episode terminated by shock

Case report: A 26-year-old patient with implanted ICD for secondary prevention (history of recurrent ventricular fibrillation episodes) referred for control follow up visit during pregnancy. She was previously diagnosed LQTS type 2 with verified mutation of KCNH2 gene. She experienced recurrent VT and syncopal attacks since the age of 5 years and underwent ICD implantation in 2009 and elective device replacement in 2011 and 2014. Analysis of endograms revealed regular appropriate shocks after ventricular fibrillation (VF) episodes mostly triggered by PVC during persistent bradycardia. The patient had previously taken low doses of beta-blockers daily. On admission she was pregnant at the 12th week of gestation. Since the first weeks of pregnancy she didn't present VT/VF episodes or ICD shocks and reported normal physical tolerance. She demonstrated physiological sinus tachycardia until the 38 weeks of pregnancy with subsequent planned caesarean delivery (due to obstetrics indications) and live child. Two weeks after delivery she continued to experience VF episodes terminated spontaneously or after adequate ICD shocks (9 episodes) (Figure 1). Now the patient remains on beta-blockers.
Questions, problems or possible differential diagnosis. This clinical case illustrates reduced risk of cardiac events and fatal arrhythmias in young woman with LQTS during pregnancy.
Answers and discussion: Data about potential risks and outcome in pregnant patients with implanted devices are lacking and treatment tactics remains controversial. Numerous cases of favourable course and even benefits in clinical and functional status during pregnancy in patients with LQTS are reported. The cardiac event risk can be modified using beta-blocker therapy. Patients with ICDs are considered to have a successful pregnancy with no fetal compromise but under thorough medical monitoring.
Conclusions: and implications for clinical practice. Pregnancy in patients with LQTS and implanted ICD is not contraindicated and treatment tactics depends on clinical situation while positive influence of physiological hemodynamical changes and hypersympathicotonia may contribute to temporary elimination of bradydependent ventricular life-threatening arrhytmias. Algorithms of ATP and shock therapy during pregnancy in women with ICD are corrected individually while remote monitoring is recommended to all patients.

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Telling the story of a caucasian woman with peripartum cardiomiopathy: from cardiogenic shock to a happy-ending second pregnancy.

AB Scardovi[1]; R De Maria[2]; A Cortellesi[1]; L Luca Arcari[1]; R Ricci[1]

[1]Hospital Santo Spirito, Cardiology, Rome, Italy; *[2]Niguarda Ca' Granda Hospital, Clinical Physiology Institute, Milan, Italy*

Background: Peripartum Cardiomyopathy (PPCM) is a rare disease, which affects previously healthy women toward the end of pregnancy or in the months following delivery, with no other identifiable cause of heart failure. Although the aetiology and pathogenesis of PPCM are still unknown, several hypotheses have been proposed, comprising viral myocarditis, apoptosis and prolactin toxicity, auto-immune mechanisms, malnutrition, hormonal changes, or the result of complex interactions of pregnancy-associated factors against a susceptible genetic background . PPCM is still a diagnosis of exclusion. Established recommendations for future pregnancies do not exist. Left ventricular (LV) recovery is considered the most reliable prognostic predictor of survival in subsequent pregnancies,but it does not guarantee an uncomplicated subsequent pregnancy. Although death is rare, marked decreases in LV function have been reported in approximately 20% of patients, with persisting dysfunction after pregnancy in about 50%.
Methods and Results: We report a case of PPCM in a 30 years old Caucasian woman, with no history or evidence of pre-existing structural heart disease. She developed cardiogenic shock 12 hours after delivery by caesarean section with spinal anesthesia of her first healthy child, at 38 weeks gestation. Transthoracic echocardiography showed a dilated left ventricle with severely depressed pump function (LVEF 20%). Endomyocardial biopsy excluded active myocarditis. She was treated with i.v. inotropes, invasive mechanical ventilation and insertion of an intra-aortic balloon-pump; lactation was inhibited by a single dose of cabergoline, two infusion of levosimendan were performed and ivabradine was added to control tachycardia. At three-month follow-up, echocardiography showed complete recovery of LV function (LVEF 57%). At 18-month follow-up the patient stopped medications for symptomatic hypotension. At 24 and 30 months follow-up, off drugs, she was asymptomatic, LVEF was 64% and exercise tolerance was normal both at cardiopulmonary exercise test and six-minutes-walking test.
Four years after the acute PPCM, having been warned of the 20% risk of disease relapse, the patient decided to undertake a second pregnancy. After an uncomplicated gestation and natural delivery she gave to a healthy fetus birth. Two years later LV and functional capacity are still normal.
Conclusions: Management of PPCM is still largely empirirc. The long term prognosis and the containdication to a subsequent pregnancy for the risk of PPCM relapse in a patient who experienced full recovery remain uncertain

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Impact of cardiac resynchronization therapy in patients with peripartum cardiomyopathy

LUIZ Camanho[1]; E B Saad[2]; C Slater[2]; LUCAS Carvalho Dias[2]; LUIS Oliveira Jr[2]; R Mourilhe-Rocha[1]

[1]State University of Rio de Janeiro and Procardiaco Hospital, RIO DE JANEIRO, Brazil; *[2]Hospital Pro Cardiaco, Electrophysiology and Pacemaker, Rio de Janeiro, Brazil*

Fundamental: peripartum cardiomyophaty (PPCM) is a rare cause of dilated cardiomyophaty in pregnant women at the time of or following childbirth. Despite maximal medical treatment, 20% to 25% of patients (pt) progress to end-stage heart failure (HF) over time. There are few data on cardiac resynchronization therapy (CRT) in this population.
Objective: to describe clinical outcome in pt with PPCM and CRT.
Methods: in a cohort of 300 consecutive pt enrolled at CRT, 4 (1.3%) had the PPCM diagnosis. All pt were receiving optimal medical treatment. In all cases, the PPCM diagnosis was defined immediately after delivery. The survival and response to CRT were evaluated.
Results: the mean age was 39 years; average ejection fraction (EF): 24,5%; left bundle branch block (LBBB) and average QRS duration: 165 ms (130 to 200 ms). Average left ventricular end-diastolic diameter was 80.7 mm and left ventricular end-systolic diameter (LVESD) was 70 mm. Functional class (FC) III (NYHA) and preserved renal function were observed in all pt. BIV-ICD was also observed in 3 pt. 75% of patients progressed to end-stage HF and subsequent death. The mean survival was 16 months. Only 1 pt presented satisfactory evolution with FC and EF

improvement and left ventricular end-systolic diameter decrease. The follow-up time was 43 months. This pt had LBBB and QRS duration of 200 ms.
Conclusion: although optimal medical treatment and CRT, this population in general presents unfavorable evolution, suggesting to be an adverse model of cardiomyophaty, and that should be early evaluated for cardiac transplantation.

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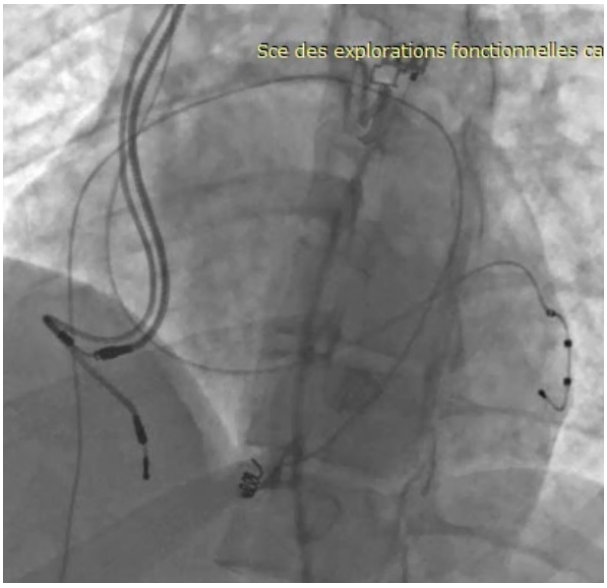
Successful pregnancy after transvenous cardiac resynchronization therapy in a woman with congenitally atrioventricular block and induced dilated cardiomyopathy

S Ouali[1]; K Sammoud[1]; M Ben Halima[1]; S Boudiche[1]; N Khedher[1]; F Meghaith[1]; MS Mourali[1]
[1]La Rabta University Hospital, Cardiology, Tunis, Tunisia

Introduction: Isolated nonimmune congenital atrioventricular (AV) block is a rare disorder, associated with a risk of sudden death in the absence of cardiac pacing. Most women with paced congenital atrioventricular block reach childbearing age. However, long term right ventricle pacing can induce dilated cardiomyopathy and pregnancy in this setting is challenging
Case: We report a case of a 31-year-old female with a history of isolated nonimmune congenital AV block and long term right ventricle pacing since 6-year old. At the age of 29, the patient achieved a non-programmed pregnancy and was admitted to our institution during the 30th week of gestation because of an exacerbation of heart failure (NYHA class III heart failure symptoms), and general physical weakness. Electrocardiogram (ECG) upon admission showed an atrial sensed and apical right ventricular-paced rhythm with QRS duration of 190 ms (Figure 1 Panel A).
Echocardiography revealed severe systolic left ventricle (LV) dysfunction, LV ejection fraction of only 35%. Significant mitral valve regurgitation was also observed. Unfortunately, a Stillbirth occurred at the 32th week of gestation despite the close monitoring. Given the underlying persistent LV dysfunction and the complete AV block requiring conventional pacemaker therapy, a biventricular pacemaker (CRT-P) was implanted, eight months later the first delivery. Postoperatively, the patient achieved total relief from her exercise tolerance and improved from New York Heart Association functional Class III to II with a QRS shortening (Figure 1 Panel B) and a significant increase of her systemic LV ejection fraction (LVEF= 47%) evaluated during a 28th week of a second gestation. The pregnancy successfully continued until term and a male infant weighting 3,200 g was born via a cesarean section.
Conclusion: A right ventricle paced induced cardiomyopathy can occurred in patients with seronegative complete AV block. These patients can be managed with cardiac resynchronization therapy and pregnancy can be achieved in this setting.



Figure

70
The clinical challenge of heart failure during the peripartum period

F Fernando Fonseca Goncalves[1]; J Pedro Guimaraes[1]; PS Mateus[1]; JI Moreira[1]
[1]Hospital Center of Tras-os-Montes and Alto Douro, Cardiology, Vila Real, Portugal

A 42-year-old woman, smoker and without other known cardiovascular risk factors, with obstetric records of four gestations, three childbirths and one abortion, shows up in the emergency ward with rest dyspnea associated with orthopnea and peripheral edema with 23 days of evolution, all beginning one day after last childbirth when she had productive cough with mucopurulent sputum, being treated therefore with steroids and empirical amoxicillin/clavulanic acid without significant symptomatic improvement. On examination the patient has tachycardia, no fever, signs of central cyanosis, peripheral edema and crackles in both inferior pulmonary thirds, without heart murmurs or pericardial friction rub audible on cardiac auscultation. Analytical assay shows leukocytosis but C-reactive protein in the upper limit of normal and an elevation in D-dimers levels for what it is then carried out a computed tomography angiogram which excludes pulmonary thromboembolism. NT-proBNP levels are high without a rise in cardiac troponin T. Virus testing in bronchial aspirate reveals positivity for Coronavirus 229 E. The electrocardiogram presents a sinus rhythm with diffuse T wave inversion. The thoracic X-ray reveals alveolar congestion with bilateral small volume pleural effusion. Subsequent transthoracic echocardiogram shows a globally hypokinetic and moderately dilated left ventricle with a severe systolic dysfunction and right ventricle systolic function in the inferior limit of normal.
After institution of standard heart failure treatment, the patient is admitted to a cardiology ward for clinical stabilization and additional diagnostic investigation. Based on the records of smoking habits, symptoms and signs presented at admission and electric and echocardiographic changes, a coronary angiography is performed and excludes significant angiographic coronary disease. In order to exclude myocarditis a cardiac magnetic resonance is done and shows a nonischemic dilated cardiomyopathy with severe left ventricular systolic dysfunction, without evidence of delayed myocardial enhancement.
Therefore, a peripartum cardiomyopathy (PPCM) is assumed as the most probable diagnosis and a therapeutic scheme of bromocriptine and rivaroxaban is begun. On the sixth day of hospital stay, already with complete symptomatic resolution, improvement of left ventricular systolic function is documented on a transthoracic echocardiogram and the patient is discharged from hospital.
In conclusion, the recognition of PPCM is fundamental because its mortality rate is considerable. Besides the standard heart failure treatment, bromocriptine seems to be associated with greater survival and better left ventricular systolic function recovery.

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Outcomes and management of arrhythmogenic right ventricular cardiomyopathy in pregnancy: a comparison of two cases.

M Marco Schiavone[1]; E Gherbesi[1]; C Gobbi[1]; M Squillace[1]; M Calcagnino[1]; M W Ossola[2]; C Bonanomi[1]; F Lombardi[1]
[1]IRCCS Fondazione Ca' Granda Ospedale Maggiore Policlinico, Cardiovascular diseases, Milan, Italy; [2]IRCCS Fondazione Ca' Granda Ospedale Maggiore Policlinico, Obstetrics and gynecology, Milan, Italy

Background: Arrhythmogenic right ventricular cardiomyopathy (ARVC) is an inherited cardiomyopathy with an estimated prevalence of 1:5000. Data on pregnancy in ARVC are limited. We reported two different cases of pregnant women affected by this rare cardiomyopathy that reflect the complexity and multiple clinical manifestations of the disease.
CASE 1: A 32-year-old pregnant woman was referred to our clinic during the 32th gestational week due to a family history for ARVC (brother). She was completely asymptomatic (NYHA I - WHO I).
The ECG showed sinus rhythm interrupted by premature ventricular contractions (PVCs), incomplete right bundle branch block (RBBB), epsilon wave in V2, inverted T waves in V1-V4.
An echocardiogram revealed a dilation of the right ventricle, mild tricuspid and mitral regurgitation.
A 24-hour Holter ECG monitoring showed frequent PVCs and a few runs of non-sustained ventricular tachycardia (NSVT). A therapy with Metoprolol was started.
While admitted she underwent a genetic testing, which revealed the same homozygous mutation of DSG2 gene described for her brother.
An elective caesarean section was then planned at 37 weeks; no complications occurred. After delivery, she was transferred to ICU for monitoring: Metoprolol was suspended and Sotalol was started.
To complete the assessment, she underwent a CMR which revealed fibro-fatty infiltration and reduced function of both ventricles.
At discharge the patient was asymptomatic at rest and there were no signs of heart failure (HF) during the follow-up period.
CASE 2: A 38-year-old pregnant woman was admitted to our clinic because of dyspnea (NYHA III - WHO III) and palpitations.
An ECG revealed sinus rhythm interrupted by PVCs, inverted T waves in V1-V5, but no evidence of RBBB.
An echocardiogram showed a severe dilation of both ventricles and a moderate left ventricular systolic dysfunction.

She was treated with i.v. Furosemide and a caesarean section was performed at 36 weeks due to HF.
In the early postpartum we observed a further reduction of systolic function (EF 30%) and a VT was recorded.
A CMR revealed fibrofatty infiltration, reduced function and dilation of both ventricles (RV volume > 100 ml/m^2). The patient was discharged with HF therapy.
An ICD was implanted three months later, after occurrence of a syncope (LVEF < 35% despite optimal medical therapy).
Conclusion: These cases strongly suggest that WHO and NYHA class, signs and symptoms of HF at a first evaluation play a major role to predict maternal and foetal outcome.
Neither HF nor other major cardiac complications occurred during pregnancy, delivery and puerperium of case 1 although both ventricles were involved. On the other hand, in the second case, fast hemodynamic changes and sympathetic overstimulation related to pregnancy determined a worsening of pre-existing HF signs and symptoms.

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A case of advanced heart failure: When not everything is as it seems

A Rodriguez Chaverri[1]; I Ponz De Antonio[1]; MD Garcia-Cosio[1]; L Moran Fernandez[1]; J De Juan Baguda[1]; F Arribas Ynsaurraga[1]; JF Delgado Jimenez[1]
[1]*University Hospital 12 de Octubre, Cardiology, Madrid, Spain*

A 33 year-old woman with dyspnea and orthopnea in the last month of pregnancy that worsened in the postpartum.ECG (Image 1) showed sinus tachycardia and T-wave changes and chest x ray (Image 2) pulmonary vasculature redistribution and bilateral pleural effusion. The echocardiogram (Image 3) revealed a severe biventricular dysfunction and functional mitral regurgitation. The cardiac MRI showed LGE restricted to the posterior septum (Image 4) and the STIR sequences were negative for edema (Image 5).

Image 1

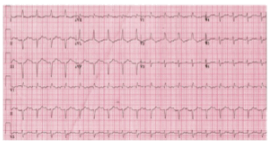
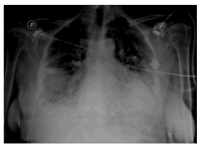


Image 2



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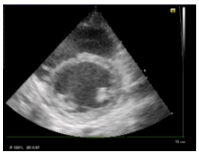


Image 4

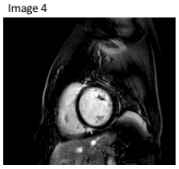
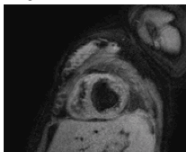


Image 5



The diagnosis of a peripartum cardiomyopathy (PPCM) was posed, and once clinical stabilization was achieved, bromocriptine was tested, which had to be stopped because of skin flushing. ACE inhibitor and beta blockers were poorly tolerated due to an increasing low cardiac output profile that required inotropic support. The patient had to be transferred to the intensive care unit due to persistent clinical worsening. Invasive hemodynamic monitoring showed a RA pressure of 20 mmHg; mPAP of 35 mmHg; PWP of 29 mmHg and a CI of 1,2 l/min/m2. In this context, a VA-ECMO was implanted as a "bridge either to recovery or to decision" strategy. In the following days, in the absence of myocardial recovery, the patient was listed for cardiac transplant which was held a week later without complications.
Peripartum cardiomyopathy is a rare cause of heart failure that affects women late in pregnancy or in the early puerperium. It has been defined as an idiopathic cardiomyopathy with the following characteristics: Firstly, the development of heart failure (HF) towards the end of pregnancy or in the months following delivery. Secondly, by the absence of another identifiable cause for HF. Lastly, by LV systolic dysfunction with an LV ejection fraction nearly always less than 45 percent.
The precise mechanisms that lead to PPCM are not fully known. Several risk factors have received attention, such as abnormal autoimmune responses, myocardial inflammation and an altered prolactin processing. However, evidence from recent studies supports the hypothesis that PPCM may develop as a result of an interaction between pregnancy-related factors (eg. late pregnancy, oxidative stress) and a susceptible genetic background. The most relevant study in this field was published in the NEJM in 2016: Forty three genes were sequenced in 172 women with PPCM. Among them, twenty six distinct rare truncating variants were identified. The prevalence of this truncating variants was significantly higher that in the reference population but similar to the cohort of dilated cardiomyopathy.
This issue, bring us back to our clinical case, as the patient's mother was diagnosed in 2013 with a dilated cardiomyopathy. Genetic testing in the mother was positive for a titin-truncanting variant and so it was in both of her daughters.
Therefore , the question I pose is: Does pregnancy actually act as a second hit in a susceptible background of different etiologies in the setting of PPCM?

Basic Science

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Enhanced activation of RSK1 in the nucleus reduces compensated hypertrophy induced by alpha1-adrenergic receptor agonist phenylephrine in mice in vivo

A Angela Clerk[1]; KA Rostron[1]; DN Meijles[2]; JJ Cull[1]; SJ Fuller[1]; PH Sugden[1]
[1]University of Reading, Reading, United Kingdom; *[2]St George's University of London, London, United Kingdom*

Funding Acknowledgements: British Heart Foundation

Background: The a1-adrenergic receptor (a1AR) agonist phenylephrine (PE), acting via ERK1/2 that phosphorylate p90 ribosomal S6 kinases (RSKs), promotes compensated hypertrophy and increases cardiomyocyte size. Both kinase families phosphorylate transcription factors producing changes in gene expression. In cardiomyocytes, potent ERK1/2 signalling causes nuclear-localisation of activated RSK1/RSK2 isoforms. This promotes cardiomyocyte growth, but hypertrophy is not sustained. Lesser ERK1/2 activation by PE causes nuclear activation of only RSK2, and this signalling is associated with a different gene expression profile.
Purpose: Our hypothesis is that activation of nuclear-localised RSK1 in addition to RSK2 promotes changes in gene expression that are not compatible with compensated hypertrophy induced by a1ARs. Our aim was to investigate if expression of nuclear-localised RSK1 is detrimental to the hypertrophic response induced in vivo by PE.
Methods/Results: Nuclear-localised (NL) RSK1 or RSK2 were expressed in cultured cells using adenoviral vectors. Immunostaining confirmed expression of NL-RSKs was confined to nuclei of HEK293, SVEC (endothelial cells) or neonatal rat cardiomyocytes. By immunoblotting with antibodies for phosphorylated (i.e. activated) RSKs, we confirmed that NL-RSKs were inactive in serum-starved cells, and activated by nuclear-localised ERK1/2 following treatment with epidermal growth factor. We generated transgenic mice for tamoxifen-inducible, cardiomyocyte-specific expression of NL-RSK1 by inserting the transgene in the ROSA26 locus, separated from the promoter by a LoxP-flanked stop cassette. NL-RSK1 mice were crossed with mice with tamoxifen (Tam) inducible CRE under control of the a myosin heavy chain promoter, producing double heterozygotes and wild-type (WT) littermates for experiments (n = 6-9 per group). Echocardiography was used to assess cardiac function/dimensions at baseline and following treatment. There was no significant difference between transgenic mice and WT litter mates up to 10 weeks of age in any of the variables studied. Tam-treatment (7 d) significantly increased diastolic (d) or systolic (s) left ventricular (LV) posterior wall (PW) thickness (16%) in transgenic, not wild-type (WT) mice indicating that enhanced NL-RSK1 alone promotes hypertrophy. PE (40 mg/kg/d, 3 d) increased LVPW ˜99% in WT or transgenic mice with corresponding decreases in LV internal diameters, but the degree of hypertrophy was significantly reduced (˜45%) in transgenic mice pretreated (4 d) with Tam.
Conclusions: Our data indicate that increased nuclear-localised RSK1 in cardiomyocytes promotes cardiac hypertrophy. However, it compromises the compensated hypertrophic response to PE. These data suggest that selective inhibition of RSK1 (rather than RSK2) may preserve the compensated hypertrophic state and, thus, reduce heart failure progression.

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MiR-126 is involved in allograft vasculopathy

W A Heggermont[1]; L Delrue[1]; L Dierckx[1]; K Dierickx[1]; S Verstreken[1]; M Goethals[1]; J Bartunek[1]; M Vanderheyden[1]
[1]Olv Hospital Aalst, Aalst, Belgium

Background: Since cardiac allograft vasculopathy (CAV) significantly limits long-term outcome after heart transplantation, its early diagnosis is crucial. Endothelium-enriched microRNAs appear to be involved in the development of CAV. However, so far, these microRNAs were not yet measured in endomyocardial biopsies and their mechanism of action in allograft vasculopathy remains elusive.
Aims: To investigate the expression of endomyocardial microRNA-126-3p and microRNA-126-5p levels in transplant recipients with (CAV+) and without CAV (CAV-), to evaluate whether these cardiac endothelial microRNAs help to predict allograft vasculopathy, and to elaborate on the possible mechanism of action of miR-126 in CAV.
Methods: We studied 39 transplant recipients, 21 with proven allograft vasculopathy and 18 without allograft vasculopathy at serial coronary angiograms. The mRNA levels of miR-126-3p and miR-126-5p, and targets PIK3R2 and SPRED1 were determined by qRT-PCR in right ventricular endomyocardial biopsies obtained at baseline routine surveillance biopsy and at follow-up within each individual patient. Human biopsy material was extracted with the miRVANA extraction kit (Ambion); cDNA synthesis and miR-qRT-PCR was performed with specific microRNA amplification kits (Qian). Furthermore, mouse cardiac endothelial cells (MCECs) were treated with methylprednisolone, tacrolimus, cyclosporine or mycophenolate in order to determine the influence of immunosuppressive agents on miR-126 and its targets.
Results: There were no baseline differences in endomyocardial miR-126-3p and -5p between CAV- and CAV+ patients. After CAV developed however, miR-126-3p levels were significantly lower in the CAV+ group, compared to their non-CAV counterparts ($p < 0.01$). Lower miR-126-3p levels were consistent with the incidence of CAV as evidenced by the ROC curve (AUC of 0.8040, $p = 0.0003$). Levels of miR-126-5p were not significantly different at that time point. Also, although there was a trend towards higher PIK3R2 and SPRED1 levels in the CAV patients, the difference was not statistically significant. When MCEC cells were treated with immunosuppressive agents for 24 hours, PIK3R2 levels were significantly lower in the treated cells versus control ($p < 0.05$). Regarding SPRED1, levels only decreased in the methylprednisolone-treated cells. Furthermore, the short treatment with immunosuppressive agents led to a significant increase in miR-126-3p (not -5p) only in the mycophenolate-treated cells.
Conclusions: Our data provide evidence that decreased microRNA-126-3p levels coincide with allograft vasculopathy. Furthermore, although further validation is paramount, the administration of immunosuppressive agents seems to influence both miR-126-3p and its targets SPRED1 and PIK3R2. Further studies are warranted to determine if serial measurement of microRNA-126-3p could help in risk assessment and early detection of post-transplant CAV.

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Cardiac-specific deletion of Nrf2 drives adverse cardiac remodelling and progression to congestive cardiac failure during chronic pressure overload stress

A Nabeebaccus[1]; I Smyrnias[1]; D Martin[1]; G Sawyer[1]; M Zhang[1]; A Brewer[1]; A M Shah[1]
[1]King's College London, School of Cardiovascular Medicine & Sciences, BHF Centre of Research Excellence, London, United Kingdom

Funding Acknowledgements: Medical Research Council (MRC) , British Heart Foundation (BHF)

Background and Purpose: Nrf2 is a key transcription factor that coordinates the expression of several cytoprotective gene regulatory pathways in multiple cell types and tissues. In the heart, Nrf2 has been identified to be essential in cardioprotection. Its activation is driven by NADPH oxidase 4-derived ROS, itself a cytoprotective enzyme upregulated in hypertrophic stress and which ameliorates hypertrophy and heart failure. Nrf2 is expressed in multiple cell types but it is not known if Nrf2 derived from cardiomyocytes, as opposed to other cell types, is the crucial player in mediating cardioprotection. This is the first study to investigate the role of cardiomyocyte-targeted Nrf2 in a murine model of heart failure.
Methods: Cardiomyocyte-specific deletion of Nrf2 was achieved by crossing a floxed-Nrf2 mouse line with a Cre-expressing line under the control of the ventricular-specific Mlc2v promotor. Cardiomyocyte-specific Nrf2-deficient male mice (csNrf2-/-) alongside matched littermate floxed controls (csNrf2fl/fl), underwent transverse aortic constriction (TAC) surgery to generate pressure-overload stress. At 2 weeks, echocardiography was performed and the hearts harvested for further characterisation by histology, immunoblotting and real-time qPCR.
Results: A significant reduction in basal levels of Nrf2 expression in csNrf2-/- compared to floxed controls was confirmed with RT-PCR in the left ventricle of hearts (80% reduction; $p = 0.02$, $n = 3$ per group). No change in mRNA levels was found in other organs. Basal cardiac function, organ and body weight of knock-out and floxed controls were similar. After 2 weeks of TAC, csNrf2-deficient mice developed significantly greater LV systolic impairment than floxed controls (37% reduction in EF, when comparing the knock-out hearts to the floxed control; $p < 0.001$, $n = 6$-10 per group). They also had significant LV dilatation with evidence of lung congestion as compared to floxed controls. Histological analysis showed pressure-overloaded csNrf2-deficient hearts had significantly more interstitial fibrosis compared to floxed

hearts (6% versus 2%; $p < 0.05$, $n = 3$ per group). Finally they had significantly increased transcripts of markers of cardiac stress (raised b-MHC and ANF) than controls.
Conclusion: This study demonstrates the successful generation of mice with a cardiomyocyte-targeted deletion of Nrf2, an important transcriptional regulator of diverse cytoprotective programs. The lack of Nrf2 in this cell type is sufficient to drive the global maladaptive cardiac remodelling response to haemodynamic stress, leading to an increase in interstitial fibrosis, ventricular dilatation and congestive cardiac failure. Further study is now needed to understand the mechanisms underlying this response.

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Comprehensive plasma and tissue profiling reveals systemic metabolic alterations in cardiac hypertrophy and heart failure

O J Mueller[1]; MB Heckmann[2]; L Ding[2]; K Rapti[2]; AY Rangrez[1]; U Rennefahrt[3]; T Ruf[2]; A Jungmann[2]; J Kreusser[2]; TM Weis[2]; J Backs[4]; N Frey[1]; HA Katus[2]
[1]University Medical Center of Schleswig-Holstein, Kiel, Germany; *[2]University Hospital of Heidelberg, Internal Medicine III, Dept Cardiology, Angiology & Pneumology, Heidelberg, Germany*; *[3]Metanomics Health GmbH, Berlin, Germany*; *[4]University Hospital of Heidelberg, Dept of Molecular Cardiology and Epigentics, Heidelberg, Germany*

Funding Acknowledgements: This work was supported by the "Bundesministerium für Bildung und Forschung" of Germany (01GR0813 to O.J.M, H.A.K. and N.F.).

Background/Introduction: Heart failure (HF) is a complex multifunctional disease. Structural cardiac remodeling induced by alterations in gene expression result in molecular, cellular, and interstitial changes. In addition, profound perturbations in cardiac metabolism affect essential cellular processes such as energy production. An improved understanding of metabolic alterations associated with other pathological processes in HF could facility the identification of novel biomarkers and effective HF-therapies.
Purpose: Aim of this study was to gain a comprehensive understanding of the holistic metabolic alterations at different stages of HF including compensated and decompensated hypertrophy, and terminal HF in a left ventricle pressure overload mouse model.
Methods: Mice were subjected to transverse aortic constriction (TAC) or sham surgery and sacrificed either 2, 4, or 6 weeks after the procedure. Metabolite profiles of cardiac tissue were investigated by broad, untargeted metabolomics including GC-MS and LC-MS/MS and compared to results of transcriptional profiling. Since HF is associated with alterations in systemic metabolism, metabolic changes in plasma, liver, and skeletal muscle of these mice were analyzed in parallel. For further mechanistic studies of a key target we used Adeno-associated virus (AAV) 9-mediated overexpression in mice subjected to TAC.
Results: Progressive alterations of key cardiac metabolic pathways and gene expression patterns indicated impaired mitochondrial function and a metabolic switch during transition to heart failure. Similar to the cardiac alterations, liver and skeletal muscle revealed significant metabolic changes such as depletion of essential fatty acids and glycerolipids in late stages of heart failure. Circulating metabolites, particularly fatty acids, reflected cardiac metabolic defects and deteriorating heart function similar as observed with a plasma-based metabolic cardiac lipid panel biomarker established for the detection of HF with reduced ejection fraction (HFrEF) in humans. Cardiac metabolic profiling further revealed decreased carnitine shuttling and transportation preceding cardiac dysfunction. Thus, we studied the therapeutic potential of Organic Cation/Carnitine Transporter 2 (OCTN2), a key factor in carnitine shuttling. Cardiac overexpression of OCTN2 significantly improved ejection fraction and reduced interstitial fibrosis in mice subjected to TAC.
Conclusions: Alterations in metabolic profiles of heart, plasma, liver, and skeletal muscle emphasizes the impact of HF as systemic disease. Overall, these systemic changes are reflected by variations in plasma metabolites that could be used as diagnosis biomarkers. In addition, our data demonstrate that metabolomics is a valuable key technology in systems biology for the identification of new drug target candidates and the elucidation of pathological HF mechanisms.

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Human cardiomyopathy islands as a novel iPSC based strategy for modeling adult onset cardiomyopathies in-vivo

O Oren Caspi[1]; SC Chrona[2]; IH Huber[2]; AG Gepstein[2]; GA Arbel[2]; GA Gruber[2]; BI Budniatzky[2]; LG Gepstein[1]
[1]Rambam Health Care Campus, Cardiology, Haifa, Israel; *[2]Technion - Israel Institute of Technology, Haifa, Israel*

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Introduction: The study of cardiomyopathies is hampered both by the inability to assess the myocardial tissue early during disease development and the lack of suitable models. The advent of human induced pluripotent stem cells (hiPSCs) technology may provide essential means for overcoming this hurdle, since it allows deriving and studying human cardiomyocytes that carry the disease-causing phenotype. However, hiPSCs based in-vitro, "disease in a dish models", are limited by the relative structural, functional and metabolic immaturity of the cardiomyocytes, the inability to assess for the effects of systemically delivered therapeutic interventions and the lack of supporting microenvironment.
Purpose: In the current study, we aimed to establish hiPSCs based in-vivo models for cardiomyopathies and assess whether such a strategy can: (1) unmask the phenotype of adult onset cardiomyopathies (e.g. arrhythmogenic right ventricular cardiomyopathy, Pompe disease); (2) obtain functional information from the engrafted hiPSCs derived cardiomyocytes (hiPSC-CMs), and; (3) assess the effect of systemically delivered therapies on hiPSC-CMs.
Methods: Heterotopic and orthotopic strategies were used to transplant hiPSCs derived cardiomyocytes (following 15-30 days of differentiation) to NOD-SCID mice. Orthotopic experiments were conducted by direct intra-myocardial delivery of the hiPSC-CMs.
Results: Orthotopic transplantation of hiPSC-CMs to the mice myocardium resulted in stable, large and discrete grafted tissue islands. The hiPSC-CMs within the islands presented both structural and molecular hallmarks of cardiomyocyte maturation following 30 days, when compared with same stage in-vitro cultured cardiomyocytes. Importantly, when hiPSC-CMs from adult onset cardiomyopathies (i.e. Arrhythmogenic right ventricular cardiomyopathy (ARVC) and Pompe disease) were transplanted, the in-vivo environment resulted in the generation of human cardiomyopathy islands (hCI) recapitulating the adult onset cardiomyopathy phenotype without the need for stressors usually required for uncovering the phenotype of these cardiomyopathies in-vitro. Additionally, The hCI strategy was used for evaluating the effect of systemic therapies on the cardiomyopathy phenotype. Heterotopic transplantation demonstrated that transplanted cells survived within the dermal thin layer of the outer ear (for up to 3 months) but was not associated with structural maturation of the hCIs nor did it promote cardiomyopathy phenotype unmasking.
Conclusions: Orthotropic hCI may serve as an attractive strategy for modeling the structural and functional alterations associated with adult onset cardiomyopathies. Apart from phenotype uncovering, this strategy may more accurately model systemic therapy effects, interaction with the immune system and adult metabolic energetics which have significant clinical importance.

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The MiR-221/-222 cluster is elevated both in biopsies of patients with myocarditis and idiopathic non-ischemic cardiomyopathy but fails to discriminate between both pathologies

W A Heggermont[1]; L Delrue[1]; R Dierckx[1]; K Dierickx[1]; S Verstreken[1]; M Goethals[1]; J Bartunek[1]; M Vanderheyden[1]
[1]Olv Hospital Aalst, Aalst, Belgium

Background: The narrow diagnostic window due to - normally - rapid recovery, the very low sensitivity of viral serology and the potential sampling error upon endomyocardial left ventricular biopsy procurement makes the diagnosis of acute myocarditis challenging. Sometimes the disease is difficult to distinguish from a new-onset idiopathic dilated cardiomyopathy.
Aims: To investigate the expression of known microRNAs involved in myocarditis and DCM (miR-221/-222), the expression of genes involved in viral replication (MDA5, RIG1, TLR3) and the expression of heart failure biomarkers (BNP, ST2) in order to improve the differential diagnosis of acute decompensated heart failure patients.
Methods: We prospectively studied left ventricular biopsies of control ($n = 11$), myocarditis ($n = 18$), and non-ischemic dilated cardiomyopathy patients (DCM, $n = 34$). Myocarditis patients had a suspected clinical history in combination with a rise in serum inflammatory markers (C-reactive protein) and clearly positive late gadolinium enhancement (LGE) on cardiac MRI. DCM patients were characterized by the presence of normal coronary arteries in combination with a dilated left ventricle, reduced LV function and either absence of LGE or a typical midwall LGE pattern on cardiac MRI. MicroRNA and mRNA levels were determined by qRT-PCR, serum protein levels by ELISA. Human biopsy material was extracted with the miRVANA extraction kit (Ambion), cDNA synthesis and qRT-PCR was performed with specific amplification kits (Applied Biosystems).
Results: On average, left ventricular ejection fraction was slightly reduced in the myocarditis group and strongly reduced in the DCM group (LVEF upon ventriculography 51% vs. 39%, $p < 0.006$). Both myocarditis and DCM patients were characterized by higher endomyocardial miR-221/miR-222 gene expression than in control patients ($p < 0.01$), whereas no changes were noted in genes related to viral replication (MDA5, RIG1, TLR3) in all groups. Both miR-221 and miR-222 levels positively correlated with left ventricular end-diastolic volume. Furthermore, although serum sST2 and NT-pro-BNP levels were significantly elevated in both patient groups, levels were significantly higher in the DCM group compared to the myocarditis group.

The best independent discriminator between myocarditis and DCM, was elevated complement C3 - rather than C-reactive protein - in serum of myocarditis patients compared to control and DCM.
Conclusions: The inflammatory miR-221/-222 cluster is of importance both in the pathophysiology of myocarditis and DCM, and correlates with left ventricular end-diastolic volume (among other markers of LV dysfunction). Nevertheless, both the miR-cluster and markers of viral replication did not help to discriminate between myocarditis and DCM. In contrast, activated complement C3 levels in serum are significantly higher in myocarditis patients compared to DCM patients, and this parameter helps to distinguish between myocarditis and idiopathic DCM.

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Boosting small heat shock proteins lowers cardiomyocyte passive stiffness in experimental heart failure with preserved ejection fraction

MT Waddingham[1]; E Dal Canto[1]; D Da Silva Goncalves Bos[1]; V Sequeria[1]; L Van Heerebeek[1]; DWD Kuster[1]; FS De Man[1]; J Van Der Velden[1]; ML Handoko[1]; EC Eringa[1]; WJ Paulus[1]
[1]VU University Medical Center, Amsterdam, Netherlands

Funding Acknowledgements: Cardiovasculair Onderzoek Nederland (CVON) RECONNECT & EARLY-HFPEF. MTW is a recipient of a CVON-RECONNECT Young Talent Program Award.

Background: Heart failure with preserved ejection fraction (HFpEF) is associated with high left ventricular (LV) diastolic stiffness, which can be attributed partly to elevated cardiomyocyte stiffness. The giant cytoskeletal protein, titin, is central to high cardiomyocyte stiffness and thus LV diastolic stiffness in HFpEF. Small heat shock proteins (sHSPs), such as aB-crystallin and HSP27, function to protect titin and consequently, prevent elevations in cardiomyocyte passive stiffness. Recently, we reported that high stiffness in isolated cardiomyoctes from patients with aortic stenosis can be lowered with the administration of exogenous aB-crystallin. This suggests that boosting sHSPs may be a viable therapeutic strategy in alleviating titin-based cardiomyocte stiffness and thus LV diastolic stiffness in HFpEF.
Aims: To examine the therapeutic effect of the HSP-inducing drug, geranylgeranylacetone (GGA) in HFpEF.
Methods: 20-week old male obese ZSF1 hybrid rats, a validated model of HFpEF, were randomised to receive GGA (200mg/kg/day) or vehicle by oral gavage for 4 weeks. At the end of the treatment period, rats were subjected to echocardiography and cardiac catheterisation to assess global LV diastolic function. Titin-based cardiomyocyte stiffness was evaluated in single Triton-permeabilised cardiomyoctes at sarcomere lengths (SLs) ranging from 1.8μm to 2.4μm.
Results: When compared to the lean control rats, obese ZSF1 rats demonstrated evidence of global LV diastolic dysfunction such as increased deceleration time (47 ± 1 vs. 57 ± 3ms, $P < 0.05$), prolonged isovolumetric relaxation time (45 ± 3 vs. 52 ± 2ms) and elevated end-diastolic pressures (5.0 ± 0.3 vs. 7.0 ± 1.8mmHg). Such abnormalities in diastolic function were not observed in GGA-treated obese ZSF1 rats. Passive force (Fpassive) was significantly higher ($P < 0.01$) at all SLs in obese ZSF1 rats compared to the lean controls, suggesting diastolic dysfunction may have arisen from elevated titin-based cardiomyocyte stiffness. Four weeks of GGA treatment in obese ZSF1 rats significantly lowered Fpassive at the physiological SLs 1.8μm (0.45 ± 0.09 vs. 0.26 ± 0.04kN/m^2, $P = 0.05$), 2.0μm (0.91 ± 0.13 vs. 0.49 ± 0.1kN/m^2 $P < 0.01$) and 2.2μm (1.45 ± 0.17 vs. 1.04 ± 0.12kN/m^2, $P = 0.05$), although no difference was observed at 2.4μm (2.14 ± 0.25 vs. 1.77 ± 0.23kN/m^2, NS) compared to untreated obese ZSF1 rats. Importantly, we found a ~2 to 3-fold greater aB-crystallin and HSP27 expression in the myofilament fraction of LV samples of GGA-treated obese ZSF1 rats, when compared to the vehicle-treated obese ZSF1 rats.
Conclusion: Four weeks of GGA treatment increased sHSPs surrounding the myofilament proteins, such as titin, likely explaining the lower cardiomyocyte passive stiffness observed in these obese ZSF1 rats. These data suggest that GGA may be a viable therapeutic strategy in alleviating high cardiomyocyte stiffness and thus LV diastolic dysfunction in HFpEF.

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Toll-Like receptor 3 mediates radiation induced heart failure

C Can Tepekoylu[1]; M Graber[1]; J Hirsch[1]; L Polzl[1]; D Lobenwein[1]; F Nagele[1]; V Sladky[2]; E Kirchmair[1]; E Demetz[3]; G Degenhart[4]; A Wegmayr[5]; D Lener[6]; A Villunger[2]; M Grimm[1]; J Holfeld[1]
[1]Innsbruck Medical University, Department of Cardiac Surgery, Innsbruck, Austria; *[2]Innsbruck Medical University, Division of Developmental Immunology, Innsbruck, Austria*; *[3]Innsbruck Medical University, Department of Internal Medicine II, Innsbruck, Austria*; *[4]Innsbruck Medical University, Department of Radiology, Innsbruck, Austria*; *[5]Innsbruck Medical University, Department of Radiotherapy and Radiation Oncology, Innsbruck, Austria*; *[6]Innsbruck Medical University, Department of Internal Medicine III, Innsbruck, Austria*

Funding Acknowledgements: MFF Tyrol

Background: Adjuvant thoracic radiation has significantly improved the survival of patients with breast cancer, Hodgkin's disease and thoracic malignancies. However, cardiovascular disease after thoracic radiation has become the leading nonmalignant cause of death in cancer survivors. Radiation causes microvascular endothelial injury resulting in impaired cardiac function. The molecular mechanism of radiation induced microvascular damage remains unknown.
Purpose: Danger associated molecular patterns (DAMPs) are released from stressed cells and are known to activate Toll-like receptor 3 (TLR3), a receptor of the innate immune system. We hypothesized that radiation leads to release of DAMPs with subsequent activation of TLR3. Concomitant inflammation causes endothelial injury resulting in impaired myocardial function.
Methods: Endothelial cells were isolated from healthy donors undergoing heart transplantation and treated with radiation therapy (10Gy). Expression levels of TLR3 and inflammatory cytokines were compared with cells treated either with TLR3 agonist poly (I:C) or a TLR3/dsRNA complex inhibitor. Cell cycle analysis via flow cytometry was performed after radiation. To investigate in vivo effects, ApoE-/- and ApoE-/-/TLR3-/- mice underwent thoracic radiation (15Gy). Heart function and morphology was analyzed via transthoracic echocardiography, microCT and histological evaluation.
Results: Radiation resulted in activation of the TLR3 pathway with upregulation of downstream proteins TIR-domain-containing adapter-inducing interferon-ß (TRIF) and transcription factor Interferon regulatory factor 3 (IRF3). Expression of the inflammatory cytokines TNF-a, IL-6, IFN-y and IL-10 was increased after radiation. TLR3 inhibition abrogated radiation-dependent inflammatory response of endothelial cells resulting in reduced endothelial apoptosis. In vivo, thoracic radiation resulted in impairment of left ventricular function with reduced ejection fraction in ApoE-/- mice (LVEF %: 44.96 ± 1.70). However, left ventricular ejection fraction of ApoE-/-/TLR3-/- mice was clearly less affected by radiation (LVEF %: 50.08 ± 1.48, $p = 0.0401$). In addition, we found decreased vascular and valvular calcifications in ApoE-/-/TLR3-/- mice.
Conclusion: Radiation leads to endothelial injury and activation of TLR3. Inhibition of TLR3 prevents from inflammation and endothelial apoptosis. ApoE-/-/TLR3-/- show superior left ventricular function after thoracic radiation compared to ApoE-/- mice. We show major involvement of TLR3 in the pathogenesis of radiation induced heart failure. TLR3 could become an effective therapeutic target for the prevention of heart disease after radiation.

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Associations between myocardial fibrosis-linked microRNAs and serum markers of fibrosis in dilated cardiomyopathy

P Pawel Rubis[1]; J Toton-Zuranska[2]; S Wisniowska-Smialek[1]; E Dziewiecka[1]; K Holcman[1]; L Khachatryan[1]; A Karabinowska[1]; M Szymonowicz[1]; E Wypasek[3]; M Kolton-Wroz[2]; P Wolkow[2]; P Podolec[4]
[1]Department of Cardiac and Vascular Disease, John Paul II Hospital, Institute of Cardiology, Krakow, Poland; *[2]Center for Medical Genomics OMICRON, Jagiellonian University Medical College, Krakow, Krakow, Poland*; *[3]John Paul II Hospital, Department of Molecular Biology, Krakow, Poland*; *[4]Jagiellonian University Medical College, Krakow, Poland*

Funding Acknowledgements: Poland National Centre of Science (no. 2013/09/D/NZ5/00252), Structural Funds of Medical College, Jagiellonian University (grant K/ZDS/007192)

Background: Fibroblast- and non-fibroblasts enriched microRNAs are involved in the pathology of cardiac fibrosis. Associations between myocardial fibrosis-linked

Table 1

Parameter	miR-21	miR-26	miR-29	miR-30	miR-133
PICP	-0.25; 0.03	-0.24; 0.05	-0.26; 0.03	0.08; 0.51	0.06; 0.64
PINP	0.19; 0.12	-0.05; 0.7	0.01; 0.9	0.09; 0.47	-0.03; 0.79
PIIICP	-0.03; 0.79	-0.02; 0.79	0.02; 0.9	-0.06; 0.65	-0.12; 0.34
PIIINP	-0.01; 0.9	0.16; 0.19	0.09; 0.47	-0.15; 0.25	-0.12; 0.31
TGF1-β	-0.31; 0.009	-0.27; 0.05	-0.11; 0.37	-0.14; 0.28	0.19; 0.12
CTGF	0.01; 0.91	0.05; 0.66	0.09; 0.45	-0.01; 0.96	-0.05; 0.65
OPN	-0.07; 0.58	0.01; 0.93	-0.07; 0.54	0.01; 0.99	-0.04; 0.73
Gal-3	-0.19; 0.12	0.05; 0.65	0.08; 0.53	-0.09; 0.41	-0.08; 0.51
MMP-2	0.04; 0.74	0.3; 0.01	0.33; 0.006	-0.03; 0.79	-0.09; 0.47
MMP-9	0.14; 0.23	0.11; 0.34	0.12; 0.31	-0.09; 0.46	-0.17; 0.16
TIMP-1	0.14; 0.26	0.28; 0.02	0.19; 0.1	-0.04; 0.73	-0.14; 0.24

microRNAs and serum markers of fibrosis in dilated cardiomyopathy (DCM) are unknown.
Methods: Seventy DCM patients (48 ± 12 years, NYHA 2.6 ± 0.7, EF 24.4 ± 7.4%) underwent right ventricular biopsy. Markers of collagen type I and III synthesis - procollagen type I and III carboxy- and amino-terminal peptides (PICP, PIIICP, PINP, and PIIINP), fibrosis controlling factors - transforming growth factor (TGF1-ß), connective tissue growth factor (CTGF), osteopontin (OPN) and galectin-3 (Gal-3), and degradation enzymes - matrix metalloproteinases (MMP-2, MMP-9) and their tissue inhibitor (TIMP-1) were measured in serum. MiR-21, miR-26, miR-29, miR-30 and miR-133a were measured in myocardial tissue, sampled during biopsy, via qPCR.
Results: Only fibroblast-enriched microRNAs: miR-21, -26, and -29 correlated with PICP, TGF1-ß, MMP-2, and TIMP-1. None of cardiomyocyte-enriched microRNAs: miR-30 and -133a correlated with any serum marker of fibrosis (Table 1).
Conclusions: Associations between myocardial fibrosis-linked microRNAs and markers of fibrosis are lower than expected. Only fibroblast-enriched microRNAs weakly correlate with some parameters, whereas cardiomyocyte-enriched microRNAs did not correlate with any serum markers of fibrosis.

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Preservation of post-infarction cardiac structure and function with formyl peptide receptor agonist treatment

RA Garcia[1]; JA Lupisella[1]; M Hsu[1]; G Fernando[1]; NL Carson[1]; H Shah[1]; S St-Onge[2]; M Carrier[2]; M Heroux[2]; M Bouvier[2]; NR Wurtz[1]; J Ostrowski[1]; B Ito[3]; J Towne[3]; FJ Villarreal[3]
[1]Bristol-Myers Squibb, Cardiovascular Drug Discovery, Pennington, United States of America; *[2]University of Montreal, Montreal, Canada*; *[3]University of California San Diego, San Diego, United States of America*

Funding Acknowledgements: Bristol-Myers Squibb Company

Background/Introduction: Dysregulated inflammation following myocardial infarction (MI) can lead to myocardial damage and inadequate infarct healing. Formyl peptide receptors play an important role in the ligand-dependent regulation of inflammation resolution. Stimulation of the resolution process via formyl peptide receptor activation is predicted to improve left ventricular (LV) structure/function relationships and prevent downstream pathological cardiac remodeling, which can lead to heart failure.
Purpose: We evaluated the capacity of Compound 43 (Cmpd43, 1-(4-chlorophenyl)-3-(5-isopropyl-1-methyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)urea), a small molecule dual agonist of formyl peptide receptor 1 (FPR1) and 2 (FPR2), to improve long-term LV and infarct scar remodeling following coronary artery occlusion in rodent MI models.
Methods: Cmpd43 was evaluated in phagocytosis, chemotaxis, signaling and cytokine response cell-based assays. In vivo, following occlusion of the left anterior descending (LAD) artery, C57BL/6 mice were treated with Cmpd43 (1 and 10 mg/kg or vehicle; PO gavage, QD). Treatment was started 24 h after occlusion and continued for 3 days to assess early inflammation or 4 weeks to evaluate passive LV mechanics and myocardial morphology. Structure/function studies in rats occurred following 60 min ischemia and reperfusion (I/R) at the LAD artery. Treatment (10 mg/kg Cmpd43 or vehicle, PO gavage, QD) was started 48 h post I/R and continued for 6 weeks.
Results: In vitro, Cmpd43 enhanced cellular phagocytosis and chemotaxis, exhibited dual agonist G-protein signaling and induced FPR2-dependent IL-10 secretion. In mice, Cmpd43 reduced LV chamber area and infarct size (30% and 49% 10 mg/kg vs. vehicle; respectively, $P < 0.05$) and preserved infarcted wall thickness (1 mg/kg, +1.6 fold vs. vehicle, $P < 0.05$). Passive LV mechanics and epicardial scar strains were improved as evidenced by ex vivo pressure-volume (PV) and pressure-strain analysis. Cmpd43 treatment yielded dose-dependent left shifts in PV curves and smaller scar strains in the circumferential (E11) and longitudinal (E22) direction. Increased arginase 1 levels were detected by in situ hybridization 3 days post-MI in the infarct border zone of Cmpd43-treated mice, suggesting a shift towards a pro-resolution phenotype in macrophages. In rats, Cmpd43 reduced LV end diastolic volume (17% vs vehicle, $P < 0.05$), preserved viable myocardium across the infarct wall (+1.4 fold vs. vehicle, $P < 0.01$) and improved LV ejection fraction (+12% vs. vehicle, $P < 0.05$).
Conclusion(s): These findings suggest that Cmpd43 treatment can limit adverse post-MI LV remodeling. Improvements in cardiac structure/function support the concept that agonism of formyl peptide receptors improves post-MI wound healing. Activation of the pro-resolution mechanism presents an innovative approach towards development of potentially effective drug therapies to prevent heart failure post-MI.

Clinical Case Award

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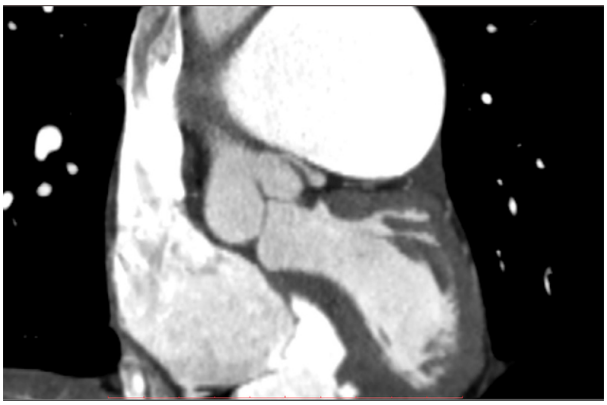
Left main coronary artery compression by a dilated pulmonary artery in a patient with pulmonary arterial hypertension

J Juan Farina[1]; A Lescano[1]; M Sztejfman[1]; M Gonzalez[1]; H Grancelli[1]; D Crippa[1]; G Romero[1]; V Daru[1]
[1]*Finochietto Clinic, Buenos Aires, Argentina*

A 56-year-old female patient diagnosed with idiopathic pulmonary hypertension (PH) with three years of follow-up presented dyspnea and chest pain in functional class III for 15 days, with two syncopal episodes not related to stress. Upon admission no evidence of heart failure was observed.
The ECG showed right ventricle (RV) hypertrophy and complete right bundle branch block. Echocardiography showed dilation of right chambers with mild depression of RV systolic function. The trunk of the pulmonary artery (PA) was severely dilated (55 mm), as well as its branches. Angiotomography of the chest confirmed the marked dilatation of the PA up to 54 mm. The course of the left main coronary artery (LMCA) was abnormal, with marked reduction of its lumen. The distance between the PA and the LMCA was narrow (3.6 mm) and the LMCA lumen was severely reduced. The calcium score was 0, not identifying atheroma plaques (Picture 1).



The case was assumed to be a LMCA compression syndrome by dilated PA. A coronary angiography (CAG) was performed, which showed the severe obstruction of the LMCA, with an almost parallel path to the wall of the left sinus of Valsalva due to the displacement generated by the PA. During the procedure the absence of plaques by intravascular ultrasound (IVUS) was registered. A stent of 4.5 mm x 20 mm was implanted with adequate result. The patient was discharged on treatment with sildenafil, macitentan, clopidogrel and acetylsalicylic acid. Six months after, there were no symptoms and new CAG was performed with no signs of complications.
Myocardial ischemia and its most frequent clinical manifestation (angina pectoris) may occur in patients diagnosed with PH with a prevalence ranging from 20-40%. Its physiopathology may involve different mechanisms:
1. Subendocardial ischemia due to RV hypertrophy.
2. Subendocardial ischemia due to an alteration of the coronary perfusion gradient.
3. Secondary mechanisms related to tachyarrhythmias and/or anemia, among others.
4. Presence of significant atherosclerotic coronary disease.
5. Extrinsic compression of the LMCA by dilation of the PA.
This last entity is an increasingly recognized cause of angina or other more serious complications (myocardial infarction, sudden death) in patients with PH. It should be suspected in all patients with PH who have a significant increase in the diameter of the main PA or in patients that presents angina or equivalent symptoms. The diagnostic confirmation is provided by angio-CT along with the CAG with IVUS, the latter procedure also allows the endovascular resolution of this intercurrence with the stent placement in the LMCA, todays therapeutic of choice over the revascularization surgery.
Considering the potential serious effects of this complication, suspicion, research and resolution of this entity are fundamental to improve the survival and prognosis of these patients.

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Acute celular rejection after heart transplant: correlation of endomyocardial biopsy with significant elevation of circulating cell-free donor-derived DNA

T Kafunkova[1]; J Krejci[1]; M Pesl[1]; P Hude[1]; E Ozabalova[1]; J Godava[1]; V Zampachova[1]; D Nikulenkov Grochova[2]; L Spinarova[1]
[1]*St. Anne's University Hospital, Brno, Czech Republic*; [2]*Cytogenetic Lab, Brno, Czech Republic*

Introduction and Background: accurate and timely diagnosis of allograft rejection is essential for long-time survival of heart transplant recipients. The endomyocardial biopsy (EMB), currently the "gold standard" for diagnostics of acute allograft rejection, is an invasive procedure with some risks of periprocedural complications and a large interobserver variability by different pathologists.
Circulating cell-free donor-derived DNA (cfdDNA) can be detected in a blood and urine of heart transplant recipients. A few days after a heart transplant cfdDNA fraction decreases to a very low level in the absence of acute celular or antibody-mediated rejection. Significant elevation of cfdDNA fraction can be detected in the blood of recipients even several months before the appearance of graft damage on EMB.
Clinical case description: 56-years-old woman 4 months after heart transplant because of dilatative cardiomyopathy was admitted for routine EMB. All of previosly performed EMBs were without any rejection (ISHLT AR grade 0). Nowdays she suffered from mild dyspnea on exertion and cought. Echocardiography didn't show any new pathology compared to previous findings (no left ventricular (LV) hyperthrophy, normal systolic and diastolic LV function, old non significant pericardial effusion). There was a new finding of 11-times elevation of cfdDNA fraction compared to baseline level (2,26% vs. 0,21%). EMB showed a new finding of mild allograft rejection (ISHLT AR grade IB). Dose of tacrolimus was lightly increased with a tight serum concentration controls and dose od prednison was increased from 10 mg OD to 20mg OD. Dose of mycophenolate mofetil was not changed. 2 weeks later she was without any complaints and control EMB showed no rejection and also cfdDNA fraction decreased to baseline level.
Conclusions: and implications for clinical practice: changes of cfdDNA fraction in the blood or urine of heart transplant recipients could serve as non invasive diagnostics of acute allograft rejection. Further research studies with large amount of patients are needed to reduce the number or even replace routine invasive EMBs with non invasive diagnostics.

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Recurrence of Takotsubo syndrome: one clinical presentation/trigger, but two different anatomical variants in the same patient. A case to reflect.

G Giulio Binaghi[1]; D Congia[1]; S Cossa[2]; R Ganga[3]; G Giardina[1]; M Melis[4]; G Matta[2]; A Pani[1]; D Pasqualucci[1]; E Serra[1]; M Porcu[1]
[1]*G. Brotzu Hospital, Department of Cardiology, Cagliari, Italy*; [2]*G. Brotzu Hospital, Department of Radiology, Cagliari, Italy*; [3]*G. Brotzu Hospital, Department of Interne Medicine, Cagliari, Italy*; [4]*G. Brotzu Hospital, Department of Neurology, Cagliari, Italy*

A 67-year-old woman access to our ED complaining diarrhea from one week and in the last hours also palpitations and dyspnea. She was an ex-alcoholic and had an history of breast cancer underwent surgical and radio therapy 18 years ago, but with subsequent pelvic bone metastasis treated with multiples orthopedic interventions. At hospitalization, ECG showed an atrial fibrillation and echocardiography (TTE) was normal. Laboratory tests evidenced hypo-K+ and Mg2+. Few hours after, spontaneous restoration of sinus rhythm occurred, but she suddenly became confused and developed seizures. A cerebral CT scan excluded an acute cerebral event. At the same time patient developed hypotension and a positive value of troponin I was detected in absence of ECG alterations, while TTE showed a severe left ventricular dysfunction (EF: 25%) due to akinesia of all basal segment with hyperkinesia of apex.

After adequate refilling, the hemodynamic status improved, but seizures persisted confirmed by EEG. Despite different intravenous neurologic therapies, she developed a refractory status epilepticus (SE) needing deep sedation and mechanical ventilation assistance. In following days SE resolved and TTE showed the recovery of left ventricle function; hemodynamic also improved, so it was possible to proceed to extubation. Cardiac MRI and coronary angiography were performed resulting normal and confirming our first diagnostic hypothesis of inverted Tako-Tsubo syndrome (TTS). A cerebral MRI showed a diffuse demyelination compatible with the history of alcoholism.
Discharged in therapy with bblocker and ACE-inhibitor; one week later the patient was re-hospitalized because of clonic seizures associated with hypo-K+ and Mg2+. ETT showed a picture like classical TTS (apical ballooning). Because of clinic scenario, the recent exams performed and the absence of ECG modification, we decided to support the patient and do not perform other invasive tests. Few days later the neurological and cardiac state resolved.
Acute neurological diseases are well-reported to be associated with TTS, however is rarer in case of SE. Probably TTS is unrecognized in this critical neurological state, a condition that need high therapeutic effort and resources. However, in literature it is emerging the idea that TTS could be the cause of Sudden Unexpected Death in Epilepsy (SUDEP).
Our patient had a recurrence of TTS onset with the same clinical presentation (seizures), but with two different anatomical forms: first, a reverse TTS, then a classical one. No similar cases are reported in literature, in fact usually the order of presentation of anatomical variants is inverted.
This can be justified by the hypothesis that previously affected ventricular regions are relatively protected from further injury during recurrent stress episodes.
This case highlights the need to better understand the physiopathology of TTS and the need to assess always cardiac function in case of epilepticus status.

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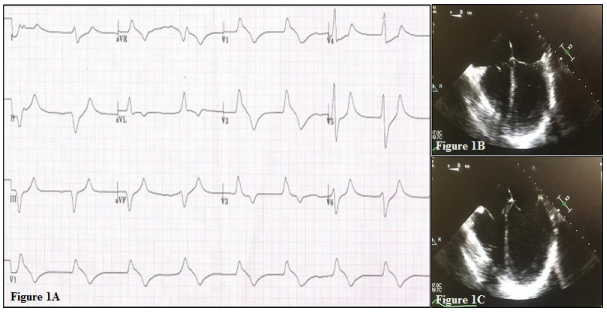
Cardiogenic shock with normal ejection fraction?

A Taher[1]; H S Lim[2]
[1]Glenfield Hospital, Cardiology, Leicester, United Kingdom; *[2]Queen Elizabeth Hospital Birmingham, Birmingham, United Kingdom*

A 17 year old man presented to his hospital with a 4 day history of diarrhoea & vomiting after returning from Dubai. He had no co-morbidities & did not smoke, drink alcohol or use illicit drugs. On presentation, he was self-ventilating but



ECG and Echocardiogram

hypotensive (sBP 60). ECG on admission showed junctional rhythm at a rate of 45-50/min of RBBB morphology [Fig 1A]. Arterial blood gas showed pH 7.28, pCO2 3.9, pO2 17.5, HCO3 13.6, BE -11.7, lactate 7.8. Echo showed preserved RV & LV systolic function with normal sizes [Fig 1 B&C]. Despite high doses of noradrenaline, vasopressin, dobutamine, adrenaline & hydrocortisone, his MAP remained between 40-50, & he became anuric. Blood tests showed Alb 32, Bil 9, Ca 2.19, Cr 368, U 11.4 CRP 38, WCC 30 with Neutrophilia of 23 & left shift on blood film. Troponin increased from 43 to 249. He was started on antibiotics & antiviral therapy, & referred to our institution for mechanical circulatory support with a presumptive diagnosis of myocarditis. On arrival, a pulmonary artery catheter was inserted & showed PASP 25, PADP 10, CO of 5L/min, index of 2.8, with BP of 90/21 & HR of 50/min. The low diastolic BP, indicative of vasoplegia did not respond to high dose vasopressors. The bradycardia failed to respond to isoprenaline. We proceeded with VA-ECMO, as he continued to deteriorate with a number of brief asystolic arrests. He became persistently asystolic following VA-ECMO support & temporary pacing was inserted. However, there was failure to capture, as he was profoundly hyperkalaemic (10mmol/l). The LV was vented via thoracotomy & a cardiac biopsy was performed. This did not show evidence of myocarditis. He was commenced on CVVH & a toxicology profile was sent. Further discussions with the patient's parents revealed a history of previous self-harm & depression. The family on this occasion found several empty boxes of verapamil 240mg. Serum levels confirmed massive verapamil overdose (OD). He was treated with IV CaCl2, high dose insulin euglycaemic infusion, glucagon and 20% lipid rescue infusion. There was return of sinus rhythm after 24h and prompt & successful weaning of vasopressors & inotropes over the following 48h. The VA-ECMO was explanted after 5 days. The patient was discharged later. Problems:1)Cardiovascular manifestation of drug OD can be difficult to recognise. 2)Mechanical circulatory support can be useful as a bridge to diagnosis and recovery. Discussion:1)Atypical presentation (brady-arrhythmia in the face of shock in a young man) should prompt a search for other possible causes of shock, including drug toxicity. 2)Verapamil OD can cause bradycardia and hypotension that is refractory to inotropes & vasopressors. Treatment of verapamil OD is complex. 3)VA-ECMO support can be used successfully for hemodynamic support in OD. Conclusions:Verapamil OD can present with a combination of cardiogenic & vasoplegic shock. This atypical shock phenotype should prompt a search for other causes, including drug toxicity.

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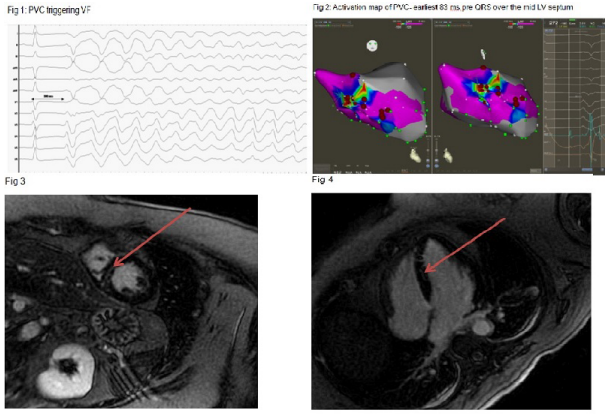
Extracorporeal membrane oxygenation supported ablation: unique management of fulminant myocarditis using a multidisciplinary and collaborative approach

V Val Rakita[1]; V Reddy[1]; W Whang[1]; G Dangas[1]; A Pawale[1]; S Pinney[1]; P Pirlamarla[1]; A Anywanwu[1]; A Lala[1]
[1]Mount Sinai Medical Center, New York, United States of America

A 55 year old female with 3 days of a viral prodrome suffered cardiac arrest at home due to refractory polymorphic ventricular tachycardia (PMVT) and ventricular fibrillation (VF). Initial work up included an elevated cardiac troponin-I of 1.2 ng/ml (normal range 0.00 - 0.40 ng/ml) and severely reduced ejection fraction on transthoracic echocardiography. Cardiac catheterization revealed normal coronary anatomy without evidence of obstructive coronary artery disease, but severely elevated filling pressures and a cardiac index of 1.7 L/min/m2. An endomyocardial biopsy was obtained and an intra-aortic balloon pump was placed to provide hemodynamic support. High dose steroids were administered in suspicion of giant cell myocarditis. She remained in refractory PMVT/VF storm sustaining innumerable defibrillatory shocks and as such the decision was made to place her on veno-arterial extracorporeal membrane oxygenation (VA-ECMO). After reviewing her electrocardiogram in consultation with our electrophysiology colleagues, it was discovered that she



Figures

had a focus of recurrent premature ventricular contractions (PVCs) triggering VF arrest. Despite full hemodynamic support with VA-ECMO, she continued to sustain shocks for VT/VF, and so decision was made to proceed to high-risk PVC ablation. During voltage mapping of the LV, PVC 1 (fig 1-2) was noted to frequently trigger VF. Activation mapping of PVC 1 (fig 3) demonstrated earliest activation over the mid-septum. Several foci were successfully ablated and she remained electrically quiescent and clinically stable post procedure. She was de-cannulated on post op day 2. RV biopsy did not show evidence of granulomas or giant cell. Serologic analysis was positive for Coxsackie virus. Cardiac magnetic resonance imaging was done on admission day 6, three days after ECMO was removed, revealing normal LV size with recovered LVEF of 48% and mild hypokinesis of the mid-inferoseptal and apical septal wall segments. On delayed enhancement imaging, there was intramyocardial scar in the mid inferoseptal, apical anterior, and apical septal walls (Fig 4-6) consistent with focal myocarditis. She received a single chamber implantable cardioverter defibrillator for secondary prevention on hospital day 8. She was discharged to home on hospital day 11.

This case highlights the importance of a multidisciplinary collaborative approach to management of a unique presentation of fulminant myocarditis. Complete mechanical hemodynamic support permitted the safe and successful ablation of PVC-inducing VF storm. Restoration of electric stability ultimately led to decannulation and myocardial recovery in the setting of fulminant myocarditis.

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Right and left heart failure due to carcinoid heart disease complicated by a PFO with right-to-left shunt: a case report

M Lichtenauer[1]; M Mirna[1]; S Eder[2]; B Wernly[1]; V Paar[1]; E Prinz[1]; UC Hoppe[1]
[1]Paracelsus Private Medical University, Internal Medicine II, Cardiology, Salzburg, Austria; *[2]Oberndorf Hospital, Department of Internal Medicine, Oberndorf, Austria*

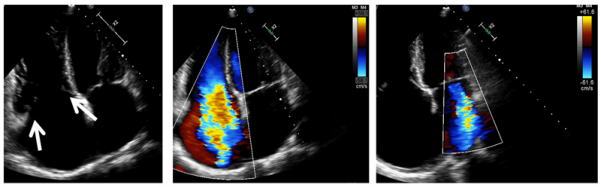
Carcinoid syndrome is a rare cause for acquired valvular heart failure. Carcinoid heart disease (CHD) occurs in 20-70% of the patients with carcinoid tumors leading to fibrotic remodeling of valvular structures, however due to degradation of serotonin in the pulmonary circulation usually only the right heart is involved. Here, we report the case of a 57 year old woman presenting with heart failure due to carcinoid syndrome. The patient was admitted to our clinic because of dyspnea and edema of the lower extremities. Transthoracic and transesophageal echocardiography showed severe tricuspid and moderate to severe mitral regurgitation. The leaflets of the tricuspid valve almost showed no motion at all. This pattern is typical for carcinoid heart disease caused by direct negative effects of serotonin in the right heart circulation leading to fibrosis of the leaflets. Furthermore, a small PFO with right to left shunt was found. We performed urine analysis screening for 5-hydroxyindoleacetic acid excretion, which proved to be severely elevated. Also serotonin (596U/l) and chromogranin A (1248µg/l) levels were elevated more than ten-fold. Next, we conducted a PET-CT scan which revealed a tumorous mass within in the liver. The primary tumor was thought to be located in the in the terminal ileum. Based on these results we hypothesized that the cause for the described symptoms was heart failure due to carcinoid heart disease. A medical therapy with the somatostatin analogue Lanreotide together with heart failure treatment was started.

During open heart surgery, it was also found that also the mitral valve was severely affected by fibrosis. We think that this was caused by direct serotonin-related effects due to the right to left shunt through the PFO leading to fibrosis of the mitral valve leaflets. A tricuspid replacement (Edwards St. Jude Epic, 33mm bioprostesis) and mitral valve repair (Edwards Physio Ring, 30 mm) was conducted successfully together with closure of the PFO and the patient showed good convalescence. This was also documented with decreasing levels of pro-BNP over the follow-up period (from 7830pg/ml to 982pg/ml).

Two months later, a hemicolectomy and liver segment resection (segment VI/VII and III) was performed. The tumor metastasis in the liver was extirpated and the (immuno-)histological analysis confirmed the diagnosis (neuroendocrine tumor of the terminal ileum).

The patient was followed-up for further 2 years and presented herself in good health without signs of recurring heart failure. At the recent follow-up exam including MRI of the abdomen new metastases were found in the liver and the patient is scheduled to undergo another liver segment resection.

This case is unique since the patient developed both right and left ventricular dysfunction due to fibrotic remodeling of not just the tricuspid valve as usually seen in carcinoid heart disease but also fibrosis of the mitral valve because of right to left shunt through a PFO.



Diagnostics - From epicardial fatty tissue to biomarkers and echocardiography

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Cytokines, Epicardial Adipose Tissue and Diastolic Function in the General Population

R Hullin[1]; G Ehret[2]; N Barras[1]; J Regamey[1]; M Kirsch[3]; M Bochud[4]; P Monney[1]
[1]University Hospital Centre Vaudois (CHUV), Cardiovascular Department, Cardiology, Lausanne, Switzerland; *[2]Geneva University Hospitals, Department of Cardiology, Geneva, Switzerland*; *[3]University Hospital Centre Vaudois (CHUV), Cardiovascular Department, Cardiac Surgery, Lausanne, Switzerland*; *[4]University Institute of Social and Preventive Medicine, Lausanne, Switzerland*

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Background: A proinflammatory state and the epicardial adipose tissue (EAT) have been suggested to play a role in impaired myocardial mechanics. This epidemiological study investigates their role for impaired relaxation in a population-based adult cohort without clinically overt heart failure or coronary artery disease.
Methods: This epidemiological study tested circulatory cytokines, EAT thickness, traditional risk factors, and multiple anthropometric measurements for prediction of impaired relaxation. EAT thickness was measured by transthoracic echocardiography using published protocols.
Results: Transthoracic echocardiography was performed in 520 participants; 14 participants were excluded for atrial fibrillation (n = 6), left ventricular ejection fraction < 50% (n = 5), or = moderate mitral regurgitation (n = 3). Mean age of included participants was 51 ± 17y; 55% were females; BMI was 25.6 ± 4.6 kg/m2. The prevalence of traditional cardiovascular risk factors corresponded to other European cohorts. Diastolic dysfunction pursuant to current guidelines was present in 4%; the prevalence of early mitral annulus e' velocity < 9 cm/s and mitral E-wave/e' ratio >8.5 was 29% and 14%, respectively. Participants with EAT thickness >median EAT value (4.5 mm) were older (57 vs 34y) and more often female (56 vs 52%); traditional risk factors were more prevalent while creatinine, smoking habits, and hemoglobin level were not significantly different. The echocardiographic parameters in this group (n = 246) were compatible with a concentric cardiac phenotype. Multivariate analysis adjusted for age, gender, and body height showed that both EAT and e' velocity share prediction by blood pressure, dyslipidemia, and anthropometric measurements of obesity. However, HbA1c, and circulatory levels of C-reactive protein or interferon y exclusively correlated with EAT whereas e' velocity was associated with circulatory levels of interleukin-6 or TNFa, and EAT thickness. Despite of the fact that EAT and e' velocity have common predictors, EAT remained an independent predictor of e' velocity in a multivariate model adjusted with measured cytokines in addition.
Conclusions: This epidemiologic study shows that both interleukin-6 and EAT thickness independently predict impaired relaxation in asymptomatic participants of a population-based cohort.

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The BNP genetic variant rs198389: cardiovascular phenotype and risk in stage A/B heart failure subjects from the STOP-HF Trial

V Cannone[1]; C Watson[2]; M Ledwidge[2]; JC Burnett Jr[1]; K Mc Donald[2]
[1]Mayo Clinic, Department of Cardiovascular Disease, Rochester, United States of America; *[2]St Vincent's University Hospital, Heart Failure Unit, Dublin, Ireland*

Funding Acknowledgements: This study was supported by the Mayo Clinic Cardiovascular Circulatory Program Award

Background: B-type natriuretic peptide (BNP) is a cardiac hormone secreted by the heart in response to myocardial stretch and volume overload. BNP possesses blood pressure lowering, natriuretic, antifibrotic and aldosterone suppressing properties. In the general population, the minor G allele of the BNP genetic variant rs198389 is associated with higher circulating values of BNP, lower blood pressure and odds of hypertension, lower cardiovascular mortality and increased lifespan.
Purpose: We aimed to investigate the clinical phenotype and cardiovascular risk associated with rs198389 genotypes in subjects at risk for heart failure (HF).
Methods: We genotyped 971 subjects with stage A/B HF from the cohort of the STOP-HF Trial.
Results: The frequencies of the rs198389 genotypes were AA: 38% (n= 367), AG: 47% (n= 455), GG: 15% (n= 149). All subsequent analyses are AA vs GG. The two genotypes did not differ in terms of age and sex. In the multivariate adjusted analysis, the GG genotype had significantly higher circulating levels of BNP (36.3 vs 50.7 pg/mL, p value < 0.001). Prevalence of hypertension was significantly lower among the homozygotes for the G allele (77.7% vs 67.1%, p value: 0.014). In the 4.95 (IQR 3.26-6.61) years follow-up analysis, the carriers of the GG genotype had lower risk of new onset left ventricular systolic dysfunction with ejection fraction < 50% and more than 5% decrease (4.4% vs 0.67%, p value: 0.032). When we evaluated the change in BNP levels over the same time period, the two groups increased by similar amount (around 5 pg/mL per annum) maintaining their significantly different set point over time. The two genotypes did not differ in terms of blood pressure, body mass index, creatinine levels, new onset of major adverse cardiovascular events and mortality.
Conclusion: In the STOP-HF Trial cohort including subjects with stage A/B HF failure, the GG genotype of the BNP genetic variant rs198389 is associated with higher BNP circulating levels, lower prevalence of hypertension and lower risk of incident left ventricular systolic dysfunction over time. Our findings suggest a cardiovascular protective role exerted by the cardiac hormone BNP in the clinical context of stage A/B heart failure and may support the concept of a natriuretic peptide-based therapy for prevention of HF.

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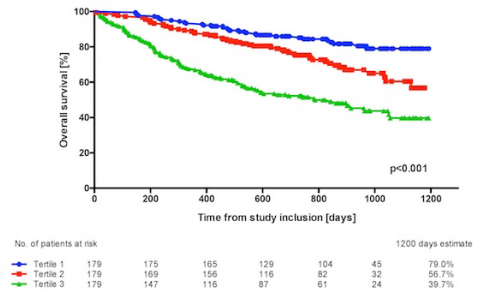
Cardiac fibrosis marker GDF-15 is associated with prognosis in treatment naive cancer patients

H Arfsten[1]; A Cho[1]; C Mayrhofer[1]; M Raderer[2]; G Goliasch[1]; R Wurm[1]; G Strunk[3]; C Zielinski[2]; M Huelsmann[1]; N Pavo[1]
[1]Medical University of Vienna, Department of Internal Medicine II, Division of Cardiology, Vienna, Austria; *[2]Medical University of Vienna, Department of Internal Medicine I, Division of Oncology and Hematology, Vienna, Austria*; *[3]Complexity Research, Vienna, Austria*

Background: The prognostic importance of growth differentiating factor-15 (GDF-15) has been investigated in numerous pathologic cardiac processes as myocardial infarction or heart failure. Elevated levels of GDF-15, which is equally implicated in cell growth and survival, have also been observed in distinct tumor entities. However, its general impact on prognosis in cancer has not been investigated yet. This study aimed to explore whether cardiac fibrosis marker GDF-15 has ability to predict long-term mortality also in an unselected cohort of cancer patients without prior anti-cancer therapy.
Methods. We prospectively enrolled 555 consecutive treatment naïve patients with primary diagnosis of cancer. GDF-15 as well as other cardiac and routine laboratory markers were determined. All-cause mortality was defined as the primary endpoint.

Figure 1. Overall survival rates for treatment-naïve cancer patients (n=555) according to tertiles of GDF-15 (p<0.001 between all groups, log-rank test).



Results: GDF-15 levels were 338pg/ml (IQR 205-534) for the total cohort and values were comparable in different tumor entities except for lower concentrations in breast cancer patients (Figure 1). Metastatic disease was characterized by higher circulating GDF-15 [266 (IQR 175-427) vs 435 (IQR 279-614), $p < 0.001$]. GDF-15 was significantly associated with all-cause mortality in the univariate analysis [crude HR for ln(GDF-15) 2.08, 95%CI:1.77-2.43, $p < 0.001$] and this effect was persistent after multivariate adjustment. Kaplan-Meier analysis revealed the high discriminatory power of GDF-15 ($p < 0.001$ between all groups according to tertiles) (Figure 2). There was a significant interaction of solid and liquid malignancies with loss of association of GDF-15 with outcome in myelodysplastic and myeloproliferative disease. GDF-15 correlated positively with the inflammatory status reflected by CRP, SAA and IL-6 ($r = 0.31$, $p < 0.001$, $r = 0.23$, $p < 0.001$ and $r = 0.14$, $p = 0.002$) and cardiac biomarkers as NT-proBNP, hsTnT or MR-proADM and CT-proET1 ($r = 0.46$; $r = 0.46$; $r = 0.59$; $r = 0.50$, $p < 0.001$ for all).
Conclusions: Increased plasma GDF-15 levels are associated with disease severity and all-cause mortality in solid tumors of treatment-naïve cancer patients. This association accompanies progressing systemic inflammation with subclinical involvement of other organ systems including the heart. GDF-15 represents a further molecule in the field of cardiooncology linking pathophysiologic conditions of both cardiac and neoplastic disease.

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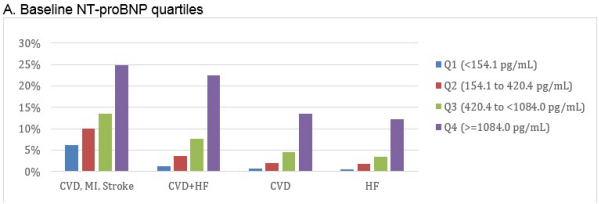
Serial monitoring of NT-proBNP predicts heart failure in patients with type 2 diabetes mellitus

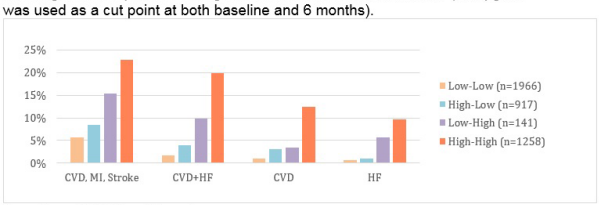
P Petr Jarolim[1]; WB White[2]; CP Cannon[3]; Q Gao[3]; DA Morrow[1]
[1]Brigham and Women's Hospital, Harvard Medical School, Boston, United States of America; *[2]University of Connecticut School of Medicine, Calhoun Cardiology Center, Farmington, United States of America*; *[3]Baim Institute for Clinical Research, Boston, United States of America*

Background: Diabetes mellitus (DM) is associated with an increased risk of microvascular and macrovascular disease. In addition, heart failure (HF) has emerged as an increasingly important complication of DM. Patients with type 2 DM (T2DM) are almost twice as likely to develop HF as patients without DM and, eventually, almost half of patients with T2DM are diagnosed with HF. In addition, some oral hypoglycemic agents increase the likelihood of developing HF, and HF itself has become a target for preventive pharmacotherapies in T2DM. Therefore, enhanced recognition of patients at risk for or who are early in the development of HF is needed to potentially guide therapeutic decision-making.

Figure: Kaplan-Meier rates for outcomes at 24 months stratified by
A. Baseline NT-proBNP quartiles



B. Categorical NT-proBNP change between baseline and 6 months (400 pg/mL was used as a cut point at both baseline and 6 months).



* p-value <0.001 for all trends

Purpose: To investigate the prognostic implications of changes in N-terminal B-type natriuretic peptide (NT-proBNP) concentration over time in patients with T2DM and ischemic heart disease enrolled in the EXAMINE trial.
Methods: EXAMINE was a phase IIIb clinical outcomes trial of alogliptin, a nonselective dipeptidyl peptidase 4 (DPP-4) inhibitor. 5380 patients with T2DM and a recent acute coronary syndrome were enrolled in the trial. NT-proBNP was measured in 5224 patients at baseline and in 4367 patients at 6 months. Cardiovascular (CV) death or hospitalization for heart failure (HF) was the endpoint of principal interest for this analysis.
Results: We observed a strong graded relationship between increasing baseline (Figure A) and 6-month NT-proBNP concentration and the incidence of major cardiovascular events. After adjusting for potential confounders, concentrations of NT-proBNP at baseline were independently associated with the development of major CV events, particularly hospitalization for heart failure. Patients who were persistently or became high at 6 months were at a significantly higher risk of adverse outcomes than those who remained low at both time points or who had a high NT-proBNP at baseline but subsequently declined to the low category (Figure B). The absolute changes in NT-proBNP by 6 months were also strongly associated with subsequent outcomes.
Conclusions: Serial monitoring of NT-proBNP in patients with T2DM and ischemic heart disease may be useful for identifying patients with T2DM at highest risk for HF. Treatment with a DPP-4 inhibitor did not meaningfully alter NT-proBNP concentration.

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Real-World application of guideline adherence score in ambulatory systolic heart failure patients, attending a dedicated heart failure clinic

A Ali[1]; N Lagzouli[1]; US Siddique[1]; P Cliffe[1]; C Zerafa[1]; P Phen[1]; J Dungu[1]; R Barbagallo[1]; HO Savage[1]
[1]Basildon and Thurrock University Hospitals NHS Foundation Trust, The Essex Cardiothoracic Centre, Basildon, United Kingdom

Introduction: Adherence to guideline recommended therapy for the treatment of chronic heart failure is associated with improved cardiovascular outcomes. The Qualify International Registry developed a global adherence score based on the prescription of ACEIs, ARBs, Beta-blockers, MRAs and Ivabradine in order to determine the outcomes in patients recently hospitalised for heart failure.
Purpose: We aimed to assess the adherence to guideline recommended pharmacotherapy for the treatment of heart failure with a reduced ejection fraction, using this global adherence score, in new attendees of a rapid access heart failure clinic (RAHFC) at a secondary care hospital and its impact on outcomes.
Methods: We implemented this score: good (1), moderate (<0.5 to < 1) and poor (= 0.5), to a cohort of 106 new patients attending a RAHFC at a secondary care hospital over a one year period. Individual medications were also recorded as having been prescribed at recommended target doses (TD), = 50% of TD and < 50% of TD and we observed the impact on readmissions for heart failure, progression to device therapy and mortality.
Results: Of the 106 attendees, 15 were diagnosed with HFpEF and excluded from the analysis. In the 91 eligible patients, 63% were men and 27% women, with mean ages of 64 ± 12 years for men and 69 ± 11 years for women. Mean ejection fraction was 28 ± 10%. Adherence was "good" in 63% of patients, "moderate" in 33% of patients and "poor" in 4% of patients. Average time to maximum tolerated doses was 70 ± 65 days. Mean NTProBNP values were 2148 ± 1623ng/L.
Overall, 94% were prescribed an ACEI or ARB, 88% prescribed a beta-blocker, 85% prescribed an MRA, and 44% were prescribed ivabradine. With the exception of ACEi (58%), less than half of patients achieved = 50% of the target dose (TD) for all classes of drugs, 44%, 49%, 31% and 8% for ARB, BB, MRA and Ivabradine respectively.
However at 12 months follow up, more frequent reviews in the RAHFC was associated with a better adherence score; 3.3 visits (good) 2.9 (moderate), 2.2 (poor). There was a significant association between the score and readmissions for heart failure; (0.4% (good), 0.5% (moderate) and 1.2% (poor)($p = 0.019$). In addition, there was an inverse correlation between the frequency of review in the RAHFC and readmissions for heart failure ($r = -0.968$). Over the period of follow up, 5 patients progressed to device therapy, 4(good), 1(moderate) and 1 patient died in the moderate adherence group.
Conclusion: Compared with heterogeneous registry data, we have shown that a higher proportion of real world heart failure patients, managed in a specialised heart failure service, had better adherence to disease modifying therapy for heart failure with a reduced ejection fraction, with a trend to better outcomes. Our data suggests more work needs to be done to ensure timely up titration to target doses, which have been shown in randomised trials, to have the most benefit for patients.

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Neurohormonal function across categories of systolic dysfunction in chronic heart failure

A Alberto Aimo[1]; G Vergaro[2]; N Ghionzoli[2]; C Prontera[2]; A Gabutti[2]; R Poletti[2]; A Giannoni[2]; C Mammini[2]; C Passino[1]; M Emdin[1]
[1]Sant'Anna School of Advanced Studies, Pisa, Italy; *[2]Gabriele Monasterio Foundation, Pisa, Italy*

Background: Latest European Society of Cardiology guidelines introduced a new categorization of heart failure (HF) patients based on left ventricular ejection fraction (LVEF): HF with reduced EF (HFrEF; LVEF <40%), HF with mid-range EF (HFmrEF; LVEF 40-49%), and HF with preserved EF (HFpEF; LVEF = 50%). No treatment has demonstrated prognostic benefit in HFpEF, and there are no clear recommendations for HFmrEF.

Methods: Patients with stable HF evaluated at a tertiary referral centre from 1999 to 2017 were considered. Circulating biomarkers (plasma renin activity - PRA, aldosterone, norepinephrine, N-terminal fraction of pro- B-type natriuretic peptide), and time-domain measures of heart rate variability (HRV; standard deviation of NN intervals - SDNN, standard deviation of the average NN intervals for each 5 min segments - SDANN, percentage of successive RR intervals that differ by more than 50 ms - pNN50, root mean square of successive RR interval differences - rMSSD) were evaluated as part of baseline assessment.
Results: Out of the entire population (n = 2791), 1000 patients (36%) had information on biomarkers and HRV (HFrEF, n = 684; HFmrEF, n = 203; HFpEF, n = 113). Samples of 113 patients, matched based on age and gender to the original populations, were derived from the HFrEF and HFmrEF groups. Median ages were 68 years (62-75), 68 (57-76), and 71 (61-79) in the HFrEF, HFmrEF, and HFpEF groups; men were 75%, 71%, and 59% in the three subsets.
All indices except for aldosterone, pNN50, and rMSSD differed significantly across LVEF categories. The neurohormonal profile in HFmrEF was better than in HFrEF, and similar to HFpEF except for lower SDNN. There was a trend towards higher aldosterone levels in HFpEF than in HFmrEF and even HFrEF.
When considering two HFrEF subgroups based on the severity of systolic dysfunction (LVEF <25% vs. = 25%, n = 113 in both cases), all parameters except for aldosterone, pNN50 and rMSSD were significantly more altered in those with LVEF <25%. By contrast, patients with LVEF = 25% resembled those with LVEF = 40% except for higher PRA and NT-proBNP.
Conclusions: The degree of neurohormonal activation is similar between HFpEF and HFmrEF, and lower than in HFrEF (especially the subgroup with more severe systolic dysfunction). By contrast, aldosterone tends to increase from HFrEF to HFpEF. These findings may help explain the systematic failure of trials on neurohormonal antagonism in HFpEF, with borderline survival benefit from spironolactone. Further assessment of aldosterone antagonists and therapeutic strategies targeting the mechanisms of HFpEF onset and progression are then warranted.

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BNP in patients with severe aortic valve stenosis undergoing valve replacement: pathophysiological determinants and long-term impact on mortality

MT Micha Maeder[1]; L Weber[1]; P Ammann[1]; M Buser[1]; NF Ehl[1]; M Gerhard[1]; PK Haager[1]; F Maisano[2]; H Rickli[1]
[1]Cantonal Hospital St. Gallen, St. Gallen, Switzerland; *[2]University Hospital, Zürich, Switzerland*

Background: In patients with aortic stenosis (AS), B-type natriuretic peptide (BNP) is a marker of disease severity and prognosis. Therefore, BNP is used as a tool for decision making regarding aortic valve replacement (AVR) in ambiguous situations. However, little is known about the pathophysiological correlates and the long-term prognostic value of high BNP in severe AS.
Methods: We measured BNP in 252 patients (age 74 ± 10 years, 58% males) with severe AS [indexed aortic valve area (iAVA) 0.4 ± 0.1 cm2/m2, left ventricular ejection fraction (LVEF) 57 ± 12%] the day before pre-AVR right heart catheterization. All patients subsequently underwent surgical (n = 157) or transcatheter (n = 95) AVR. The median follow-up was 3.1 (interquartile range, 2.3-4.3) years.
Results: The median BNP plasma concentration in the entire cohort was 188 (78-452) ng/l. Patients with supramedian BNP (BNP = 188 ng/l) were older (78 ± 9 vs. 72 ± 10 years), more symptomatic (44 vs. 20% in NYHA class III/IV), more likely to be on loop diuretics (62 vs. 39%), spironolactone (2 vs. 8%), and digoxin (16 vs. 1%), had lower body mass index (BMI; 27 ± 5 vs. 29 ± 5 kg/m2), estimated glomerular filtration rate (66 ± 29 vs. 80 ± 26 ml/min/1.73 m2), hemoglobin (130 ± 19 vs. 138 ± 15 g/l), forced expiratory volume within the first second (81 ± 21 vs. 91 ± 21 %predicted), and LVEF (53 ± 14 vs. 61 ± 10%), and had higher mean pulmonary artery pressure (mPAP; 31 ± 11 vs. 20 ± 6 mmHg), and mean pulmonary artery wedge pressure (20 ± 8 vs. 12 ± 5 mmHg; p < 0.05 for all comparisons). There was a trend toward a lower iAVA in patients with supramedian versus inframedian BNP (0.40 ± 0.12 vs. 0.43 ± 0.12 cm2/m2; p = 0.051). Parameters independently associated with higher BNP (ln-transformed values) included higher age, lower BMI, lower hemoglobin, lower LVEF, and higher mPAP (r2 for the entire model: 0.59), the strongest correlation being that with mPAP (r = 0.66). Patients with supramedian BNP had both higher 30 day mortality post AVR (p = 0.03) and higher long-term mortality (log rank p = 0.001).
Conclusions: In patients with severe AS, BNP is a marker of more advanced disease in terms of both hemodynamics and non-cardiac co-morbidities, and thereby a predictor of long-term post-AVR mortality. Importantly, non-cardiac factors known to be associated with higher BNP including older age, lower BMI and lower hemoglobin have significant impact on BNP also in the setting of severe AS which has to be taken into account when using BNP for decision making regarding AVR.

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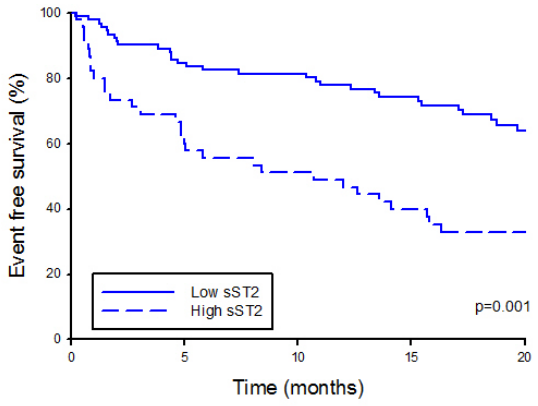
Elevated suppression of tumorigenicity 2 associated with poor outcome in heart failure with preserved ejection fraction

C Clotilde Roy[1]; A Slimani[1]; C De Meester[1]; M Amzulescu[1]; A Pasquet[1]; D Vancraeynest[1]; C Beauloye[1]; J-L Vanoverschelde[1]; B Gerber[1]; A-C Pouleur[1]
[1]Cliniques Saint-Luc UCL, Cardiology, Brussels, Belgium

Introduction: Soluble suppression of tumorigenicity 2(sST2) receptor is a well known biomarker implicated in inflammatory diseases. It has already been shown that sST2 is associated with worse outcome in HFrEF. In HFpEF, data are rather limited.
Purpose: We sought to evaluate the association of sST2 with clinical, laboratory and imaging findings and its prognostic value in HFpEF patients.
Methods: Between January 2015 and June 2017, we prospectively enrolled 137 consecutive patients with HFpEF (79 ± 8 years, 61% women). Elevated sST2 was determined by an age and sex-adjusted cutoff value (cutoff 55 ng/ml) corresponding to mean + 2 standard deviations in 31 controls (75 ± 6years, 61% women). All patients underwent complete 2D echo and cMR. Patients were followed up for a composite outcome of all-cause mortality and first HF hospitalization.
Results: In HFpEF patients, median sST2 level was 44.5 ng/ml (IQR: 31.6-62.2 ng/ml). Elevated sST2 (n = 46) had an impaired right ventricular function (FAC 39 ± 10% vs 43 ± 8%, p = 0.017; TAPSE 17.4 ± 5.6mm vs 19.2 ± 5.2mm, p = 0.067; RVEF by cMR 53.5 ± 9.8% vs 58.1 ± 7.8%, p = 0.008) and higher proportion with pathologic RV/RA gradient (n = 20 (40%) vs n = 23 (26%), p = 0.034). They were similar for other clinical, laboratory and imaging characteristics. Multivariate analysis showed that only RVEF by cMR was associated with high sST2 level (OR: 0.94 [0.89-0.99] p = 0.010).
During a mean follow-up of 20 ± 8months, seventy one patients (52%) reached the combined end point. Cox analysis identified GFR, hemoglobin, sST2 , use of loop diuretic and E/e' ratio as significant predictors of outcome. GFR (HR= 0.98 [0.96-0.99], p < 0.001) and sST2 (HR= 3.64 [1.37-9.65], p = 0.009) were significantly associated with the composite outcome even after adjusting for important clinical and imaging covariables.
Kaplan Meier event free survival curve showed that HFpEF patients with high sST2 had poorer 20months prognosis than those with low sST2 (p = 0.001, Figure)
Conclusions: In HFpEF, sST2 is associated with impaired right ventricular function and with a poorer prognosis with higher rate of all cause mortality and first HF hospitalization.

Event free survival Kaplan Meier curve according to sST2 level



Low sST2	91	77	72	59	35
High sST2	46	27	23	17	12

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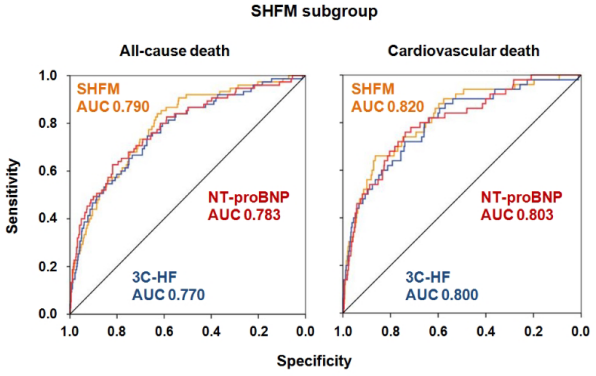
N-terminal fraction of pro-B-type natriuretic peptide vs. clinical risk scores for prognostic stratification in chronic systolic heart failure

A Alberto Aimo[1]; C Arzilli[2]; G Vergaro[2]; A Ripoli[2]; M Senni[3]; M Emdin[1]; C Passino[1]
[1]Sant'Anna School of Advanced Studies, Pisa, Italy; *[2]Gabriele Monasterio Foundation, Pisa, Italy*; *[3]Ospedale Papa Giovanni XXIII, Bergamo, Italy*

Background: The Seattle Heart Failure Model (SHFM) or the Cardiac and Comorbid Conditions (3C-HF) scores may help define patient risk in heart failure (HF). Direct

comparisons between them or versus N-terminal fraction of pro-B-type natriuretic peptide (NT-proBNP) have never been performed.
Methods: Data from consecutive patients with stable systolic HF (left ventricular ejection fraction < 50%), and 3C-HF data were examined. A subgroup of patients had SHFM data available. The endpoints were 1-year all-cause or cardiovascular death.
Results: The whole population included 2023 patients, 798 (39%) with SHFM data. Mean age was 71 years, 75% were men, and 47% had ischaemic HF. At 1 year time-point, 198 deaths were recorded (10%), 124 of them (63%) from cardiovascular causes. While areas under the curve (AUC) were not significantly different, NT-proBNP displayed better reclassification capability than the 3C-HF score for the prediction of 1-year all-cause death, and (at least for net reclassification improvement) cardiovascular death. Adding NT-proBNP to the 3C-HF score resulted in a significant improvement in risk prediction.
Among patients with SHFM data available (n = 798), the AUC values for all-cause death were higher for the SHFM score (0.790) and NT-proBNP (0.783), and lower for the 3C-HF score (0.770). For cardiovascular death, the prognostic performances were slightly better, AUC values being 0.820 for the SHFM score, 0.803 for NT-proBNP, and 0.800 for the 3C-HF score. The combination of 3C-HF score and NT-proBNP displayed a similar prognostic performance than the SHFM score for both endpoints. Adding NT-proBNP to the SHFM score performed better than the SHFM alone in terms of reclassification, but not discrimination.
Conclusions: Among patients with chronic systolic HF, NT-proBNP levels had better reclassification capability for all-cause and cardiovascular death than the 3C-HF score. The inclusion of NT-proBNP to the 3C-HF score resulted in significantly better risk stratification. In a subgroup with SHFM data, the SHFM and 3C-HF scores and NT-proBNP yielded similar AUC values. The combination of the 3C-HF score and NT-proBNP had a similar prognostic performance than the SHFM score, while adding NT-proBNP to the SHFM improved reclassification over the SHFM score.



217
Prevalence and prognostic implications of longitudinal ejection fraction change in heart failure

O Ola Vedin[1]; G Savarese[2]; U Dahlstrom[3]; CSP Lam[4]; LH Lund[2]
[1]Uppsala University Hospital, Department of Medical Sciences, Cardiology, Uppsala, Sweden; [2]Karolinska Institute, Stockholm, Sweden; [3]Linkoping University Hospital, Linkoping, Sweden; [4]National Heart Centre Singapore, Singapore, Singapore

Background: In addition to the use of ejection fraction (EF) as a mere categorization tool in heart failure the clinical significance of EF change over time is becoming increasingly recognized but remains poorly described.
Purpose: We evaluated incidence and predictors of EF change and its associations with outcomes in a large cohort of patients with HF with reduced (HFrEF), mid-range (HFmrEF), and preserved EF (HFpEF).
Methods: Patients in the Swedish Heart Failure Registry with at least two EF assessments were categorized as having EF increase (transition from a lower to a higher EF category), stable EF, or EF decrease (transition from a higher to a lower EF category). Multivariable logistic regression models assessed predictors of EF increase and decrease. Multivariable Cox regression models evaluated associations between EF change and all-cause mortality and the composite of all-cause mortality and HF hospitalization.
Results: Of 4,957 patients at baseline, 63% had HFrEF, 19% HFmrEF and 18% HFpEF. Over a median follow-up of 1.4 years (interquartile range 0.5-3.0 years), 1,030 patients (21%) had an EF increase (10% HFrEF to HFmrEF, 6% HFrEF to HF with improved EF and 5% HFmrEF to HF with improved EF), 3,235 patients (65%) stable EF, and 692 patients (14%) an EF decrease (4% HFpEF to HFmrEF, 3% HFpEF to HFrEF and 7% HFmrEF to HFrEF). After adjustments, predictors of EF increase included shorter HF duration (< 6 vs = 6 months), female sex, higher eGFR (= 60 vs < 60 ml/min), no diabetes, no ischemic heart disease, higher mean arterial pressure (= 90 vs < 90 mmHg) and planned follow-up in HF nurse-led clinic. Predictors of EF decrease included atrial fibrillation, diabetes, history of stroke, higher mean arterial pressure (= 90 vs < 90 mmHg), no ACE-i/ARB, no ICD/CRT and no planned follow-up in HF nurse-led clinic. Cumulative crude incidence of all-cause mortality and the composite outcome are depicted in Figure 1. After adjustment, as compared with stable EF, increased EF was associated with lower all-cause mortality (HR 0.69; [95% CI 0.59-0.80]) and decreased EF with higher all-cause mortality (HR 1.15, [1.01-1.31]). Increased EF was also associated with lower risk of the composite outcome (HR 0.66 [0.58-0.75]) and decreased EF with higher risk (HR 1.14 [1.02-1.28]).
Conclusion: In this large nationwide contemporary heart failure cohort EF change occurred in over one third of all patients. Important predictors of change included demographic, clinical, co-morbidity and treatment factors. An increase in EF over time was associated with improved outcomes. A decrease in EF portended a poor prognosis but may be preventable by optimal HF therapy.

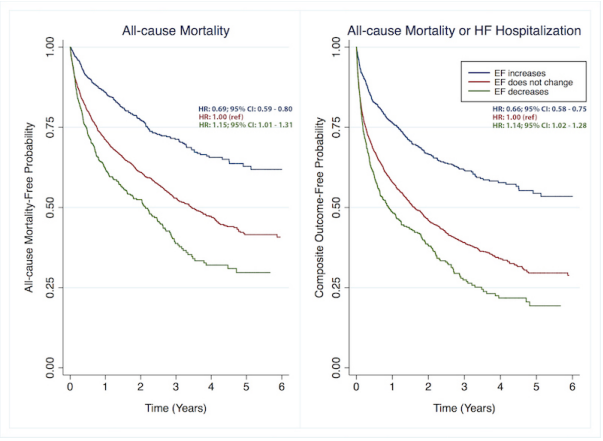


Figure 1

Poster Session 1

Atrial Fibrillation - Pathophysiology and Mechanisms

P218

Predictive value of interatrial block for atrial fibrillation in old subjects enrolled in the PREDICTOR study at 5 years follow up. A population-based study in central Italy .

A Cortellesi[1]; A Boccanelli[2]; G Mureddu[3]; G Cesaroni[4]; N Agabiti[4]; L Arcari[1]; AB Scardovi[1]
[1]*Hospital Santo Spirito, Cardiology, Rome, Italy*; [2]*Quisisana clinic, Rome, Italy*; [3]*Hospital San Giovanni Addolorata, Rome, Italy*; [4]*Epidemiology Department, Lazio region, Rome, Italy*

Background: Bayés and other authors found interatrial block (IAB) to be a substrate for the development of supraventricular arrhythmias [mostly atrial fibrillation (AF)]; a condition that was subsequently referred to as Bayés syndrome. IAB is associated with AF in multiple clinical scenarios. However, the role of IAB as predictor of arrhythmias in many other situations has not yet been evaluated. Large and comprehensive studies exploring this connection in specific subsets of individuals are still lacking.
Methods and Results: The PREDICTOR study is a population-based cross-sectional study that aimed to assess the prevalence of both preclinical and clinical heart failure (HF) in the elderly. A sample of 2001 randomly selected subjects, 65- to 84-year-old residents in the Lazio Region (Italy), underwent physical examination, biochemistry/N-terminal pro brain natriuretic peptide (NT-proBNP) assessment, electrocardiography, and echocardiography. We performed a retrospective analysis on 1489 elderly patients enrolled in the PREDICTOR study in sinus rhythm that had a baseline electrocardiogram and echocardiographic exam available for interpretation. IAB was defined as a P wave duration >120 m/sec with or without biphasic morphology in the inferior leads (II,III and aVF). Among the study population, at a administrative 5 years follow-up 90 patients were admitted to the emergency department or hospital ward due to a new occurrence of AF. The presence of IAB at the baseline ECG was associated to a higher probability of developing AF (HR = 1,71 (95%CI:1,10-1,66) p = 0.017).
Conclusions: in a large sample from an elderly general population the presence of IAB is associated to the development of AF.

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Clinical prognostic values of left atrial dysfunction after catheter ablation for atrial fibrillation

K Masai[1]; A Goda[1]; M Sugahara[1]; T Oshita[1]; Y Ohta[1]; A Daimon[1]; T Mine[1]; M Asakura[1]; M Ishihara[1]; T Masuyama[1]
[1]*Hyogo College of Medicine, cardiovascular, Nishinomiya, Japan*

Background: Left atrial (LA) function is important factor in atrial fibrillation (AF). We investigated whether several LA functions predict recurrent AF after catheter ablation (CA).
Methods: We studied 64 patients (39 males, age 65 ± 8 yrs) who underwent CA for AF. Transthoracic echocardiography (TTE) was performed after the CA, and all patients had sinus rhythm. LA functions were calculated using the following formula; (1) Reservoir function = {[maximum LA volume (LAVmax) - minimum LA volume (LAVmin)] / LAVmin} × 100, (2) Booster function = {[Pre-A volume (LAVpre-A) - LAVmin] / LAVpre-A} × 100, LAVpre-A was defined as LA volume at the onset of the P-wave on electrocardiogram. (3) Conduit function = [(LAVmax - LAVpre-A) / LAVmax] × 100.
Results: Recurrent AF was detected in 24/64 (38%) during the follow-up period (11.5 ± 7.0-month). Univariate analysis revealed lower reservoir function, decreased booster function, larger LA diameter, elevated E wave, and higher prevalence of persistent AF as significant variables. On multivariate analysis, booster function was only independently associated with recurrent AF (p = 0.037, OR 1.141 for each 1% decrease in AEF index, 95%CI 1.019-1.313). Moreover, patients with decreased LA booster function (<10.6%) had a higher risk of recurrent AF (log-rank p = 0.0009).
Conclusion: LA booster dysfunction after sinus rhythm conversion might predict a recurrence after CA for AF.

Atrial Fibrillation - Epidemiology, Prognosis, Outcome

P220

Is dietary salt intake a predictor of future development of atrial fibrillation in the general population?

H Hiroyuki Takase[1]; M Machii[1]; D Nonaka[1]; K Ohno[1]; T Sugiura[2]; N Ohte[2]; Y Dohi[3]
[1]*Enshu Hospital, Hamamatsu, Japan*; [2]*Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan*; [3]*Nagoya Gakuin University, Seto, Japan*

Background: Atrial fibrillation (AF) is a common arrhythmia and several conditions have been proposed as risk factors contributing to the onset of AF. Dietary salt consumption, which is a modifiable factor in our life style, is associated with hypertension and cardiovascular diseases independently of its effects on blood pressure.
Purpose: We tested the hypothesis that dietary salt intake predicts new onset of AF in the general population.
Methods: Consecutive 12,769 subjects without AF (male = 7,749, 52.8 ± 12.2 year-old) who visited our hospital for a physical check-up were enrolled in this study. After baseline examination, subjects were followed up for 1,821 days (median) with the endpoint being the new onset of AF. Individual salt intake was estimated using a spot urine by a previously reported method.
Results: Salt intake was 12.1 ± 3.1 g/day in male and 8.3 ± 2.2 g/day in female subjects at baseline. During the follow-up period, 87 subjects developed AF (1.44 per 1000 person-year) with the incidence being more frequent in male than female subjects (2.10 vs. 0.39 per 1000 person-year). Non-adjusted hazard ratio (HR) (95% confidence interval [CI]) of salt intake for the new AF was 1.169 (1.108-1.234). In analysis where subjects were divided into gender-specific quartiles according to the baseline salt intake (salt intake; 7.4 ± 1.7, 9.5 ± 1.8, 11.3 ± 2.0 and 14.3 ± 3.0 g/day in the first, second, third, and fourth quartiles, respectively), the incidence of AF were increased across the quartiles (0.73, 1.31, 1.72, and 1.99 per 1000 person-years). However, multivariate Cox proportional hazard analysis adjusted for age, gender, body mass index, systolic blood pressure, heart rate, serum creatinine, uric acid, fasting plasma glucose, low-density lipoprotein cholesterol, triglyceride, haemoglobin, B-type natriuretic peptide and current smoking habit at baseline revealed that salt intake did not predict the new AF (HR:0.970, 95%CI:0.906-1.039).
Conclusions: Although salt intake is associated with the development of AF in the general population, other factors rather than salt intake have much more prominent impact on the development of AF, suggesting the complementary role of salt intake for the prediction of AF.

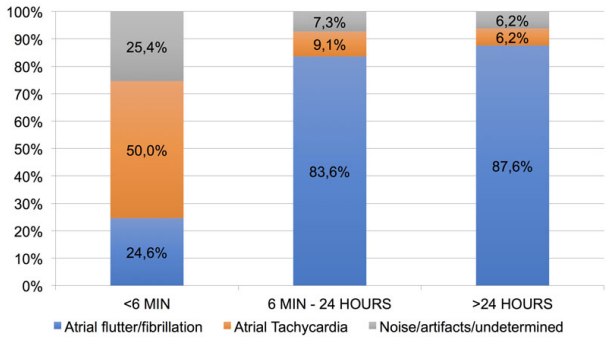
P221

Diagnostic yield and clinical implications of atrial high-rate episodes detection in patients with a cardiac implantable device

F Davi[1]; M Moretti[1]; S Agosti[1]; PF Vianello[1]; P Ameri[1]; C Brunelli[1]; G Bertero[1]; M Canepa[1]
[1]*University of Genoa, Genoa, Italy*

Background: The detection of AHREs (atrial high rate episodes) in patients with cardiac implanted electronic devices (CIEDs) and no history of atrial fibrillation has been associated with increased thromboembolic risk. The aim of this study was to analyze the prevalence and clinical predictors of AHREs and occult atrial fibrillation (AF) in an unselected population with the aforementioned characteristics.
Methods: This prospective study included all consecutive patients referred at two outpatient clinics (Ospedale Policinico San Martino Genova, Mon-Wed-Thurs; Ospedale di Novi Ligure, Wed) undergoing a routine interrogation of a CIED with an atrial lead. Clinical characteristics were collected using a structured questionnaire and the devices of patients with no history of AF and/or anticoagulant therapy were interrogated for the presence of AHREs. If AHREs were detected, EGMs (electrograms) were analyzed to further characterize the arrhythmia detected by the CIED.

Results: In a 6-month period (Jan 2017-May 2017) 1189 patients were screened and 322 were included in the final population. The mean age was 76.6 ± 9.7 years and the mean CHA2DS2-VASc score was 4.1 ± 1.8. The majority of these patients (81.4%) had a bicameral pacemaker. A total of 133 patients (41.3%) had no AHREs; 118 (36.6%) had at least one AHRE < 6 min; 55 (17.1%) had at least one AHRE >6 min and < 24 hours; 16 (5.0%) had at least one AHRE >24 hours. At EGM analysis, AF was detected in 29 patients (24.6%) in the first group (< 6min); in 46 patients (83.6%) in the second group (<6min < 24hours) and in 14 patients (87.6%) in the third group (<24hours, p < 0.0001, see Figure). At univariate analysis of clinical predictors, only age was significantly related to the occurrence of clinically significant AHREs (<6min) (p < 0.02).
Conclusions: This study demonstrates a significantly high prevalence of clinically relevant AHREs and occult AF in an unselected outpatient population with CIEDs. Further studies are warranted for ensuring systematic AHREs assessment at CIED interrogation, whose therapeutic management remains a matter of debate.



P222

Subclinical systolic dysfunction of the left ventricle in patients with chronic atrial fibrillation and preserved ejection fraction

K Kalliopi Keramida[1]; P Kostakou[1]; A Michalopoulos[1]; V Giannaris[1]; E Tryfou[1]; V Kostopoulos[1]; CD Olympios[1]; N Kouris[1]
[1]Thriassio General Hospital, Athens, Greece

2D speckle tracking echocardiography can assess subclinical myocardial dysfunction by strain at the longitudinal, circumferential and radial level, even when classical echocardiographic parameters, like ejection fraction (EF) are within the normal limits. The aim of this study was to test the hypothesis that chronic atrial fibrillation (AF), apart from the diastolic function impairs systolic deformation of the left ventricle (LV), even if it is not apparent from the reduction of EF.
Patients and Methods: 40 consecutive patients (29 males and 11 females) with chronic AF and preserved EF (58 ± 4%) and 20 healthy controls (9 males and 11 females) underwent a comprehensive 2D echocardiographic study, while strain analysis was performed off-line by GE EchoPac software version 110. Global longitudinal strain of the LV (LVGLS) was assessed from the standard three apical views, while circumferential strain (LVCS) from the parasternal short axis view at the level of papillary muscles. Exclusion criteria were presence of moderate/severe valvular disease, coronary artery disease and LV hypertrophy.
Results: Patients with chronic AF revealed significantly impaired LVGLS (-13.6 ± 3.5% vs -21.2 ± 1.3%, p < 0.0001) and LVCS (-15 ± 4.8 vs -22.5 ± 2.2, p < 0.0001). LVEF and LV end-diastolic diameter (LVEDD) did not differ between the two groups, while left atrial dimensions [left atrial diameter (LAD) and left atrial volume indexed (LAVi)] were significantly larger in patients with AF, as expected (Table 1).
Conclusion: Chronic AF impairs the deformation properties of LV despite the preserved EF. This observation is in line with the diastolic dysfunction of this group of patients that is almost always present, proving the interaction and the probable common pathophysiologic mechanism of systolic and diastolic dysfunction.

	Chronic AF	Controls	p value
LVEDD (mm)	48.8±4.5	47.5±3.4	0.29
LVEF (%)	58±4	60±3	0.20
LAD (mm)	43±5.5	35±2.4	<0.0001
LAVi (ml/m^2)	43.4±10.6	23.5±4.2	<0.0001
LVGLS (%)	-13.6±3.5	-21.2±1.3	<0.0001
LVCS (%)	-15±4.8	-22.5±2.2	<0.0001

Table 1. Echocardiographic LV parameters of patients with chronic AF and healthy controls.

Implantable Cardioverter / Defibrillator

P223

Indications and clinical outcome of subcutaneous ICD therapy in patients with heart failure

C Christoph Schukro[1]; M Sponder[1]
[1]Medical University of Vienna, Vienna, Austria

Background: Subcutaneous implantable cardioverter-defibrillators (S-ICD) are an innovative and less invasive alternative to transvenous ICD (TV-ICD) in selected patients. We aimed to investigate the indications for implanting S-ICD in clinical practice, as well as the prevalence of shock delivery and complications in patients with heart failure.
Methods and Results: From December 2012, data of 236 patients (30.5% female; age 48.6 ± 16.8 years) were gathered from 12 centres in Austria. Follow-up data over a period of 1.7 ± 1.1 years were available for 231 patients (in total 359.2 patient-years). Predominant underlying diseases were ischemic cardiomyopathy (iCMP; 32.0%), whereas dilated cardiomyopathy (dCMP) was found in 17.3%. The most frequent indications for implantation were sudden cardiac death survival (27.4%, of which only 1.3% had iCMP and dCMP, respectively), as well as primary prevention for iCMP (23.9%) and primary prevention for dCMP (12.8%). Appropriate shocks were documented in 16 patients (6.9%), iCMP being the predominant underlying disease in 8 patients. Arrhythmia conversion was successful in all patients, efficacy of the first shock was 96% in 48 of 50 episodes (both unsuccessful first shocks were found in patients with iCMP). Inappropriate shock were found in 12 patients (5.2%), of which 3 patients had iCMP and dCMP, respectively. Clinical complications needing surgical revision occurred in 8 patients (3.5%), of which 1 patient with surgical pocket revision had iCMP.
Conclusions: Overall, S-ICD were mostly implanted for primary prevention in patients with heart failure (36.7%). Clinical and functional complication rate was comparably low in this collective. In conclusion, S-ICD is a safe and efficient alternative in ICD candidates with heart failure, when no cardiac pacing is needed.

Cardiac Resynchronization Therapy

P224

Is the typical left bundle branch block pattern on the ECG caused by variable ventricular activation sequences?

L Riedlbauchova[1]; T Adla[2]; V Suchanek[2]; M Lozek[3]; J Tomis[1]; J Hozman[4]; V Tomek[3]; J Veselka[1]; J Janousek[3]
[1]University Hospital Motol, CardioVascular Center, Prague, Czech Republic; *[2]Motol University Hospital, Department of Radiology, Prague, Czech Republic*; *[3]Motol University Hospital, Children's Heart Centre, Motol University Hospital, Prague, Czech Republic*; *[4]Czech Technical University in Prague, Faculty of Biomedical Engineering, Prague, Czech Republic*

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Introduction: The presence and extent of ventricular dyssynchrony is currently estimated from the morphology and width of the QRS complex. However, similar ECG pattern may be caused by various ventricular activation sequences. This may then contribute to interindividualy different response to cardiac resynchronization therapy (CRT).
Methods: Electroanatomical (CARTO) mapping and MRI scan during spontanous rhythm was performed in 11 patients with typical left bundle branch block (LBBB, QRS 170 ± 14ms) and heart failure of ischemic (CAD, n = 2) and nonischemic (DCM, n = 9) etiology. Local activation time was set for each of 17-segment model of the left ventricle (LV). Presence and extent of scarring was analysed in the same 17-segment LV model using software Segment (Medviso).
Results: Regardless of the etiology, presence of typical LBBB was associated with diffuse prolongation of impulse conduction over the ventricles with right-to-left activation sequence (Fig.1). Basal lateral wall was a constant site of late activation. Heart was always abnormally rotated with its apex pointing towards the axila. In patients with DCM, focal scarring was either not present or in form of mid/ epicardial deposits only and generally didn't exceed >6% of the LV myocardial mass. Only individuals with CAD displayed focal scar (nontransmural anteroapically in one case, transmural inferiorly in the other one). Similar finding of subendocardial scarring was also present in 1 patient with DCM (Fig.2). Despite that all 3 patients presented with typical LBBB and CARTO mapping demonstrated activation sequence and site of late activation similar to the other individuals with LBBB. Reverse remodeling (?LVESV>15% and/or ?LVEF>5%) was evident in 10 patients. Only the one man with DCM and subendocardial scarring was CRT nonresponder.

Conclusion: It seems that typical LBBB is associated with a constant activation ventricular sequence regardless of the etiology and scar localization.

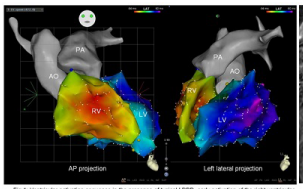


Fig.1: Ventricular activation sequence in the presence of typical LBBB- early activation of the right-ventricular free wall (red), interventricular delay 38ø18ms followed by interventricular septum activation. Site of the latest activation is located always in the basal or midventricular third of the LV lateral wall (violet).

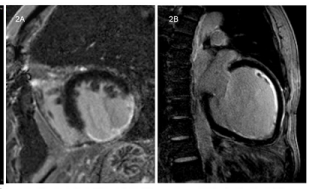


Fig.2: Scar localization in CAD patient with old transmural myocardial infarction inferolaterally (2A) and extent of subendocardial scarring in the only CRT nonresponder with idiopatic DCM (2B)

P225

QRS width can predict outcomes in cardiac resynchronization therapy: the size really matters.

J Juan Martinez Milla[1]; AM Romero-Daza[2]; C Garcia-Talavera[1]; B Arroyo[1]; A Garcia-Ropero[2]; A Miracle[1]; J Benezet-Mazuecos[1]; M Cortes-Garcia[1]; JM Rubio Campal[1]
[1]Foundation Jimenez Diaz, Madrid, Spain; [2]Mount Sinai Medical Center, Cardiology, New York, United States of America

Background: Cardiac Resynchronization Therapy with Defibrillator (CRT-D) has proven to reduce major adverse cardiac events (MACE) in patients with reduced LVEF, impaired New York Heart Association (NYHA) class and wide QRS complex. It has not been widely studied the width of the paced QRS (pQRS) in the patients outcomes. Our objective is to determine if there is any relationship between the pQRS duration and cardiovascular events.
Methods: All consecutive patients with CRT-D implant from January 2010 to June 2016 in our center were included. Electrocardiograms before and after CRT-D implantation were analyzed. Demographic data, incidence of appropriate ICD shocks, heart failure (HF) admissions and MACE were collected.
Results: We studied 100 patients (median age 73 years ± 10 years, 82% males). Baseline QRS duration was 162 ms (± 31 ms), pQRS mean duration was 142 ms (± 25ms). The mean follow-up was 34 ± 22 months and 17 patients (17%) had a MACE. After a multivariate analysis there was a significant relationship between the QRS duration and the risk of MACE (Hazard Ratio 1.02, 95% confidence interval, 1.00 to 1.03; P = 0.048). During follow-up there were no significant associations between the QRS duration, mortality, ICD shocks or NYHA class.
Conclusions: Paced QRS width is associated with negative outcomes in CRT-D patients. We estimate that for every millisecond the QRS is wider the probability of having a MACE is increased by 2%. Narrower paced QRS may represent a novel target during follow up of these patients.

Baseline characteristics	
Baseline Characteristics	
Age (y)	71 ± 10
Males	82 (82%)
Ischemic Cardiomyopathy	50 (50%)
Baseline QRS duration (ms)	162 ms ± 31 ms
Baseline LVEF (%)	23 ± 7
Clinical follow-up (36 ± 22 months)	
Heart failure admissions	24(24%)
MACE	18 (24%)
ICD shocks	10 (10%)
Follow-up LVEF (%)	32± 13
Paced QRS duration (ms)	142 ms ± 25ms
NYHA class (III-IV)	16 (16%)

P226

Response to cardiac resynchronization therapy in heart failure patients with mitral regurgitation

A Anna Vachulova[1]; M Sasov[1]; P Margitfalvi[1]; B Liska[1]; R Hatala[1]
[1]Clinic of Cardiology SZU and NUSCH a.s., Bratislava, Slovak Republic

Cardiac resynchronization therapy (CRT) is widely acknowledged as effective device therapy for patients with failing hearts with complete left bundle branch block. However, at least 30% of patients with CRT do not benefit from it. Definition for these "non-responders" (NR) includes absence of functional improvement (NYHA) and insufficient increase in ejection fraction of LV (<5%). Functional mitral regurgitation (MR) is a common finding in HF patients and is strongly associated with a poor prognosis.
The aim of this study was to analyse CRT response in patients with moderate to severe MR.
Patients and Methods: We retrospective screened all consecutive CRT recipients from our center with moderate to severe MR who were implanted during a 2-year period (01/2015-12/2016). We used univariant statistical analysis by Fisher test.
Results: Overall, 192 patients received CRT devices in our institution during the analyzed period. At the time of implantation, moderate to severe MR was present in 53 pts (27%). Complete follow-up data for 17.5 ± 5.4 months were available in 23 pts: 15 with CRT-D and 8 with CRT-P (20 men, mean age 65 ± 13.4 years). Ischemic etiology of HF was diagnosed in 13 pts (57%), in 9 pts (39.1%) permanent atrial fibrillation was present.
At the time of implantation following parameters were observed: mean NYHA functional class 2.7 ± 0.5, mean LVEF 26 ± 7%, severe MR was present in u 3 pts (13%), the 73 ± 0,5,
typical LBBB (strict Strauss criteria) was present in 13 pts (56.5%), mean QRS duration was 165 ± 32ms. 8 pts (7 men) were NR (35%). In 4-16 months after CRT implantation 5 (22%) pts died. Mean MR stage was in responders 3.2 ± 0.1 and in NR 3.1 ± 0. Following risk factors for becoming NR were: serum creatinine >140 μmol/l (p = 0.001), any kidney disease (p = 0.040) and AF presence (p = 0.049), Most importantly, pts implanted as class I indication (ESC) were NR in 37%, pts indicated as class IIa indication were NR in 62%.
Conclusion: Hemodynamically significant MR is common (27%) in pts undergoing CRT devices implantation. Kidney disease, atrial fibrillation and class II indication for CRT are associated with increase of non-response (up to 60%). Thus, strict adherence to class I indication (ESC) for CRT is crucial in HF pts with MR for minimizing non-response to CRT.

P227

Prognosis and predictor of CRT Hyper-responder

Y Yoshifumi Ikeda[1]; K Kato[1]; K Goto[1]; T Nagase[1]; Y Shiki[1]; S Tanaka[1]; S Asano[1]; H Mori[1]; M Tawara[1]; K Matsumoto[1]
[1]Saitama International Medical Center, Cardiology, Hidaka, Japan

Background: Cardiac resynchronization therapy (CRT) is effective treatment for drug-resistant severe heart failure patients with left ventricular dyssynchrony.Some of CRT patients will become hyper responders, but the long-term effects and predictors of hyper responder are still unknown.
Methods: We performed this retrospective analysis of 167 patients underwent CRT at our institute between April 2007 and December 2016. Normal responder and hyper responder were defined as more than 15-29% and 30% reduction of left ventricular end systolic volume using ultra sonic cardiography.
Results: The mean age was 65.9 ± 19.3 years (36-86 years old). The average period of postoperative monitoring was 34.6 ± 22.7months (mean 32 months).Number of responder and non responder was 96 (57.4%) and 71 (42.6%), In those, normal responder and hyper responder was 32 and 64 cases. Normal responder group and hyper responder group did not differed significantly according to patients characteristics for example, age, percentage of sex, category of NYHA, Body size, LVEF and LVESV. Overall mortality using kaplan-meier survival curve was 27.1% during follow-up time. There was significantly difference in mortality between responder and non responder (log rank test p = 0.001). Hyper responder tended to have a better survival rate than normal responder without significantly difference(P = 0.064). In univariate analysis, CLBBB, QRS over 150ms, optimal LV lead posision and continuously optimized AV delay have tendency of predictors of hyper responder (CLBBB, optimal LV lead position and continuously optimized AV delay with significantly difference). According to multivariate analysis using cox proportional hazard models, to continuously optimized AV deplay was an only significantly independent factor to detect hyper responder (HR 1.7:p = 0.006)
Conclusion: The long-term prognosis of hyper responders of CRT is good, and it is desired that all CRT patients become hyper responders. Therefore, continuous AV delay adjustment is an important factor.

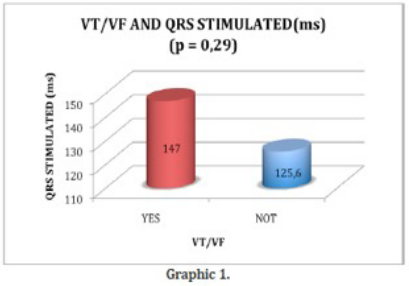
P228

Relationship between width and fragmentation of QRS stimulated in ICD-CRT in primary prevention and ventricular arrhythmia

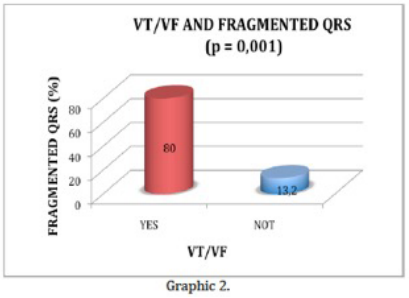
N G Uribe Heredia[1]; R Peinado Peinado[2]; J Balaguer Recena[1]; LG Piccone Saponara[3]; R Arroyo Espliguero[4]; S Moreno Reviriego[1]; ME Jimenez Martinez[4]; E Novo Garcia[4]; JL Garcia Gonzalez[4]; B Garcia Magallon[4]; MA San Martin Gomez[4]; C Toran Martinez[4]; E Diaz Caraballo[4]; S Garcia Ortego[4]; I Rodriguez Guinea[4]
[1]University Hospital of Guadalajara, Arrhythmia unit, Guadalajara, Spain; *[2]University Hospital La Paz, Arrhythmia unit, Madrid, Spain*; *[3]Hospital General de Ciudad Real, Nefrology, Ciudad Real, Spain*; *[4]Guadalajara University General Hospital, Cardiology Department, Guadalajara, Spain*

Introduction: In view of the limited published evidence of the determinants of future major ventricular arrhythmia events in patients with implantable cardioverter defibrillator implantation with cardiac resynchronization therapy in primary prevention (ICD-CRT), we developed this study in order to identify those patients with a higher probability of VT/VF, performing in them a closer follow-up and reinforcing the treatment in an early manner.
Methods: Retrospective descriptive study. A total of 43 patients who received an ICD-CRT according to the European Guidelines from January 2010 to December 2013 were evaluated. was programmed according to the narrowest paced QRS measured by the polygraph in the time of implantation. The presence of QRS fragmentation in at least 2 contiguous leads (notching in the ascending branch of the R wave, nadir of the S wave and/or presence of more than one R wave). Follow-up up to 3 years. Variables are compared using Chi2 test and Student's T test. SPSS 20.0. Statistical significance p <0.05, 95% IC.
Results: A total of 43 patients, mean age was 71.2 ± 9.9 years, 9.1% women, the mean ejection fraction was 31.7 ± 9.1% at the time of device implantation. 48.8% ischemic. 62.8% were in advanced stages of heart failure (NYHA III-IV) and 34.9% permanent atrial fibrillation. The mean baseline QRS was 164.1 ± 29.4ms and the biventricular pacing was 128.1 ± 21.9ms. At a mean follow-up of 33.3 ± 7.8 months, 11.6% (5 patients) had at least one VT/VF. The mean time from device implantation to the first episode of VT/VF was 20.2 ± 9.9 months, all of them male, of which 80% were ischemic, the mean QRS stimulated in these patients was higher than those who did not have TV/VF (147 ± 38.9ms Vs 125.6 ± 18.1ms) although no statistically significant differences were obtained (Graph1). Stimulated QRS fragmentation was more frequent among patients who had VT/VF, 80% Vs 13.2% p = 0.001 (Graph 2).
Conclusions: In our study, the measurement of the width of the QRS stimulated in patients with ICD-CRT implanted in primary prevention was not related to the occurrence of VT/VF. In contrast, the presence of fragmentation in the stimulated QRS was related to the increased probability of this type of arrhythmia.

VARIABLES	TV/FV	P	
SI	NO		
Age (years)	66,6 + 12,1	71,75 + 9,6	0,280
QRS Width Stimulated(ms)	147 + 38,99	125,55 + 18,0	0,288
Fragmented QRS on the ECG stimulated(%)	80	13,2	0,001
LVEF post TRC	35 + 14,88	44,53 + 11,06	0,089



Graphic 1.



Graphic 2.

P229

Comparsion of clinical response to de novo vs. upgrade cardiac resynchrinzation therapy: results from a long-term, high-volume, single-center registry

W Walter Richard Schwertner[1]; A Kosztin[1]; A Kovacs[1]; E Zima[1]; L Geller[1]; V Kutyifa[2]; B Merkely[1]
[1]Semmelweis University Heart Center, Budapest, Hungary; *[2]University of Rochester, Rochester, United States of America*

Background: Approximately 10-20% of patients with previously implanted cardiac defibrillator (ICD) or conventional pacemaker (PM) develops heart failure and becomes CRT candidates due to the chronic right ventricular pacing. However recent guidelines do not provide a comprehensive recommendation for CRT upgrade.
Purpose: We assessed the long-term clinical benefits who were upgraded to CRT from a conventional PM or ICD and compared to de novo implantations in our high-volume, single-center experience.
Methods: In our retrospective registry participants underwent CRT implantation according to the current guidelines. Patients registered from 2004 to 2017, with decreased ejection fraction (EF= 35%) wide QRS (= 120 ms) and symptomatic (NYHA II-IV class) heart failure. Primary endpoint was all-cause mortality, secondary endpoint was echocardiographic response. We performed Kaplan-Meier, Cox regressional analyses and propensity score matching by baseline ejection fraction (EF = 30% vs. <30%) and NYHA class (NYHA II vs. III-IV).
Results: From 1336 (288 upgraded vs. 1048 de novo CRT implanted) patients 701 reached (176 CRT-upgrade, 525 de novo CRT) the primary endpoint during the mean follow up time of 5.8 years. Patients in the upgrade group were older (71 vs. 67 years; p <0.01), had higher serum creatinine level (116 vs. 99 µmol/l; p <0.01), prior myocardial infarction (47% vs. 40%; p = 0.03) and atrial fibrillation (48% vs. 34%; p <0.001). By univariate analysis all-cause mortality was 46% higher in the Upgrade CRT group compared to De Novo CRT group (HR 1.46; 95% CI: 1.23-1.73; p <0.001). However multivariate analysis did not show a significant difference between the upgrade vs. de novo CRT groups (HR 1.17; 95% CI: 0.96-1.13; p = 0.13), after adjusting for relevant clinical covariates. We found similar improvements 12 months after the procedure, (?LVEF de novo 6.8% vs. upgrade 4.8%; p = 0.25) when echocardiographic response was evaluated. Based on propensity score matching, selecting 214-214 pair of patients confirmed our results independently from baseline EF and NYHA parameters.
Conclusions: CRT upgrade patients show higher risk of all-cause mortality compared to de novo CRT group, it is derived from co-morbidities. After adjusting relevant parameters they show similar long-term clinical response.

Chronic Heart Failure - Pathophysiology and Mechanisms

P230

REMODEL: Demonstration of REverse ReMODELing Effects of sacubitril/valsartan

S Kalantari[1]; DM Medvedofsky[2]; JG Grinstein[2]; ST Tayazime[1]; GK Kim[1]; NS Sarswat[1]; JR Raikelkhar[1]; BS Smith[1]; FM Maffessanti[1]; DB Beiser[1]; PW Ward[1]; GS Sayer[1]; RL Lang[1]; NU Uriel[1]
[1]University of Chicago Medicine, Chicago, United States of America; *[2]MedStar Hospital, Cardiology, Washington DC, United States of America*

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Background: Sacubitril/valsartan, an angiotensin receptor-neprilysin inhibitor, significantly reduced cardiovascular mortality and heart failure hospitalizations as compared to a target-dose enalapril-based regimen for patients with heart failure reduced ejection fraction. The pathophysiology underlying the benefit of sacubitril/valsartan and its effects on remodeling remain unknown. Here we seek to further elucidate the benefits of sacubitril/valsartan on ventricular remodeling, functional status, and quality of life.
Methods: In this prospective, single-arm longitudinal study, 40 patients who were on optimal guideline directed medical therapy were initiated on sacubitril/valsartan after an appropriate wash-out period from prior ACEI or ARB therapy. The primary end-point was the degree of reverse remodeling (change in LV and RV size, volume, shape, and function) as assessed by 2D and 3D-TTE with surface analysis at 3 months compared to baseline using paired t-tests. Secondary endpoints were peak VO2, 6-minute walk distance, and quality of life parameters.
Results: There was significant reduction in left ventricular and left atrial volumes with an increase in left ventricular ejection fraction as well as improvement in LV conicity index at 3 months (Table 1). Interim analysis revealed improved 6-minute walk distance (428 ± 105 vs 451 ± 115 m; p = 0.006) and a trend towards improvement in peak VO2 (18.5 ± 5.7 vs 19.2 ± 5.6; p = 0.19) at 3 months.

Conclusion: Compared to a background of historical guideline directed medical therapy, transition to sacubitril/valsartan led to significant reverse remodeling and improved functional status.

Table 1.

N = 36	Baseline	3 month	P value
LVEDD (cm)	6.2 ± 0.8	6.0 ± 0.8	< 0.01
LVESD (cm)	5.3 ± 0.9	4.9 ± 1.0	< 0.01
LVEDV (ml)	247 ± 68	222 ± 58	<0.01
LVESV (ml)	170 ± 58	148 ± 50	< 0.01
LV EF (%)	32 ± 7	35 ± 7	< 0.01
LV conicity (%)	0.75 ± 0.03	0.76 ± 0.03	0.03
LV sphericity (%)	0.73 ± 0.05	0.72 ± 0.06	0.11
LA volume (ml)	96 ± 39	87 ± 30	< 0.01
RVEDV (ml)	149 ± 50	142 ± 43	0.05
RVESV (ml)	77 ± 35	72 ± 30	0.11
RV EF (%)	50 ± 10	50 ± 9	0.97
Septal curvature (%)	0.86 ± 0.2	0.82 ± 0.2	0.35
Free-wall curvature (%)	1.13 ± 0.1	1.16 ± 0.07	0.29

P231

Evaluation of left intraventricular synchrony in asymptomatic left bundle branch block patients by non-invasive parameters obtained from radionuclide ventriculography

A Agustin Pastor Fuentes[1]; R Mata[1]; J Perea[1]; A Nunez Angulo[1]; J Pais[1]
[1]*Hospital Universitario Getafe, Getafe (Madrid), Spain*

Background: Radionuclide ventriculography (RNV) has been used to assess left ventricular ejection fraction (LVEF) and ventricular synchrony by means of phase and amplitude parametric images and their quantitative-derived parameters, where mean phase angle (PA) represents mean time of ventricular contraction onset and the standard deviation (SD) of the PA relates to synchrony of ventricular contraction. Objective: To study global and regional LVEF data and LV synchrony parameters obtained by a RNV in patients (P) with an asymptomatic left bundle branch block (LBBB)
Methods: LVEF and LV synchrony data obtained from a RNV in 18 normal ECG P were compared with the same parameters in 45 asymptomatic LBBB P with no previous cardiac history, who were referred for evaluation because of the abnormal ECG finding. SD of PA was derived from the phase histogram obtained in the best left anterior oblique view, and expressed both in grades (°) or milliseconds (ms). Regional LVEF was derived from each of the four segments that ventricular blood pool was divided (Septal, Apex, Inferior-Lat, Post-Lat) in the same left anterior oblique view.
Results: In 18 LBBB P, mean LVEF was < 50% and > 50% in the remaining 27 P (40 ± 7% vs 60 ± 6%p<.001). Other results are expressed in the table below. In the whole LBBB group, a weak but good and inverse correlation between SD of PA and LVEF was found (r= - 0.53, p < 0.001), so the greater SD of PA, the less LVEF.
Conclusions: Abnormal LV systolic function is encountered in 40% of asymptomatic ambulatory P with LBBB. All LBBB P, show left intraventricular mechanical asynchrony data estimated by RNV parameters, although higher in P with depressed LVEF. We may speculate that abnormal LVEF in 40% of LBBB group is due to an undiagnosed primary cardiomyopathy since regional wall motion is globally affected in this group compared with control P and those LBBB P with preserved EF or due to a LV remodeling because of LBBB-dependent electrical asynchrony itself

RESULTS

	CONTROL	LBBB/EF>50%	LBBB/EF <50%
SD(°)	20 + 12	39 + 21**	56 + 17***
SD (ms)	45 + 25	92 +57 **	129 + 40***
Septal (%)	50 + 7	45 + 9 *	26 + 10 ***
Apex (%)	60 + 8	62 + 7	44 + 10 ***
Inferior-Lat (%)	61 + 11	66 +11	51 + 14***
Inferior-Post(%)	69 + 12	74 + 12	56 + 15***

*: p<.05 vs control;**:p<.01 vs control;***:p<.001 vs control and LVEF>50%

P232

Skeletal muscle metabolism characteristics of HFpEF and HFrEF patients

N Scherbakov[1]; L Klug[2]; S Von Haehling[3]; HD Duengen[4]; M Boschmann[2]; W Doehner[1]
[1]*German Center for Cardiovascular Research, partner site Berlin, Berlin, Germany*; [2]*Charité - Campus Berlin Buch (CBB), Experimental & Clinical Research Center, ECRC, Berlin, Germany*; [3]*University Medical Centre Göttingen, Innovative Clinical Trials, Department of Cardiology and Pneumology , Göttingen, Germany*; [4]*Charite - Campus Virchow-Klinikum (CVK), Department of Cardiology, Berlin, Germany*

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Background: Heart failure (HF) is associated with insulin resistance (IR) and there is a clear difference between the HF with reduced ejection fraction (HFrEF) and preserved ejection fraction (HFpEF). However, tissue metabolism is still not well characterized in these patients.
Purpose In this pilot study we investigated in situ skeletal muscle glucose metabolism in HFpEF and HFrEF vs. healthy controls.
Methods: Vastus lateralis muscle tissue perfusion and glucose metabolism were studied using the microdialysis technique at fasting condition and during an oral glucose challenge. Interstitial fluid energy substrate metabolites as well as tissue perfusion were assessed using ethanol dilution method. Eight men with HFrEF (age 59 ± 14 yrs, BMI 26.5 ± 3.5 kg/m^2, NYHA I-III, LVEF 32 ± 9%) and six men with HFpEF (age 65 ± 10 yrs, BMI 26.8 ± 5.8 kg/m^2, NYHA I-II, LVEF 54 ± 2) participated in this cross-sectional study after a 12h overnight fasting. Nine healthy men of similar age and BMI served as controls.
Results: In fasting condition there were no significant differences in tissue perfusion and marker metabolite levels. However, after the glucose load, tissue perfusion and glucose supply tended to be lower in HFrEF, not in HFpEF vs. controls (Fig. A, B). Furthermore, tissue lactate (indicator for anaerobic glycolysis) tended to be higher in HFrEF vs. HFpEF and controls (Fig. C). Postprandial tissue pyruvate (indicator for aerobic glycolysis) did not differ significantly between the groups (Fig. D,E). Finally, tissue glycerol (indicator for lipid mobilization) decreased similarly in all groups after the glucose load (Fig. F).
Conclusions: Postprandial muscle tissue perfusion and glucose supply might be reduced in HFrEF but not HFpEF patients that is in line with differences in insulin resistance observed in patients with HFrEF and HFpEF. However, this finding is not associated with an impaired aerobic glucose metabolism in HFrEF patients at resting.

P233

Morphological structure of diaphragm in patients with different class of heart failure

GP Arutyunov[1]; KV Ilina[2]; EA Kolesnikova[1]; AG Arutyunov[1]; EV Tulyakova[2]
[1]*The Russian National Research Medical University named after N.I. Pirogov , Moscow, Russian Federation*; [2]*Moscow City Hospital No 4, Moscow, Russian Federation*

Patients with heart failure (HF) have respiratory muscles disorders and as a result high risk of pneumonias, poor prognosis and lethal outcomes. The purpose: To study the morphological features of diaphragm and its role in ventilation disorders in patients with HF. Materials: 32 diaphragm autoptat (14 male, 16 female) with different lethal outcomes (8 myocardial infarction, 9 stroke, 5 pulmonary embolism, 10 pneumonia) were taken in 1 hour after death. Pats were selected from research data base of patients with NYHA I-IV class HF. Inclusion criteria: patients with CAD, arterial hypertension and NYHA I-IV class HF with stable standard doses of drug therapy.Exclusion criteria: patients = 75 years, with COPD, obesity, diabetes mellitus, alcohol abuse.
Methods: percentage composition of muscle, connective, adipose tissue, collagen and number of fibroblasts were studied in diaphragm autoptat. Results of functional status (vital capacity, forced vital capacity were taken from research data base. Test were done during dynamic examination no longer then within 3 months of lethal outcome date.
Results: Pats with NYHA I HF had 90% of muscle tissue, 6% connective tissues, 4 % adipose tissue, 5 fibroblasts. Pats with NYHA II HF had 80% of muscle tissue, 15% connective tissues, 8 % adipose tissue, 25 fibroblasts. Pats with NYHA III HF had 70% of muscle tissue, 20% connective tissues, 11 % adipose tissue, 23 fibroblasts. Pats with NYHA IV HF had 60% of muscle tissue, 35% connective tissues, 18 % adipose tissue, 10 fibroblasts. Collagen content in connective tissue - 2% in pats with NYHA I, 5% in pats with NYHA II, 8% in pats with NYHA III, 15% in pats with NYHA IV.Conclusion: The diaphragm undergoes structural changes with the increase in functional class of HF - connective tissue, collagen and adipose tissue is growing while muscle tissue is decreasing. Respiratory functional disorders directly correlate with the products of inflammation process - the high content of collagen and connective tissue. At the same time the other members of inflammatory

process - fibroblasts grow from I to III NYHA class and tend to decline in patients with IV class HF.

P234
Clinical phenotypes and prognosis of patients with chronic heart failure with mid-range ejection fraction

AA Nasybullina[1]; OV Bulashova[1]
[1]*Kazan State Medical University, Kazan, Russian Federation*

The European Society of Cardiologists of 2016 proposed the allocation of patients with heart failure (HF) with mid-range ejection fraction (HFmrEF). As studies have shown, patients with different ranges of ejection fraction differ in a number of clinical signs and prognosis.
Goal: Study of clinical variants and outcomes of patients with chronic heart failure (CHF) with mid-range left ventricular ejection fraction.
Material and methods. The study included 76 patients without acute decompensation of CHF I-IV functional class NYHA, 66.1 ± 10.4 years, with a duration of CHF of 8.5 years. The causes of CHF were ischemic heart disease in 89.5% and hypertension in 10.5%. Heart failure with preserved ejection fraction (HFpEF) was observed in 55.3%, HFmrEF - 23.7%, reduced EF (HFrEF) - 21,1%. The results of a walking test, a scale for evaluating the clinical status, and quality of life were evaluated. Fatal and non-fatal cardiovascular events (CVE) were analyzed during the first year: cardiovascular mortality, myocardial infarction, cerebral stroke, acute decompensation of CHF, thrombotic complications.
Results: Comparative analysis, depending on the range left ventricular ejection fraction, showed that HFmrEF occupies an intermediate position between HFpEF and HFrEF for a number of clinical characteristics (sex, scale for evaluating the clinical status, quality of life were evaluated, weighed heredity, duration of CHF). However, patients with HFmrEF, in contrast to HFpEF, were older in age (p = 0.04), with a predominance of III-IV NYHA stage, which was confirmed by comparing the results of the walking test (182.5 [110, 272], m 350 [250, 400], p <0.001).
Analysis of the structure of the CCC showed that the HFmrEF also occupies an intermediate position between the HFpEF and HFrEF in the frequency of all CVE (17.6%, 10.8%, 18.8%, respectively), myocardial infarction (5.9%, 0%, 6.2%), thrombotic complications (5.9%, 5.4%, 6.2%). However, cardiovascular mortality in HFmrEF was significantly lower than with HFpEF and HFrEF (0%, 2.7%, 12.5%), as well as the incidence of acute decompensation of CHF (0%, 2 , 7%, 6.2%).
Conclusion: Despite the similarity of some clinical characteristics, patients with HFmrEF have a special clinical profile and a prognosis for cardiovascular mortality and the incidence of acute decompensation of heart failure.

P235
Predictors of non-recovery of left ventricular systolic function in breast cancer patients with chemotherapy induced left ventricular dysfunction

HJ Hyun Ju Yoon[1]; KH Kim[1]; JY Cho[1]; HJ Park[1]; JC Park[1]
[1]*The Heart center of Chonnam National University Hospital, Gwangju, Korea Republic of*

Background and objectives: Non-recovery of left ventricular (LV) function is known to be a predictor of poor prognosis in patients with chemotherapy induced LV dysfunction (LVD). Although the incidence or natural history of chemotherapy induced LVD in patients with breast cancer has been changed after the introduction of target therapy with trastuzumab, the predictors of LV functional non-recovery in patients with breast cancer that developed LVD in association with trastuzumab use after conventional chemotherapy has been poorly studied. Therefore, the aim of the present study was to investigate the predictors of LV functional non-recovery in breast cancer patients with LVD in association with trastuzumab use after conventional chemotherapy.
Methods: Among 826 patients treated with trastuzmab after chemotherapy for breast cancer, a total of 243 patients with chemotherapy induced LVD were divided into 2 groups; recovery group (n = 195, 51.4 ± 10 years) vs non-recovery group (n = 48, 49.6 ± 10 years). Chemotherapy induced LVD was defined as LV ejection fraction (EF) of < 55% or the decrease in LVEF >10% from the baseline LVEF on follow-up echocardiography after chemotherapy. LV functional recovery was defined as the improvement of LVEF > 10% on follow up echocardiography as compared to the LVEF measured at the time of diagnosis of chemotherapy induced LVD. Clinical, laboratory, and echocardiographic findings were compared.
Results: On follow up echocardiography, chemotherapy and trastuzumab induced LVD was improved in 195 patients (80.2%), whereas LVD was persisted in 48 patients (19.8%). In univariate analysis, low levels of hemoglobin and albumin, larger LV end-diastolic and end-systolic dimension, lower LVEF and global longitudinal strain, and higher pulmonary artery systolic pressure were significantly associated with non-recovery of LVD. In multivariate regression analysis, severe LV dysfunction (HR10.09, CI = 4.232-24.05, p < 0.001), pulmonary hypertension (HR 2.783, CI = 1.277-6.065, p = 0.010), and anemia (HR 2.149, CI = 1.091-4.232, p = 0.027) were independent predictors of non-recovery of LV function in breast cancer patients with chemotherapy and trastuzuamb induced LVD.
Conclusion: Non-recovery of LV function in breast cancer patients with chemotherapy and trastuzumab induced LVD was not uncommon (19.8%), and severe LV dysfunction, pulmonary hypertension and anemia were independent predictors of sustained LV dysfunction. Therefore, careful monitoring and intensive medical management for LV dysfunction in breast cancer patients with these characteristics should be considered.

P236
No short-term cardiac toxicity of novel biological therapies for advanced non-small cell lung cancer in routine clinical practice

L Loredana Mrak[1]; R Marcun[2]; T Cufer[1]; M Podbregar[3]
[1]*University Clinic of Respiratory and Allergic Diseases Golnik, Department of Medical Oncology, Golnik, Slovenia*; [2]*University Clinic of Respiratory and Allergic Diseases Golnik, Department of Cardiology, Golnik, Slovenia*; [3]*University Medical Centre of Ljubljana, Cardiovascular Intensive Care Unit, Department for Anesthesiology and Surgical Intensive Care, Ljubljana, Slovenia*

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Background and Purpose: New biological therapies significantly improved overall survival rates for patients with advanced non-small cell lung cancer (NSCLC). The effects of such treatment on heart function in routine clinical practice are currently poorly known. The aim of the study was to evaluate short-term effects of biological therapies for advanced NSCLC on heart function among patients treated in our routine clinical practice.
Methods: This was a single center, prospective, observational pilot study which included 17 consecutive patients (10 female, 64 ± 9 years) with advanced NSCLC treated with biological therapy at one academic center. Patients received a clinical evaluation before, after two and after four months of treatment, at that time points also NT-proBNP, troponin T and echocardiographic examination were performed.
Results: 8 patients were treated with programmed cell death 1 receptor blocking antibodies (6 with pembrolizumab, 2 with nivolumab), 9 with a tyrosine kinase inhibitor (1 with gefitinib, 2 with erlotinib, 1 with afatinib, 5 with osimertinib). Normal cardiac function was required at baseline. After two and four months of treatment no patient developed symptoms of heart failure, body weight was stable, troponin T and NT-proBNP (248 ± 116 ng/L, 289 ± 117 ng/L, 242 ± 81 ng/L, respectively, p = 0.9) remained within normal range Dimensions of heart cavities remained normal. Left ventricular ejection fraction remained normal (69.6 ± 1.6%, 70.3 ± 1.8%, 72.2 ± 1.2%, respectively, p = 0.8) as did diastolic left ventricular function. Left ventricular filling pressure (E/e': 10.5 ± 0.8, 10.3 ± 0.9, 10.0 ± 0.7, respectively, p = 0.9) and right ventricular pressure remained unchanged.
Conclusion: This pilot study showed no short-term cardiac toxicity of novel biological therapies for advanced NSCLC in routine clinical practice. Further studies are necessary to confirm short and long-term cardiac safety of novel biological therapies.

P237
Cardiovascular risk profiles in cardio-oncology - time matters.

J Ferreira-Martins[1]; L Tan[1]; L Venneri[1]; J Cevallos[1]; N Pareek[1]; E Ciburiene[1]; P Moliner-Borja[1]; V Chambers[1]; RS Khattar[1]; AJ Baksi[1]; SD Rosen[1]; AR Lyon[1]
[1]*Royal Brompton Hospital, London, United Kingdom*

Introduction: Referrals to Cardio-Oncology services occur before, during and after cancer treatment. It is not known whether patients referred prior to cancer therapy have a different cardiovascular risk profile to those referred with late cardiovascular complications after cancer treatment.
Purpose: To determine whether patients referred before and after cancer treatment differ with regards to 1) the burden of cardiovascular comorbidities; 2) cardiac biomarker profile; 3) left ventricular ejection fraction (LVEF) and tissue characteristics assessed by cardiac magnetic resonance (CMR); as well as 4) their pharmacologic cardiac treatment.
Methods: First appointments in a Cardio-Oncology service were categorized either as "Pre-treatment" (Pre), during treatment (excluded) or "Post-treatment" (Post) if the purpose was an assessment before initiation of cancer treatment or an evaluation of cardiovascular complications after cancer therapy, respectively. A retrospective analysis of clinical, biomarker, CMR and treatment information from a specifically designed database of patients referred between February 2011 and October 2017 was included.
Results: 384 patients were referred during the study period (Pre n = 214; Post n = 170). The commonest primary neoplasia was breast cancer (Pre n = 42, 19.6%; Post n = 75, 48.4%). Pre-existing cardiovascular co-morbidities were significantly more

prevalent in the Pre- than in the Post-treatment group (61.2% vs 26.5%, p < 0.0001): arterial hypertension (Pre 47.2% vs Post 22.4%, p < 0.0001), ischaemic heart disease (Pre 16.8% vs Post 0.6%, p < 0.0001) and valvular heart disease (Pre 6.5% vs Post 1.2%, p < 0.001). Despite this, a significantly higher proportion of patients in the Post-treatment group had Troponin T >15ng/L (Pre 3.6% vs Post 11.7%, p < 0.01) and higher BNP levels (Pre 107 ± 115ng/L vs Post 164 ± 243ng/L, p < 0.01). LVEF was significantly lower in the Post-treatment group (Pre 65.1 ± 11.8% vs Post 54.5 ± 12.4%, p < 0.0001). However, the presence of late gadolinium enhancement was more common in the Pre treatment group (Pre 39.3% vs Post 26.2%, p = 0.016) possibly reflecting a higher prevalence of pre-existing cardiovascular comorbidities. More patients in the Post-treatment group were on beta-blockers (Pre 39.9% vs 54.2%, p < 0.01) and angiotensin-converting enzyme inhibitors/angiotensin receptor blockers (Pre 48.3% vs Post 71.7%, p < 0.0001).
Conclusion: Cardio-Oncology services offer care to distinct cancer populations - those at risk and those who have developed cardiovascular complications. Patients referred after cancer treatment have evidence of cancer therapy-related cardiotoxicity with an unfavorable biomarker and cardiac function profile. This is despite a lower prevalence of pre-existing cardiovascular comorbidities and higher use of cardiac medication. Personalised care is advised to improve outcomes in cancer survivors and populations before and after treatment have different requirements.

P238
Cardiotoxicity of treatment hepatitis C by triple combination of antiviral drugs

J Jakub Simka[1]; R Pudil[1]; S Plisek[2]
[1]*Faculty of Medicine in Hradec Kralove, Charles University, 1st Department of Medicine, University Hospital Hradec Kralove, Hradec Kralove, Czech Republic*; [2]*Faculty of Medicine in Hradec Kralove, Charles University, Department of Infectious Diseases, University Hospital Hradec Kralove, Hradec Kralove, Czech Republic*

Background: Antiviral drugs are considered as drugs that may be potentially cardiotoxic. Due to prolongation of the QTc interval may affect the incidence of severe ventricular arrhythmias.
Purpose: The aim of the retrospective study was to assess the effect of three antiviral drugs on the QTc interval and find patients who are at increased risk of developing malignant ventricular tachyarrhythmias.
Methods: The study includes 23 patients (14 men, 9 women, 46 ± 18 years) treated by combination of three antiviral drugs: interferon alpha, ribavirin, and NS3/4A protease inhibitor. We evaluated 12 leads electrocardiogram (ECG) before treatment, 3 ± 1 months after treatment and 6 ± 1 months after treatment. Bazett's formula was chosen to calculate QTc interval. ECGs assessment was digitized by the program ImageJ.
Results: Before initiation of therapy, the following mean parameters were obtained: Heart rate (HR): 69 ± 12 / min, QTc: 412 ± 35 ms. After 3 months: HR: 72 ± 11 / min, QTc: 412 ± 33 ms. After 6 months: HR: 64 ± 12 / min., QTc: 405 ± 28 ms. In the follow-up population, the QTc interval was prolonged after 3 months of treatment in 53 % of patients and after 6 months of treatment in 43% of patients. QTc prolongation over 450 ms was noted in 1 (4 %) patient. New treatment-related repolarization changes were detected in 1 (4 %) patient.
Conclusion: The study shows that combination therapy of 3 antiviral drugs significantly does not prolong the QTc interval and does not cause severe pathological changes on ECG. Patients undergoing this treatment are not endangered by the development of heart disease as an undesirable side effect. ImageJ was first used to evaluate ECGs in this study and has proved to be an appropriate and very accurate interval-measuring program.
The study was supported by project Progres Q40/03.

P239
Right ventricular to arterial elastance ratio, internal work, and late gadolinium enhancement as prognostic markers in pulmonary hypertension.

H Hamdy Shams Eddin[1]; KH Elmaghraby[1]; S Demitry[1]; A Aboelnour[1]
[1]*Assiut University, Assiut, Egypt*

Background: External cardiac work i.e. the P-V loop area, correlates poorly with heart's energy demands until IW component is added. Ea/Emax measures ventriculo-arterial coupling. LGE is known to be present within RVIPs in PH, but its prognostic role is insufficiently explored.
Purpose: To investigate the impact of right ventricular internal work (RVIW), arterial to ventricular end-systolic elastance ratio (Ea/Emax), RV insertion point (IP) late gadolinium enhancement (LGE); and its temporal change on outcome in pulmonary hypertension (PH).
Methods: Cardiac magnetic resonance (CMR) of 124 PH patients (aged 60 ± 13, 85 Females) was retrospectively examined for RV volumetric and functional indices and RVIP LGE %. Right heart catheterization (RHC) performed within 2 ± 1 months of CMR was reviewed. Ea/Emax was derived as RV end-systolic volume (ESV)/RVSV. Internal work was estimated as RVESV × (RV end-systolic pressure-RV diastolic pressure).Patients were followed from date of CMR for up to 5 years for MACE (death, hospitalized RV failure, initiation of parenteral prostacyclin, sustained ventricular arrhythmia, or referral for lung transplantation). Follow-up CMRs for 44 patients were examined for temporal change of LGE (? LGE).
Results: 48/124 (39%) patients had MACE. The strongest predictor of MACE was Ea/Emax (OR = 1.46, P = 0.01), followed by RVIW, versus mPAP, RV mass, RVEF, and IP LGE. Similar results were obtained for time-to-MACE (Ea/Emax HR = 1.44, p <0.001). Using Vanderpool et al.'s proposed Ea/Emax cut-off of 1.94 produced an early split in time-to-MACE (Log rank = 5.31, p = 0.02). ? LGE (median=-1.97, range=-25.87 to 16.48) predicted time to MACE.
Conclusions: Higher Ea/Emax and RVIW herald worse prognosis in PH. Not only is RVIP LGE static, but also it can decrease over time in PH. This is the 1st study addressing this concept. Failure to reduce RVIP LGE % (? >1.97) predicts worse prognosis.

P240
Could inferior vena cava diameter replace the central venous catheter to estimate central venous pressure?

R Mosaddegh[1]; M Chardoli[1]; M Ahmadi[1]
[1]*Iran University of Medical Sciences & Health Services, Emergency Medicine Management Research Center, Firoozgar Hospital, Tehran, Iran (Islamic Republic of)*

Introduction: It is important to know hemodynamic status of the patient when we need to resuscitate the patient whose heart condition is unknown. Bedside ultrasound is a quick and noninvasive method of hemodynamic monitoring. The researcher wants to compare the accuracy of inferior vena cava (IVC) ultrasound with central venous catheter (CVC) in estimating the Central Venous Pressure (CVP).
Methods: Adult patients who need to insert a CVC enrolled in the study. The CVP was measured used the CVC in place. The diameter of the IVC was measured in the expiration with a portable two-dimensional ultrasound and the Caval index was calculated. The cut of point, sensitivity, specificity, positive predictive value and negative predictive value of Caval index was calculated to estimate central venous pressure then.
Results: Ninety-nine patients with median age of 69 years old was enrolled in the study. The mean of CVP and IVC diameter before and after fluid challenge was 5.25 ± 3.59 vs 6.68 ± 3.43 (P value: 0.003) for CVP and 7.44 ± 5.13 vs 9.84 ± 5.29 (P value: 0.002) for IVC diameter. There is no significant difference between area under receiver operating characteristic curve of CVP vs IVC diameter (AUC 0.973 vs 0.974 P value: 0.78). The best cut off point to estimate CVP off less than 8 cm H20 was IVC diameter of less than 10.9 mm with sensitivity and specificity of 90.79 and 100 percent respectively.
Conclusion: Measuring the IVC diameter with bedside ultrasound in emergency department could estimate the CVP of the patients with good correlation and good sensitivity and specificity with CVC measuring of CVP. This method is fast, non-invasive and accurate and could replace the invasive method of CVC measuring the CVP.

P241
N-terminal prohormone brain natriuretic peptide is a weak indicator of cardiac function and haemodynamic response to exercise in chronic heart failure

M Parovic[1]; NC Okwose[1]; SJ Charman[1]; S Cassidy[1]; P Doherty[2]; K Bailey[3]; J Skinner[3]; PM Seferovic[4]; GA Macgowan[5]; D Djordje Jakovljevic[6]
[1]*Newcastle University, Institute of Cellular Medicine, Newcastle upon Tyne, United Kingdom*; [2]*University Of York, Department of Health Sciences, York, United Kingdom*; [3]*Royal Victoria Infirmary, Cardiology, Newcastle upon Tyne, United Kingdom*; [4]*Clinical center of Serbia, Cardiology, Belgrade, Serbia*; [5]*Freeman Hospital, The Cardiothoracic Centre, Newcastle upon Tyne, United Kingdom*; [6]*Buckinghamshire New University, Research Centre for Society and Health, Chalfont St Giles, United Kingdom*

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Background/Aim: Heart failure is associated with high mortality and poor quality of life. N-terminal prohormone brain natriuretic peptide (NTproBNP) plays a critical role in the diagnosis and management of patients with chronic heart failure. There is no evidence that NTproBNP can predict overall cardiac function and haemodynamic response to exercise in heart failure. Cardiac power output is a unique haemodynamic measure of overall cardiac function and is one of the strongest predictors of mortality in chronic heart failure. The aim of the present study was to assess the relationship between NTproBNP, rest and exercise haemodynamics and quality of life.

Methods: A single-centre pilot study recruited 20 patients (mean age 68 ± 7 years) with stable chronic heart failure due to left ventricular systolic dysfunction (LVEF = 31 ± 8%). Blood samples for NTproBNP were taken and all patients completed a maximal graded cardiopulmonary exercise stress testing using cycle ergometer with non-invasive gas exchange and haemodynamic (Bioreactance, Cheetah Medical, USA) monitoring. Quality of life was assessed using Minnesota Living with Heart Failure Questionnaire. Cardiac power output, expressed in watts, was calculated as the product of mean arterial blood pressure and cardiac output.
Results: The average value (± SD) for NTproBNP was 820 ± 1056 ng/L. Rest and peak exercise values for haemodynamic variables were: cardiac power output, 1.19 ± 0.21 vs. 2.93 ± 0.75 watts; cardiac index 3.1 ± 0.4 vs. 6.7 ± 1.1 L/min/m2; stroke volume index 48 ± 8.8 vs 63.1 ± 14.1 ml/beat/m2; heart rate 67 ± 7 vs. 111 ± 21 beats/min; peak oxygen consumption 1423 ± 353 ml/min; peak work rate 82 ± 20 watts; and quality of life score 27 ± 18. The NTproBNP was not significantly correlated with measures of cardiac function at rest i.e. cardiac power output (r= -0.04, p = 0.87), cardiac index (r= -0.02, p = 0.95), stroke volume index (r= -0.17, p = 0.48), mean arterial blood pressure (r= 0.14, p = 0.55), and heart rate (r= 0.22, p = 0.34). There was a weak to moderate negative relationship between NTproBNP and peak exercise haemodynamic function i.e. cardiac power output (r= -0.51, p = 0.02), cardiac index (r= -0.50, p = 0.02), stroke volume index (r= -0.04, p = 0.86), mean arterial blood pressure (r= -0.30, p = 0.20), and heart rate (r= -0.26, p = 0.27). In contrast, the NTproBNP correlated well with exercise tolerance i.e. peak oxygen consumption (r= -0.60, p = 0.01), and work rate (r= -0.62, p < 0.01), but not with quality of life (r= -0.03, p = 0.92).
Conclusion: Present findings demonstrate only weak to moderate strength relationship between N-terminal prohormone brain natriuretic peptide and measures of cardiac function at rest and in response to exercise. The NTproBNP should not be considered as an indicator of cardiac function and haemodynamic response to exercise in chronic heart failure.

P242

Role of NT-proBNP and sST2 meanings in the acute myocardial infarction in the development of left ventricle systolic dysfunction in the post-infarction period.

F Fatima Akhmatova[1]; Il Chukaeva[1]; VN Larina[1]
[1]*Russian National Research Medical University, Moscow, Russian Federation*

Introduction: One of the adverse effects of myocardial infarction (MI) is heart failure (HF), it is developed under the influence of several factors. The study of the multicomponent nature of cardiac function disorders in the acute period of MI can contribute to predicting left ventricular (LV) dysfunction in the post-infarction period.
Purpose: to study the role of changes in the acute MI period of natriuretic peptide (NT-proBNP) and stimulating growth factor (sST2) in the development of systolic LV dysfunction in the early and late post-infarction period.
Methods: 27 patients with MI were included into the study, the age was 52 [44;64] years, the criteria for exclusion were the occurrence of complications in the acute period of myocardial infarction and chronic heart failure. The study groups were formed on the first day of MI according to the change of the level HF markers in serum: the group 1 - an increase in NTproBNP concentration of more than 300 pmol/l and sST2 - more than 35 ng/ml were registered in14 patients; the group 2 - NTproBNP of less than 300 pmol/l and sST2 of less than 35 ng/ml were registered in 13 patients. The groups differed significantly in the median concentration of NTproBNP and sST2], ? = 0,006. The median age in the groups did not differ significantly. The LV function of patients was assessed according to the results of echocardiography on the 1st day, 14th day of MI (early post-infarction period) and in 6 months (late post-infarction period). The LV ejection fraction (LVEF %), LV end-diastolic dimension (LV EDD, mm) and LV end-systolic dimension (LV ESD, mm), left atrial dimension (LAD, mm) were determined. Statistical analysis was performed using Mann-Whitney U Test.
Results: There was no signs of LV dysfunction in the groups in the first day MI: in the group 1 LVEF - 52,5 [44,0; 68,0]%, LV EDD - 47,0 [42,0; 56,0] mm, LV ESD - 33 [30,0; 44,0] mm, LAD - 36,5 [35,0; 38,0] mm; in the group 2 LV EF - 56,0 [55,0; 68,0]%, LV EDD - 45,0 [40,0; 50,0] mm, LV ESD - 31 [26,0; 36,0] mm, LAD - 36,0 [34,0; 41,0] mm, p>0,05. As of for the14th day of MI the group 1 showed signs of LV systolic dysfunction - reduction of LVEF, however, the differences were unreliable: LVEF in the group 1 - 47,9 [34,5; 60,0]%, in the group 2 - 57,0 [55,0; 59,7]%, p>0,05. The remaining echocardiographic parameters also did not differ statistically. After 6 months MI in the group 1 the significant systolic LV dysfunction was determined in comparison with the group 2: LVEF in the group 1 - 48,4 [35,0; 53,6]%, in the group 2- 60,5 [52,0; 64,0]%, ? = 0,03. The remaining echocardiographic indicators were of no statistically significant differences.
Conclusion: The change in two markers of heart failure - the natriuretic peptide NT-proBNP and stimulating growth factor sST2 - in first day of myocardial infarction is associated with the development of left ventricular systolic dysfunction in the late post-infarction period.

P243

QRS duration impact on recovery of left ventricular ejection fraction in patients with Heart Failure

A Ana Neto[1]; D Seabra[1]; L Marques[1]; H Guedes[1]; A Andrade[1]; P Pinto[1]
[1]*Hospital Centre do Tamega e Sousa, Cardiology, Penafiel, Portugal*

Introduction: Heart failure (HF) is the end-stage of several cardiac diseases. The recovery of left ventricular ejection fraction (rLVEF) is an important prognostic factor in these patients (pts). A majority of pts with HF have ECG disturbances, some with delayed intraventricular conduction (DIVC). Delayed activation of the lateral wall of the left ventricle can produce dyssynchronous contraction, which impairs ventricular pump efficacy. Mechanical desynchrony is usually associated with abnormalities of intraventricular conduction (IVC), particularly left bundle branch block (LBBB).
Aims: Evaluate the presence of DIVC in pts followed in a HF clinic (HFC) and their correlation with recovery of LVEF, after at least 3 months of optimal medical therapy (OMT).
Methods: Unicentric and retrospective study; included pts with reduced ejection fraction (EF) and admitted in the HFC with a previous diagnosis of HF for at least 6 months or had prior hospitalization for acute HF. Assessed QRS duration (QRSd) after OMT, HF etiology (ischemic and non-ischemic), EF (before and after OMT). rLVEF was defined as an increase = 10% in LVEF assessed by echocardiography. Pts were divided in two groups: rLVEF (G1) and non-rLVEF (G2). Excluded pts who already had definitive pacemaker at HFC admission. CRT pts data was evaluated before the device implantation.
Results: Included 276 pts, with mean age of 60.5 ± 13.1 years. 24.6% were female. Mean QRSd was 129.6 ± 30.8 milliseconds (ms). 42.0% had ischemic etiology, with no significant differences between HF etiology and QRSd. 27.9% had LBBB and 44.2% non-LBBB delayed IVC. 30.1% had rLVEF after OMT. In univariate analysis, there were an inverse correlation between QRSd and EF at admission and this correlation remained after OMT (p < 0.001). Mean QRSd was inferior in rLVEF pts (p = 0.004). Conclusion: In this cohort of HF pts, a majority of pts showed delayed intraventricular conduction. An inverse correlation was showed between mean QRSd and admission EF, and this correlation remained after OMT. rLVEF was associated with shorter QRSd. These results highlight the importance of electrical desynchrony in myocardial contraction efficacy and, therefore, in prognosis of HF pts.

P244

Global strain of left ventricular myocardium and ejection fraction in STEMI patients

V Valentin Oleinikov[1]; V Galimskaya[1]; A Golubeva[1]; S Kupriyanova[1]
[1]*Penza State University, Penza, Russian Federation*

Aim: to compare different types of global strain of left ventricular (LV) myocardium in patients with ejection fraction (EF) more than 50%, and EF less than 50% 24 weeks after STEMI.
Methods: the study included 99 patients with STEMI (51.3 ± 8.6 years), confirmed by ECG, coronary angiography (CAG), troponin I level, CK-MB. The control group consisted of 50 healthy volunteers (52.2 ± 9.4 years). Echocardiography was performed on the MyLab device (Esaote, Italy) with ejection fraction (EF) determination by Simpson method at 7-9th days from the disease onset and 24 weeks after. The global longitudinal (GLS), circumferential (GCS) and the radial (GRS) strain (-%) were determined using X-Strain ™ software.
Results: Patients were divided into two groups 24 weeks after STEMI: the first group - 76 patients with LVEF > 50%, the second - 23 patients with EF < 50%. GLS values were 17.42 (95% CI 7.96, 26.88) in the 1st group, in the 2nd group - 13.45 (95% CI 3.17, 23.73) (p < 0.01); GCS - 20.07 (95% CI 6.51, 33.63) and 15.07 (95% CI 0.59, 29.55) (p < 0.01), respectively. GRS values in groups 1 and 2 were 32.69 (95% CI 12.75, 52.63) and 25.8 (95% CI 3.0, 48.6) (p < 0.01). GLS was 21.56 (95% CI 20.75, 22.38) in the control group, and differed from group 1 and group 2 by 18% (p < 0.01) and 37% (p < 0.01); GCS - 26.05 (95% CI 24.84, 27.27), 23% (p < 0.01), 42% (p < 0.01), respectively; GRS - 37.65 (95% CI 34.82, 40.48) differed from the strain values by 13% (p < 0.01), and 32% (p < 0.01), respectively, in groups 1 and 2.
Conclusion: EF decrease is accompanied by a reliable reduction in deformation parameters. The global strain parameters differed in patients with preserved EF from those of healthy individuals to a lesser extent.

P245

The usefulness of pulse oximetry for the evaluation of left ventricle ejection fraction in patients with heart failure

A Alexey Naimushin[1]; R Beigel[1]; S Matetzky[1]
[1]*Sheba Medical Center, Ramat Gan, Israel*

Background: The rapid determination of cardiac output (CO) is important for the evaluation of patients presenting to the emergency room, outpatient clinic or during hospitalization. The most accepted technique for CO measurement in the clinical setting is the thermodilution method. Yet, this method requires the use of sophisticated invasive equipment, time consuming measurements and experienced personnel. Pulse oxymetry is a useful method for monitoring patients in different clinical scenario yet it use for CO evaluation had yet to be studied. We sought to evaluate the use of pulse oxymetry for evaluation of CO.
Methods: We evaluated 32 consecutive patients with systolic heart failure (ejection fraction < 40%) and without know lung disease, during their treatment in our day care congestive heart failure unit. Oxygen saturation was measured at admission and if it was less then 95% at room air the second test was done after nasal oxygen supplementation of 3 l/min. The time to correction of basal saturation to +3% after oxygen supplementation was measured.
Results: Average LVEF was 30.25 ± 5.32% with an average basic saturation of 91.9 ± 1.53% without any correlation (r=-0.05). The average time for saturation correction to +3% was 38.5 ± 6.45 seconds and demonstrated a good correlation with systolic function (r=-0.9).
Conclusion: Pulse oxymetry can be a useful parameter for the quick evaluation of patients with known heart failure in regard to left ventricular ejection fraction.

P246

Left ventricular remodeling and endothelial dysfunction in postmenopausal women

N Natalia Lareva[1]; A Govorin[1]; E Luzina[1]
[1]*Chita State Medical Academy, Chita, Russian Federation*

Purpose: To assess the relationship of endothelial dysfunction and left ventricular remodeling in postmenopausal women.
Methods: 203 postmenopausal women were included in the study: 142 with surgical menopause (44,3 ± 5,4 years, menopause duration 3,8 ± 2,4 years); and 61 with natural menopause (46,2 ± 4,7 years, menopause duration 4,3 ± 2,1 years). All patients underwent general clinical examination, ambulatory blood pressure monitoring (Cardiotens-01, Meditech, Hungary), echocardiographic examination with systolic and diastolic left ventricular function assessment. Endothelial function was assessed by the level of metabolites of nitric oxide and the number of desquamated endotheliocytes. Statistical methods such as Cruskell-Walles criteria and chi-square test were used.
Results: Only 39 postmenopausal women (19,2%) had normal LV geometry; 89 pts (43,8%) demonstrated LV concentric hypertrophy, 57 pts (28,1%) - concentric remodeling and 18 women (8,9%) - eccentric hypertrophy. Nobody of included postmenopausal women had LV systolic function failure. Patients with LV concentric hypertrophy had LV diastolic dysfunction in 84,3% cases (75 pts); with LV concentric remodeling - in 52,6% cases (30 pts), with LV eccentric hypertrophy - in 31,6% cases (6 pts), this difference was statistically significant. Nitroxide-producing endothelial function was inhibited in all women included in the study, with a minimum level of nitric oxide metabolites recorded in patients with concentric LV hypertrophy; in the same group the maximum number of desquamated endotheliocytes was recorded (by 40-60% more than in patients with other types of LV remodeling, $p < 0.05$). The functional state of the endothelium in patients with LV diastolic dysfunction was changed to a greater degree than in those who had no diastolic filling disorders (the total number of nitric oxide metabolites was 12-17% lower in comparison with those patients who did not have disturbed LV relaxation processes). Significantly more pronounced in patients with impaired diastolic filling were the processes of desquamation of endotheliocytes: their number was 3.1 times higher than in healthy individuals, which was 148% of the level of this indicator in the group of women with normal parameters of diastolic function. Conclusions. Thus, violations of LV structure and function in postmenopausal women are interrelated with changes in the functional state of the endothelium. Most endothelial dysfunction is expressed in patients with concentric LV hypertrophy, as well as with its diastolic dysfunction. This relationship, perhaps, causes the rapid progression of cardiovascular complications in patients with violations of LV geometry that occur with an increase in the LV myocardial mass and changes in the characteristics of its cavity, as well as in patients with worsened diastolic filling of the LV.

P247

Evaluation of right ventricular diastolic function in patients with coronary artery disease: gender differences

A N Alexey Sumin[1]; EV Korok[1]; OG Arhipov[2]
[1]*RAMS Scientific-Research Institute for Complex Studying of Cardiovascular Diseases, Kemerovo, Russian Federation*; [2]*Sanatorium Topaz, Mysky, Russian Federation*

Background: Right ventricular dysfunction is an independent predictor of cardiovascular mortality after coronary artery bypass grafting. Early diagnosis of right ventricular (RV) dysfunction is important for an accurate assessment of the patient's prognosis. There are few studies focused on the gender differences in the evaluation of RV diastolic function in patients with coronary artery disease (CAD).
Purpose: To assess the detection rate of RV diastolic dysfunction in men and women with CAD.
Methods: 719 patients with CAD who underwent outpatient examination were included in the study. All patients were assigned to two groups according to their gender: Group 1 - men (n = 432, 61 [55, 67] years), and Group 2 - women (n = 287, 62 [56, 67] years), and echocardiography (ECHO-CG) was performed. Preserved RV diastolic function was considered with the Em / Am ratio in the range of 0.8-2.1, the Em / e't ratio < 6, and the deceleration time of early diastolic mitral and tricuspidal flows >120 msec. Alterations in the above set ranges and reduced distribution velocity of early tricuspid flow (DVETF) < 35 cm/s were defined as RV diastolic dysfunction.
Results: DVETF was higher in women compared with men. There were no differences found in the other ECHO-CG parameters in both groups (Table). RV diastolic dysfunction was commonly found in both groups, compared to RV systolic dysfunction (50.5% and 45.6% vs. 17.6% and 15%, respectively). There were no significant differences between the study groups (p>0.05).
Conclusion: There were no gender differences in the detection rate of RV diastolic dysfunction in CAD patients. However, RV diastolic dysfunction was more common than RV systolic dysfunction.

Right ventricular diastolic indexes

Parameters	Group 1 men (n = 432)	Group 2 women (n = 287)	?
$?_m/?_m$	1.2 [1.0;1.5]	1.2 [1.0;1.4]	0.536
DTE_t, ME [LQ, UQ] msec	177 [155;207]	170 [148;200]	0.100
DVTF, ME [LQ, UQ] cm/sec	38 [33;43]	39 [34;45]	0.001
$?'_t$, ME [LQ, UQ] cm/sec	13 [10;16]	13 [11;16]	0.513
$?'_t$, ME [LQ, UQ] cm/sec	15.4 [12.2;19.6]	16.1 [12.9;19.6]	0.238
$?'_t/?'_t$, ME [LQ, UQ]	0.8 [0.7;1.0]	0.8 [0.7;1.0]	0.819
$?_t/?'_t$, ME [LQ, UQ]	4.0 [3.2;4.9]	3.9 [3.2;4.9	0.416

Em / Am - the ratio of early and late diastolic transmitral flows; DT?t, - deceleration time of early diastolic tricuspidal flows; DVTF - distribution velocity of early tricuspidal flow; et, - early diastolic tricuspid annular velocity; a't - late diastolic tricuspid annular velocity; e't / a't, Et / e't is the ratio of the early filling velocity of the right ventricle to the early diastolic tricuspid annular velocity.

P248

Longitudinal strain abnormalities predict worse outcome in patients with recovered ejection fraction

J J Jort Merken[1]; HP Brunner-La Rocca[1]; J Weerts[1]; J Verdonschot[1]; J Schroder[1]; M Hazebroek[1]; V Van Empel[1]; SRB Heymans[1]; C Knackstedt[1]
[1]*Maastricht University Medical Centre (MUMC), Cardiology, Maastricht, Netherlands*

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Background: Due to modern heart failure (HF) therapy, some patients show normalization of left ventricular ejection fraction (LVEF), classified as patients with heart failure with recovered LVEF (HFrecovEF). Still, the question remains whether this means full recovery of left ventricular systolic function or just normalization of LVEF. Global longitudinal strain (GLS) analysis at echocardiography may provide additional insight to study systolic function.
Purpose: Here, we determined the percentage of persistent GLS abnormalities in patients with HFrecovEF, and determined its prognostic value.
Methods: A total of 212 patients with HFrecovEF were included in one center. HFrecovEF was defined as an initial LVEF <35% and improvement to 55% or higher. GLS was determined on routine echocardiography using a dedicated software. GLS was considered normal <-21.5% and abnormal >-21.5%. Patient characteristics and adverse events during follow-up were taken from the medical records. All

etiologies (diseased myocardium, abnormal loading conditions, and arrhythmias) for an initial decreased LVEF were included. The primary endpoint was death or HF hospitalization.
Results: Despite normalization of LVEF after a follow-up of 56 ± 21 months (range 12-90 months), 168 (79%) of patients with HFrecovEF displayed a pathologic GLS. These patients showed a significant worse outcome of all cause death and HF hospitalization (p-value = 0.039) as compared to patients with normal GLS (Figure 1).
Conclusions: In conclusion, the majority of patients with HFrecovEF still have an abnormal systolic function of the LV, measured by GLS. Patients with HFrecovEF and an abnormal GLS exhibit a significantly worse outcome. Whether these patients would benefit from continuation of HF therapy, requires further investigation.

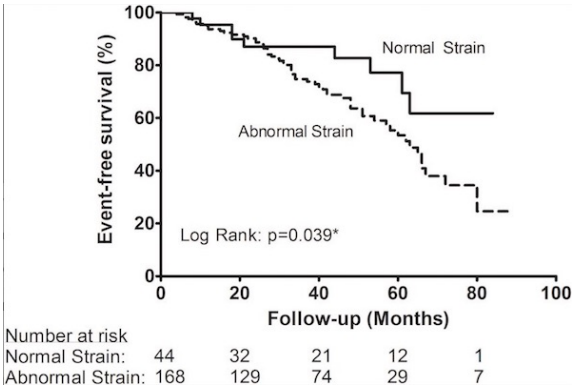


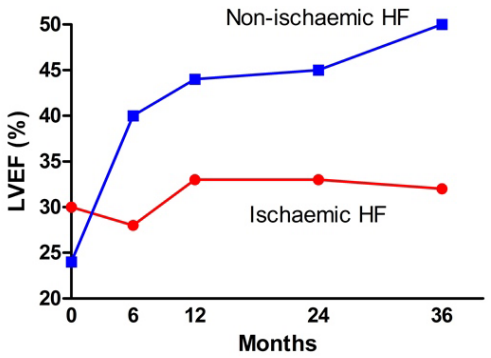
Figure 1

P249

Left ventricular remodelling and prognosis of patients with de novo heart failure: differences between ischaemic and non-ischaemic aetiology

J C Van Den Berge[1]; JF Veenis[1]; JJ Brugts[1]; K Caliskan[1]; OC Manintveld[1]; KM Akkerhuis[1]; JW Deckers[1]; AA Constantinescu[1]
[1]*Erasmus Medical Center, Department of Cardiology, Rotterdam, Netherlands*

Background: As a result of optimal medical heart failure (HF) therapy, left ventricular (LV) function may improve in HF patients. However, studies on LV remodelling were mostly performed in outpatients with chronic HF, and rarely in patients admitted with de novo HF. Moreover, there are no studies investigating LV remodelling in relation to ischaemic or non-ischaemic aetiology.
Purpose: Therefore, we studied the LV remodelling and prognosis of patients admitted with acute decompensated de novo HF. Furthermore, we investigated whether there was a difference in LV remodelling and prognosis between patients with ischaemic and those with non-ischaemic HF.
Methods: We included all consecutive patients admitted with de novo HF in the period 2008 through 2016. Patients with a history of any cardiac disease or a left ventricular ejection fraction (LVEF) at admission above 40% were excluded. LV remodelling was assessed by serial measurement of LV end diastolic (LVED) diameter, LV end systolic (LVES) diameter and LVEF by echocardiography.



	Baseline	6 months	12 months	24 months	36 months
Non-ischaemic HF	24 (17-31)	40 (32-50)	44 (38-55)	45 (36-55)	50 (38-62)
Ischaemic HF	30 (24-37)	28 (23-35)	33 (26-43)	33 (29-37)	32 (27-44)

Figure.

Results: We included 123 patients (mean age 49 ± 14 years, 57% male, 42% ischemic HF) with acute decompensated de novo HF. At discharge, the median LVED and LVES diameter were 58 mm (IQR 53-65) and 47 mm (IQR 39-55), respectively, whereas the mean LVEF was 28% (IQR 22-36). In the total population, the LVED, LVES and LVEF improved over time, especially in the first six months (LVED -4 mm [p < 0.001], LVES -6 mm [p < 0.001] and mean LVEF +6% [p = 0.01]). In patients with ischaemic HF, we could not observe an improvement in LVED (p = 0.28), LVES (p = 0.58) and LVEF (p = 0.19) during the first six months (Figure). In contrast, in the first half year after discharge, patients with non-ischaemic HF had significant remodelling with improved LVED (p < 0.001), LVES (p < 0.001) and LVEF (p < 0.001; Figure). A total of 30 patients (24%) reached the composite end-point during 3 years of follow-up. In patients with non-ischaemic HF only 17% reached the composite end-point of death, HF rehospitalisation, left ventricular assist device (LVAD) implantation or heart transplantation during 3 years of follow-up , compared to 35% of the patients with ischaemic HF (p = 0.02).
Conclusions: In patients admitted with de novo HF, we found improving left ventricular diameters (both LVED and LVES) and increasing LVEF over time, with the most improvement in the first 6 months after discharge. This LV remodelling was observed in patients with non-ischaemic HF but not in those with ischaemic HF. The prognosis of patients with non-ischaemic aetiology of de novo HF was more favourable than the prognosis of their counterparts with ischaemic HF.

P250

Myocardial deformation in STEMI patients with different types of left ventricle remodelling

V Galimskaya[1]; A Golubeva[1]; S Kupriyanova[1]; V Valentin Oleinikov[1]
[1]*Penza State University, Penza, Russian Federation*

Aim: to compare the deformation characteristics of left ventricle myocardium, determined using the speckle tracking technique, 3 months after STEMI in patients with different types of cardiac remodeling.
Methods: 74 patients (51.3 ± 8.6 years) with STEMI confirmed by ECG, coronary angiography (CAG), troponin I, and CK-MB were included in the study. Inclusion criteria: significant stenoses of one infarct-related coronary artery, PCI for the first hours after the pain onset. Exclucion criteria: history of myocardial infarction and other cardiovascular diseases. All patients underwent echocardiography on the MyLab device (Esaote, Italy) at the 7th day and 3 months later. End-diastolic volume index (EDVi) was evaluated. Using the X-Strain™ software, the Global longitudinal (GLS), circumferential (GCS) and radial (GRS) strain (-%) were determined. The criterion for pathological remodeling was considered to be an EDVi increase of more than 20% on the following measurement 3 months after the STEMI.
Results: After 3 months, the patients were separated onto two groups depending on the EDVi increase: one group included 43 (58%) people without echocardiographic signs of LV remodeling; group 2 comprised 31 (42%) patients. In the 1 and 2 group GLS had the following values: 17.71 (95%CI 16.23, 19.18) and 14.39 (95%CI 12.66, 16.13) (p <0.01), respectively; GCS - 20.84 (95%CI 18.97, 22.69) and 15.57 (95%CI 13.38, 17.76) (p <0.01). The GRS values in group 1 were 33.95 (95%CI 30.99, 36.91), in the 2nd group 28.79 (95%CI 25.31, 32.28) (p <0.05). Conclusion: the global longitudinal, circumferential and radial strain were significantly less in patients with rapidly progressive LV remodeling after STEMI, than in the group without pathological remodeling.

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Heart rate variability and left ventricle ejection fraction in patients after the acute Q-wave myocardial infarction

NU Zakirov[1]; YG Kevorkova[1]; A Amayak Kevorkov[1]; Z Fazylbekova[2]
[1]*Republican Specialized Center of Cardiology, Tashkent, Uzbekistan*; [2]*Tashkent Pediatric Medical Institute, Tashkent, Uzbekistan*

Purpose: to estimate interrelations between heart rate variability (HRV) and left ventricle ejection fraction (LVEF) in patients after the acute Q-wave myocardial infarction (Q-AMI).
Materials and Methods: Study included 96 male patients (average age of 52.78 ± 9.05 y. o.) survived after the primary Q-AMI. The diagnosis of Q-AMI was established in accordance with the ESC criteria (2012). All patients underwent Holter ECG monitoring (HMECG) with the estimation of HRV and transthoracic echocardiography. HMECG performed on standard therapy on 10-14 day of the Q-AMI and after the 6 month of follow up. Standard therapy included antiplatelet agents, beta-blockers, ACE inhibitors or ARB, statins and amiodarone (if necessary). Interpretation of HRV parameters was made with estimation of SDNN, SDANN, RMSSD and pNN50. As a decrease in the total HRV, a reduction of SDNN = 100 ms was assumed. Statistical analysis was performed using nonparametric ANOVA ?2 test. Differences were considered significant for p <0.05.

Results: It was noted that afer the 6 month level of the SDNN, SDANN and pNN50 values increased on therapy by more than 20%, and the rMSSD - more than 12%. In patients with reduced HRV at 6 months of follow-up, were noted significantly lower initial values of the LVEF (49.28 ± 11.89% vs. 51.98 ± 10.39%; p = 0.038), compared with patients with normal HRV. There was also a significant positive correlation between baseline LVEF values and SDNN (R = 0.21, p = 0.041) and SDANN (R = 0.22, p = 0.034) after the 6th month follow-up. Also, group of patients with a significant baseline decrease in EF <40% compared with patients with baseline EF>40% were further analyzed. It was noted that patients with significantly reduced EF, at baseline, had reliably lower rates as SDNN (84.8 ± 25.9 ms vs. 103.5 ± 28.9 ms, p = 0.035) and SDANN (75.3 ± 21.9 ms vs. 92.9 ± 26.9 ms, p = 0.038).
Conclusions: Group of patients with reduced total HRV at 6 months of follow-up demonstrates significantly lower initial values of the LVEF and there is a significant positive correlation between baseline LVEF values and total HRV level on 6th month of follow-up. Low level of LVEF on 10-14 day of Q-AMI may be consider as a 6-month predictor of decreasing of HRV which in combination points to worsening of prognosis for such category of patients.

6 month dynamics of HRV indicators

	Initial	6 month	ANOVA χ^2	p
SDNN, ms	102.7±32.5	124.0±34.4	30.556	0.000
SDANN, ms	91.2±29.6	110.1±30.0	25.043	0.000
rMSSD, ms	23.4±12.7	26.3±12.2	12.517	0.000
pNN50, %	5.0±7.2	6.0±6.9	9.000	0.003

P252

Effect of high beta-blocker dose on the long term prognosis of patients with heart failure with reduced ejection fraction

M Marie Lazarova[1]; FM Malek[2]; MT Taborsky[1]; AI Ignaszewski[3]
[1]University Hospital Olomouc, cardiology, Olomouc, Czech Republic; *[2]Na Homolce Hospital, Cardiology, Prague, Czech Republic*; *[3]St Paul's Hospital, Cardiology, Vancouver, Canada*

Background/Introduction: Pharmacotherapy of patients with HFREF with reaching target medication doses is one of the key factors contributing to better prognosis, especially concerning beta-blockers. Despite this fact, the general HF patient population reach target medication doses only in a small percentage according to clinical practice data and registries.
Purpose: We aimed to evaluate the effect of target and more than target beta-blocker dose on a long term prognosis of HFREF patients.
Methods: We analyzed data of 739 HFREF patients who were followed during years 1975-2011 and achieved long-term clinical stabilization and reverse left ventricle remodeling. We analyzed the established pharmacotherapy of this patient group, especially concerning beta-blocker doses.
Results: 739 HFREF patients who stabilized their disease in long term period and reached LV reverse remodeling were followed for 6.4 (median) years. 65.9% of patients had non-ischemic cardiomyopathy (NICMP). Their median LV ejection fraction (LVEF) improved from 25.0% at baseline to 50.0% at the time of the latest data collection. 79.7% of patients survived 18.1 years after diagnosis of HF according to Caplan-Meier survival analysis, that is much better long term prognosis than general HF patient population. 78.1% of the patients were receiving recommended target or higher than target doses of beta-blockers. The most frequently used beta-blocker was carvedilol, target dose of 50 mg daily and more had 40.6% of beta-blocker patients. Target daily bisoprolol dose of 10 mg and more and metoprolol dose of 200 mg and more had 27.0% and 10.5% of beta-blocker patients, respectively.
Conclusion: The prognosis of patients with HFREF who developed LV reverse remodeling was much more favorable than in the general population of HF patients. Optimal pharmacotherapy, especially reaching of target beta-blocker doses might have significantly contributed to this.

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Clinical and humoral determinants of congestion in HFrEF patients

I Ivana Jurcova[1]; J Benes[1]; M Kotrc[1]; A Jabor[1]; J Kautzner[1]; J Kovar[1]; P Jarolim[2]; V Melenovsky[1]
[1]Institute for Clinical and Experimental Medicine (IKEM), Cardiology, Prague, Czech Republic; *[2]Brigham and Women's Hospital, Boston, United States of America*

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Purpose: Congestion is a classical feature of heart failure (HF) that is present in some but not all HF patients. The goal was to identify clinical and humoral factors associated with congestion and its impact on prognosis.
Methods: 371 stable HFrEF patients underwent clinical examination, echocardiography, blood sampling, Minnesota Living with HF Questionnaire (MLHFQ) and were longitudinally followed. Death, LVAD implantation or heart transplantation were considered as an adverse outcome. Patients scoring between 3-5 in question 1 of MLHFQ were considered congestion-positive.
Results: Congestion was present in 31% of patients. After a median follow-up of 521 days, 37% of all patients had an event. In Cox analysis, the presence of congestion was associated with 68% higher risk of an adverse outcome (p = 0.003). Patients with congestion were more symptomatic (NYHA 2.9 ± 0.5 vs 2.7 ± 0.6, MLHFQ sum: 61 ± 18vs 41 ± 21) and had more often edema at the time of the examination (50% vs 17%) than those that were congestion-free (all p?0.001). Presence of congestion was strongly (?0.001) associated with RV dysfunction, tricuspid regurgitation, dilated inferior vena cava, cardiac cachexia (15 vs 31%), furosemide daily dose, hyponatremia, hypoalbuminemia, but unrelated to age, HF duration and etiology, sex, systolic blood pressure, body mass index, left ventricular function, cardiac output, hemoglobin, eGFR and MRA or ACEi/ARB dose. The levels of mid-regional pro-adrenomedullin (MR-proADM), BNP, copeptin, endothelin-1, GDF-15, FGF-13 and adiponectin were significantly (p < 0.05) associated with congestion; on the contrary no relation between congestion and the level of insulin, cortisol and troponin was found.
Conclusion: Congestion is associated with distinct set of humoral factors and predominantly with the RV but not LV function. Congested patients suffer with more pronouced HF symptoms and have shorter survival.

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Left atrial dysfunction as a pathophysiological determinant of clinical status, right ventricular dysfunction and pulmonary hypertension in HFrEF patients with significant mitral regurgitation

G Palmiero[1]; L Ascione[1]; A Ferro[1]; E Melillo[1]; R Ascione[1]; S Severino[1]; P Caso[1]; V Monda[1]
[1] AO dei Colli-Monaldi Hospital, Department of Cardiology, Naples, Italy

B: Functional mitral regurgitation (FMR) and left atrial function (LAF) are determinants of clinical status but little is known about the effects of FMR on LAF in HFrEF patients.

Table 1

	FMR (n = 38)	SFMR (n = 59)	P
Age (yrs)	62,5±14,9	66,0±9,7	ns
Men (%)	5 (13,1%)	9 (15,2%)	ns
Ischaemic aetiology (%)	24 (63,1%)	46 (79,6%)	ns
NYHA Class	2,0±0,8	2,7±0,8	0,0001
LVEDV (ml)	174,3±52,9	256,3±72,1	0,0001
LVEF (%)	30,1±3,5	28,4±5,6	ns
LAVI (ml/m^2)	46,3±17,3	67,9±23,2	0,0001
E/E'	17,4±6,9	27,7±10,5	0,0001
sPAP (mmHg)	34,3±7,4	50,6±13,3	0,004
TAPSE (mm)	19,6±2,9	16,5±4,2	0,02
EROA (mm^2)	0,11±0,4	0,23±0,8	0,0001
LAAEF (%)	28,0±9,4	19,1±8,9	0,0001
LAPEF (%)	25,1±8,1	18,1±7,5	0,0001
TLAEF (%)	45,8±10,4	33,5±11,0	0,0001
LAEI (%)	92,7±44,8	54,7±26,4	0,0001

P: To assess the effects of significant FMR (SFMR) on LAF and their consequences on RV function and pulmonary pressures.
M: 97 patients with HFrEF in sinus rhythm with mild-to-severe FMR were enrolled. MR severity was assessed and patients dichotomized based on the presence of SFMR (3-4+) at TTE. LAF was evaluated using the phasic method. LA volumes were measured at 3 time-points (before mitral valve opening, at P-wave onset and at MV closure) and LAF parameters thus calculated: reservoir as LAEI, conduit as LAPEF, pump as LAAEF and total emptying function as TLAEF. LA dysfunction (LA-Dys) was defined for TLAEF values below the median and the 2 gruops subdivided on its presence.
R: The groups were well matched (Table 1). Pts with SFMR displayed higher larger LV and LA volumes, higher LV filling and pulmonary pressures and lower TAPSE and LAF values compared to those in FMR group. SFMR/LA-Dys+ group showed a worse clinical status and higher incidence of pulmonary hypertension (PH) and right ventricular dysfunction (RV-Dys) (Fig. 1)

C: SFMR seems to affect LAF in HFrEF patients and SFMR and LA-Dys to play a complimentary role in determining clinical status, RV-Dys and PH in HFrEF patients.

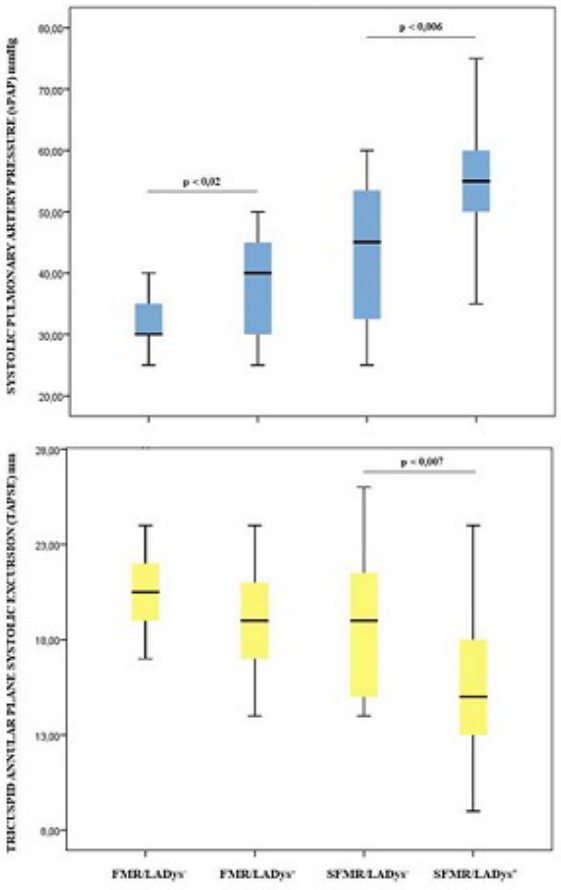

Fig. 1

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Initial experience of pharmacological treatment with sacubitril-valsartan: baseline clinical characteristics and follow-up at one year of clinical use

RA Montiel Quintero[1]; I Irene Menduina Gallego[1]; M Grova Marco[1]; E Perez Nogales[2]; JM Medina Gil[2]; M Galvan Ruiz[1]; M Singh[1]; M Fernandez De Sanmamed Giron[1]; A Garcia Quintana[1]
[1]*University Hospital Dr Negrin, Cardiology, Las Palmas De Gran Canaria, Spain*; [2]*University Hospital Insular of Gran Canaria, Las Palmas De Gran Canaria, Spain*

Introduction: An important novelty, with incorporation in the current guidelines of heart failure(HF) is sacubitril/valsartan. This has shown reduced risk of death and hospitalization in patients with chronic HF and reduced left ventricular ejection fraction (LVEF).Propouse: To describe the baseline demographic and clinical characteristics, in addition to the one-year follow-up of patients who were prescribed sacubitril/valsartan. Method: We analyzed 106 patients with HF and reduced LVEF assessed in the cardiology outpatient clinic of two universitary hospitals between October 2016 and October 2017, who were treated with sacubitril/valsartan.
Results: an average age of 63.56 years (+/-11.68), being 68.87% (n = 73) men. 51.52% (n = 51) were in NYHA II and 47.47% (n = 47) remaining in NYHA III. 74.53% (n = 79) were hypertensive, 49.06% (n = 52) diabetic and 51.89% (n = 55) dyslipemic. 30.19% (n = 32) had atrial fibrillation, 38.46% (n = 40) complete block of the left branch of Has of His and of these 55 %% (n = 22) received resynchronization therapy. 49.52% (n = 52) was ischemic heart disease and 40% (n = 42) idiopathic dilated cardiomyopathy. 75.47% (n = 80) of the subjects had the LVEF severely depressed (< 35%). The average LVEF was 30.4% (+/-6.94). The mean value of serum creatinine was 1.11 mg/dL (+/-0.33), serum potassium 4.48 mEq/L (+/-0.52) and NTproBNP 4072 pg/mL. The mean systolic blood pressure at the start of treatment was 127.14 mmHg (+/-21.69). 95.19% (n = 99) received betablockers, 44.23% (n = 46) spironolactone, 39.05% (n = 41) eplerenone, 80.58% (n = 83) loop diuretics and 24.27% (n = 25) ivabradine. In the majority (59.43%; n = 63), sacubitril / valsartan was started with the low dose (24/26 mg). With respect to follow-up, the mean time was 198.24 days (+/-137.6). At the end of the follow-up only 27.35% (n = 29) of the patients had achieved the target dose. The majority (35.84%, n = 38) received intermediate doses and 27.35% (n = 29) received low doses. Mean serum creatinine at follow-up was 1.16 mg/dl (+/-0.38) and only 17.07% (n = 14) reported values above 1.5 mg/dL. The mean NTproBNP at follow-up was 2323.01, with a reduction of 42.95% with respect to the baseline. 20.75% (n = 22) went to the emergency room or was admitted due to decompensation of the HF. The mortality was 4.71% (n = 5). Conclusion: When compared to the profile of patients in the Paradigm HF clinical trial, the subjects in our series were in worse functional class, had higher levels of pro-BNP and lower LVEF. In addition, a significant percentage of the patients who started with this treatment had resynchronization therapy, which is why we conclude that our patients are in more advanced stages of the ICC, which is why we should emphasize the beginning of this innovative and effective treatment in more early stages of the disease in order to improve the prognosis and quality of life.

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The role of sacubitril-valsartan treatment on right ventricular function and cardiorespiratory response in patients with chronic heart failure. Single-centre experience from Myltiple patient program o

C Christina Chrysohoou[1]; E Oikonomou[1]; G Vogiatzi[1]; E Paschalidis[1]; N Maggas[1]; V Katsi[1]; A Avgeropoulou[1]; I Kallikazaros[1]; D Tousoulis[1]
[1]*University of Athens, Athens, Greece*

Introduction: Cardiorespiratory response, right ventricular and global diastolic function is known to deteriorate the clinical course of patients with chronic compensated systolic heart failure, even under optimal treatment. In this work we sought to evaluate the role of sacubitrrl/valsartan initiation in patients with chronic heart failure showing clinical deterioration under optimal medical treatment in NYHA clinical status II-III.
Methods: 46 patients consecutive patients (90% male, mean age 55+/-8 years old, 60% ischemic heart failure) with chronic compensated heart failure, due to ischemic (IHF) or dilated cardiomyopathy (DCM)-NYHA classification II-III-, who were enrolled in the Sacubitril-Valsartan multiple patient program were evaluated. Cardiorespiratory exercise response and bi-ventricular Doppler indices were evaluated at first visit and 6 months after. The pulsed tissue Doppler imaging of the systolic and diastolic function of mitral and tricuspid annulus was characterized by the systolic waves Smv and Stv, and the diastolic waves: Emv and Amv; E was the early filling wave in transmitral velocity. Left atrial maximal volume and global longitudinal strain of the left ventricle (GLPS) were measured. Serum urine, creatinine levels, potassium and sodium were also measured. All of them received b-blockers, 90% eplerenone or spironolactone, 25% ivabradine and 90% diuretic treatment. Sixty six percent of them started with the dose of 50mg of sacubitrl/valdartan; while 80% finally received the full dose of 200 mg bid. One third of them were on clinical status NYHA III.
Results: Four of the patients discontinued the program due to hypotension or renal function worsening. All patients expressed improvement in clinical status; while diuretic therapy was down titrated in all of them and discontinued in 30%. As compared with the initial examination, tricuspid annulus systolic wave velocity increased by 6.6% (p = 0.04); maximum volume of left atrium was decreased by 8.4% (p = 0.004); GLPS average was improved by 50% (p = 0.001) and E/Emv ratio was decreased by 22% (p = 0.04). Moreover, improvement in Stv was more prominent in DCM as compared to IHF patients; while no such difference was detected in average GLPS. In cardio respiratory exercise VE/VCO2 and VO2 max showed a trend in improvement (p = 0.1), with no difference detected between DCM and ICM patients; although there was a significant increase in METS achieved (p = 0.04).
Conclusion: Sacubitril/valsartan initiaition was associated with improved left diastolic function and right ventricular function, along with functional status improvement in patients with chronic heart failure. These finding underline the beneficial role of sacubitril/valsartan initiation on the hemodynamic course of patients with systolic heart failure and clinical status deterioration.

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Sacubitril/valsartan (SV) in chronic symptomatic heart failure with reduced ejection fraction; early clinical experience from a large UK tertiary centre.

D Ali[1]; J Hyland[1]; F Riley[1]; S Kirkland[1]; L Hinitt[1]; S Al Bared[2]; R Parekh[1]; C Watson[1]; H Nicholson[1]; J Mccann[1]; F Umar[1]; P Banerjee[1]
[1]*University Hospitals of Coventry and Warwickshire NHS Trust, Cardiology, Coventry, United Kingdom*; [2]*University of Medicine Victor Babes, Timisoara, Romania*

Objective: Sacubitril valsartan (SV) is now approved to be used as an alternative to ACE-inhibitors (ACE-i)/Angiotensin Receptor Blockers (ARB) in patients with symptomatic chronic heart failure with reduced ejection fraction (HFrEF). We report our clinical experience of SV use in HF patients at a large UK cardiac centre, using dedicated nurse-led , cardiologist supported, SV clinic.
Methods: HFrEF patients seen in the HF clinic and started on SV from April 2016 till July 2017, were retrospectively evaluated. Change in New York Heart Association (NYHA) class, eGFR, up-titration to target dose and tolerability to SV were assessed. Six month and 1-year outcomes, in term of death and HF hospitalisation were evaluated. Patients were seen in nurse-led HF clinic at 4 weekly intervals until up-titration to maximum tolerated dose.
Results: A total of 140 patients were included and in 77 patients (55%) up-titration to the target dose was achieved. In 43 patients (31%) and in 23 patients, an improvement of NYHA class and LVEF respectively, was seen. Fourty four patients (31%) had symptomatic systolic blood pressure drop of >10mmHg at follow-up preventing target dose up-titration. At 6 months there were 8 (6%) HF admissions and 5 in hospital deaths. One year outcome was observed in 68 patients with a mortality of 7% (n = 5) and HF admission of 6% (n = 4). Fifteen patients (10%) had a worsening of the eGFR >10 and in 11 patients (8%) SV was stopped to due intolerability.
Conclusion: The clinical use of SV in our centre has a high rate of tolerability with significant improvement in NYHA class (31%) and low HF hospitalization and mortality rate. However, in a large proportion of patients, the target dose was not achieved (45%), mainly due to reported dizziness and postural blood pressure drop.

Outcome measures	
Outcome measures (N = 140)	
Up-titration achieved (target dose 97/103mg BD)	77 (55%)
Reduction in Loop Diuretic dosage	30 (27%)
SV intolerability and stopped	11 (8%)
Mineralocorticoid receptor antagonist (MRA) dose reduced due to hyperkalemia	2 (2%)
MRA dose stopped due to hyperkalemia	1 (1%)
Postural hypotension with drop of systolic blood pressure at (>10mmHg)	44 (31%)
Mortality (6 months n = 140) Mortality (1-year n = 68) HF admission (6 months n = 140) HF admission (1 year n = 68)	5* (4%) 5 (7%) 8 (6%) 4 (6%) *(2 HF related, 3 non-HF related death)
Hyperkalaemia (>6.0 mmol/L) Deterioration in eGFR>10	4* (3%) 15 (10%) *(2 patients admitted to hospital)
NYHA class improvement (by 1 class) Improvement in LVEF Mean EF (pre-entresto) Mean EF (post-entresto)	43 (31%) 23* out of total 34 patients (66%) *(7 patients from LVEF <35 to >55%) 23% 30%

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Atrial deformation imaging predicts invasively measured pulmonary vascular resistance in advanced heart failure patients

V Marinho[1]; J Moura Ferreira[1]; P Alves[1]; C Domingues[1]; J Milner[1]; J Ferreira[1]; S Costa[1]; R Baptista[1]; F Franco[1]; MJ Ferreira[1]; R Martins[1]; F Goncalves[1]; M Pego[1]
[1]*University Hospitals of Coimbra, Cardiology, Coimbra, Portugal*

Introduction: Advanced heart failure (HF) patients often have high pulmonary vascular resistance (PVR) which prevents candidacy to heart transplantation. Atrial myocardial deformation analysis assessed by speckle tracking echocardiography is a research imaging technique that provides information about all the components of atrial function: reservoir, conduit and booster pump.
We aimed to evaluate atrial myocardial deformation analysis as predictors of invasively measured PVR in advanced HF patients.
Methods: Retrospective, observational study that included 15 advanced HF patients that performed echocardiography and hemodynamic assessment in the same week. Atrial myocardial deformation was evaluated by speckle tracking imaging from acquired apical 4 chambers and two chambers cine loops, using EchoPAC workstation. Strain and strain rate addressing reservoir (S), conduit (E) and booster pump (A) functions were determined. Invasive hemodynamic pressure curves were reviewed, and relevant hemodynamic data was collected.
Results: Scatter plots and Pearson correlations were computed to examine the intercorrelations of the variables. PVR was significantly correlated with strain-S (4C) r(12)= -0,706, p = 0,01, strain-S (2C) r(10)= - 0,767, p= 0,01, strain-E (2C) r(9)=-0,754, p = 0,019, strain-A (4C) r(10)=-0,772, p = 0,009, strain rate -A (4C) r(11)= 0,616, p = 0,044. A regression model to predict PVR including strain-A (4C) was statistically significant F (1,8)= 11,764, p= 0,009. The adjusted R2 value was 0,55, meaning that 55% of the variance in PVR was explained by the model.
Conclusion: All the components of atrial function - reservoir, conduct and booster pump - evaluated by atrial myocardial deformation speckle tracking analysis are correlated with invasively assessed PVR in advanced HF patients.

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Cardio-renal syndrome type 2: a retrospective study.

S Antit[1]; B Ben Kaab[2]; MB Menjour[2]; I Slama[1]; S Belakhel[2]; I Boussabeh[1]; M Thameur[1]; L Zakhama[1]; S Benyoussef[1]
[1]*Interior Security Forces Hospital, Department of Cardiology, Marsa, Tunisia*; [2]*Interior Security Forces Hospital, Department of medicine interne, Marsa, Tunisia*

Background: Chronic heart failure (CHF) is a serious disease, and its prevalence is steadily increasing. Among patients with CHF, 30-60% have chronic renal impairment, defining cardio-renal syndrome (CRS) type 2. Patients with CRS type 2 have a higher morbidity and mortality and have a therapeutic problem. The objective of our study was to evaluate the therapeutic and prognostic impact of CKD in CHF patients.
Methods: This was a retrospective study involving 70 patients with CHF (LVEF = 50%) divided into two groups: Type 2 cardio-renal syndrome (SCR) group: patients with creatinine clearance < 60ml / min, a control group: patients with creatinine clearance = 60 ml / min
Results: Patients with CRS type 2 were older (66 years versus 54 years, p = 0.001). The risk of developing CRS type 2 was correlated with the female genus and the presence of high blood pressure. The presence of a CRS type 2 worsens the clinical picture of the CHF, as dyspnea stage IV was more severe (68% versus 38%, p = 0.03) and blood pressure was higher for Systolic (141 versus 122, p = 0.002) and diastolic (86 versus 75 p = 0.01) in the CRS type 2 group.
Biologically, patients with CRS type 2 had more anemia with lower average hemoglobin. (12.9 versus 13.9, p = 0.01).
Therapeutically, nitrates were used more often in patients with CRS type 2 (20% versus 5%, p = 0.05).
As for the evolution of our patients, the occurrence of outbreaks of heart failure and mortality were significantly higher in the SCR group type 2.
Conclusion: The occurrence of a SCR worsens the initial picture of heart failure, exposes it to more cardiovascular events, and aggravates the patient's prognosis. Management must be early and prevention of cardiovascular risk factors remains the most effective way to limit the incidence of CHF and CRS.

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Sacubitril/Valsartan in systolic heart failure: a short term follow up.

VIPIN Mughilassery Thomas[1]; AHMED Siddiqui[1]; SWAPNA Thomas[2]; NAWAS Mohammed[1]; TAHA El Shafie[1]
[1]*Al Ain Hospital, Cardiology, Al Ain, United Arab Emirates*; [2]*Amrita Institute of Medical Sciences, Kochi, India*

Background: Angiotensin Receptor/Neprilysin Inhibitor(ARNI),Sacubitril/Valsartan has been shown superior to Enalapril in reducing the risk of cardiovascular deaths & hospitalisation in heart failure patients with Reduced Ejection Fraction (HFrEF).
Objectives & Methods: To analyse the efficacy,tolerability,adverse effects and clinical outcome in patients treated with ARNI in our hospital population.Patients were in NYHA II-IV with LVEF < 40%.Followed up to twelve months for heart failure rehospitalisation,improvement in NYHA functional class,adverse effects and total mortality.
Results: A total of 30patients were treated with ARNI(mean age 66.6 ± 13.5 years; 63.3% male,36.7% female).
Of these,17(56.7%)had Ischemic cardiomyopathy and 13(43.3%) had non-ischemic cardiomyopathy.

14(46.7%) had GFR < 60mL/min/1.73m2. Worsening of renal function occurred in 23.3%.Asymptomatic hypotension occurred in 6.7%.Progressive elevation of BNP in 43.3% of patients.Improvement in functional class by one class, occurred in 56.7% of patients and partial improvement in 30%.There were a total of 37 rehospitalisation among the 30patients up to 9months prior to commencement of ARNI and 17 rehospitalisation with heart failure after starting ARNI. Total mortality during the follow up was 10%.

Conclusion: This short term clinical study data show that ARNI is well tolerated in our cohort population of HFrEF with improvement in functional class and reduction in hospitalisation rate.

Age	66.6±13.46yrs
Sex	male 69.5% , female 30.5%
Ischemic v/s non-ischemic	56.7% v/s 43.3%
CKD	46.7%
Worsening renal function	23.3%
Asymptomatic hypotension	6.7%
Symptomatic hypotension	nil
history of CRT-D	30%
worsening BNP	43.3%
NYHA class improvement by 1 class	56.6%
Total re-hospitalization : before ARNI	44 events
Total re-hospitalization: after ARNI	17 events
Total mortality	10%

Clinical profile of the patients (total n = 30)

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Characteristics and long-term prognosis of patients with heart failure and mid-range

J Abdulla[1]; J Lauritsen[1]; F Gustafsson[2]
[1]*Glostrup hospital, Division of cardiology, Department of medicine, Copenhagen, Denmark*; [2]*Rigshospitalet - Copenhagen University Hospital, Department of Cardiology B, The Heart Centre, Copenhagen, Denmark*

Background: The European and American societies of cardiology have introduced a new category of CHF with borderline reduced LVEF of 40-49%, called HF with mid-range EF (HFmrEF). Despite publication of a considerable number of epidemiological studies, the clinical characteristics and long-term prognosis of patients with HFmrEF are still inadequately addressed and the results concerning mortality and hospitalization have varied considerably across the published studies.
Purpose: To assess by a meta-analysis the clinical characteristics, all-cause and cardiovascular mortality and hospitalization of patients with HFmrEF compared with HF reduced EF (HFrEF) and HF preserved EF (HFpEF).
Methods: Data from twelve eligible observational studies including 109,257 patients were pooled using fixed effects model.
Results: HFmrEF patients were significantly different and occupied a mid-position between HFrEF and HFpEF: mean age 73.6 ± 9.8 vs. 72.6 ± 9.8 and 77.6 ± 7.2 years, male gender 59% vs. 68.5% and 40%, ischemic heart disease 49% vs. 52.6% and 39.4%, hypertension 67.3% vs. 61.5% and 76.5%, atrial fibrillation 45.2% vs. 39.6% and 46%, chronic obstructive pulmonary disease 26.4% vs. 24.9% and 30.5%, estimated glomerular filtration rate 62 ± 30 vs. 63.3 ± 23 and 59 ± 22.5, use of renin-angiotensin system inhibitors 79.6% vs. 90.1% and 68.7%, beta-blockers 82% vs. 89% and 73.5% and aldosterone antagonists 20.3 vs. 31.5% and 26%, p-values <0.05 (Fig.1). After a mean follow-up of 31 ± 5 months, all-cause mortality was significantly lower in HFmrEF compared with HFrEF and HFpEF (26.8% vs. 29.5% and 31%), risk ratio (RR) 0.95 [0.93-0.98; 95% confidence interval (CI)] p <0.001 and 0.97(0.94-0.99; 95% CI) p = 0.014, respectively. Cardiovascular mortality was lowest in HFmrEF (9.7% vs. 13% and 12.8%) RR = 0.81(0.73-0.91) p <0.001 and 1.10(0.97-1.24;95%CI) p = 0.13, respectively. HF hospitalization in HFmrEF compared to HFrEF and HFpEF was 23.9% vs. 27.6% and 23.3% with RR = 0.89(0.85-0.93) p <0.001 and RR = 1.12(1.07-1.17) p <0.001, respectively (Fig.2).
Conclusion: The results of this study support that HFmrEF is a distinct category characterized by a mid-position between HFrEF and HFpEF and with lowest all-cause and cardiovascular mortality.

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Temporal trends in clinical characteristics, management of heart failure patients with mid-range ejection fraction in Japan: from the HIJ-HF studies

K Kei Tsukamoto[1]; Y Matsui[1]; K Nagara[1]; S Haruki[1]; T Kogure[1]; N Kikuchi[1]; H Hattori[1]; A Suzuki[1]; E Kawada[1]; T Suzuki[1]; T Shiga[1]; N Hagiwara[1]
[1]*Tokyo Women's Medical University, Department of Cardiology, Tokyo, Japan*

Introduction: Temporal trends in clinical characteristics and management of heart failure (HF) patients with mid-range ejection fraction (HFmrEF) remain to be elucidated in Japan.
Methods: From a multicenter hospital-based cohort consisted of hospitalized HF patients between 2001 and 2002 (HIJ-HF 1 study), and between 2013 and 2014 (HIJ-HF 2 study), we studied HFmrEF patients. The baseline characteristics and details of medical treatment are compared between HIJ-HF 1 study and HIJ-HF 2 study. Mid-range left ventricular ejection fraction (LVEF) was defined 40% or more and 49% or less.
Methods and Results: From the HIJ-HF 1 (2001-2002, n = 2,808) and HIJ-HF 2 (2013-2014, n = 1,245) studies, we enrolled 517 and 234 consecutive HFmrEF patients, respectively. As compared with the patients in the HIJ-HF 1 study, those in the HIJ-HF 2 study had similar sex prevalence, and were characterized by higher age, lower body mass index (BMI), higher brain natriuretic peptide, higher prevalence of ischemic heart disease (IHD) and dyslipidemia. From HIJ-HF 1 study to HIJ-HF 2 study, use of renin-angiotensin system inhibitors, ß-blockers was significantly increased, while that of digitalis was decreased. The use of Aldosterone antagonists and loop diuretics was similar.
Conclusions: Comparing the HFmrEF patients 10 years ago, age was higher, BMI was decreased, and the rate of IHD was increased. Along with implementation of evidence-based medications for the treatment of heart failure, it was suggested that systemic management is necessary.

	HIJ-HF 1 (n=517)	HIJ-HF 2 (n=234)	P value
Age (years)	68 ± 15	73 ± 14	<0.001
Male	314 (61)	135 (58)	0.431
BP (mmHg)			
Systolic	120 ± 17	132 ± 33	<0.001
Diastolic	67 ± 11	75 ± 16	<0.001
Heart rate (bpm)	71 ± 11	75 ± 26	<0.001
Atrial fibrillation	200 (39)	60 (26)	0.001
sustained VT/VF	26 (5)	11 (5)	0.847
Ischemic heart disease	175 (34)	101 (43)	0.014
BMI (kg/m^2)	21.5 ± 3.9	22.7 ± 4.7	0.004
BNP (pg/ml)	345 ± 424	773 ± 766	<0.001
LVEF (%)	45 ± 3	44 ± 2	0.010
Hypertension	295 (57)	148 (63)	0.088
Dyslipidemia	142 (27)	86 (37)	0.706
Diabetes mellitus	164 (32)	71 (30)	0.010
Hemodialysis	13 (3)	16 (7)	0.004
Medication			
β-blockers	183 (35)	159 (68)	<0.001
ACE inhibitor/ARB	335 (65)	171 (73)	0.025
MRA	216 (42)	84 (36)	0.127
Loop diuretics	387 (75)	174 (74)	0.885
Digitalis	180 (35)	33 (14)	<0.001
Ca blocker	150 (29)	94 (40)	0.002
Statins	85 (16)	105 (45)	<0.001

ACE(), angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BMI, body mass index; BNP, brain natriuretic peptide; eGFR, estimated glomerular filtration; HF, heart failure; NYHA, New York Hear Association; LVD6, left ventricular end-diastolic diameter; LVDs, left ventricular end-systolic diameter.; LVEF, left ventricular ejection fraction; MRA, Mineralocorticoid receptor antagonist; VT, ventricular tachycardia; VF, ventricular fibrillation.

Patients' characteristics

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Characterisation of patients with heart failure and mid-range ejection fraction at a tertiary centre.

C Cox Catrin[1]; D Bromage[1]; T Godec[2]; S Piper[1]; T Mcdonagh[1]
[1]*King's College Hospital, London, United Kingdom*; [2]*London School of Hygiene and Tropical Medicine, London, United Kingdom*

Background: The 2016 ESC heart failure (HF) guidelines newly classified patients with LV ejection fraction between 40-49% as 'mid-range' (mrEF).(1)

Table 1

EF		Mid-range	Reduced	P-Value	Preserved	P-Value
Age		71.0 (15.1)	68.9 (14.1)		72.4 (14.7)	
Gender	Female	36 (37.9)	84 (33.3)		69 (57.5)	**
Place of care	Cardiology	29 (30.5)	93 (37.1)		22 (18.3)	
	General Medicine	57 (60.0)	140 (55.8)		92 (76.7)	*
CABG		4 (23.5)	9 (14.5)		0 (0.0)	*
PCI		4 (23.5)	16 (25.4)		6 (40.0)	
Device Therapy		16 (16.8)	69 (27.5)	*	19 (15.8)	
Hypertension		75 (79.0)	162 (65.2)	*	104 (86.7)	
BMI		30.0 (8.7)	28.1 (6.6)	*	32.1 (8.2)	
Hb		114.8 (20.0)	121.4 (19.7)	**	114.87 (20.1)	
QRS		111.7 (30.0)	122.5 (35.6)	**	117.5 (43.2)	

Data presented as mean (SD), median (IQR) or n (%). P-value compared to HFmrEF. P Values * < 0.05 ** < 0.01 *** < 0.001.

Purpose: We aimed to characterise a population with HFmrEF in a tertiary Heart Failure unit in London.

Methods: This was an observational study of 467 consecutive patients, admitted between February 2015 and March 2016. Data was collected at the time of admission into the National Heart Failure Audit database. The co-primary endpoints were in-hospital mortality, admission duration and time to readmission, within 12 months.

Results: 95 patients (20.3% of the study population) had HFmrEF. Unsurprisingly, when compared to patients with preserved or reduced ejection fraction (pEF or rEF, respectively), patients with HFmrEF had intermediate values for most parameters. However, patients with HFmrEF were more likely to be male and managed on cardiology wards than patients with HFpEF (Table 1). They were less likely to have a device, hypertension or high body mass index, and likely to have higher haemoglobin than patients with HFrEF. There was no association between EF group and in-hospital mortality after adjustment for other predictors of mortality (P = 0.890). Furthermore, there was no association with admission duration or 1 year readmission rate using Cox Proportional Hazards modelling (P = 0.318 and P = 0.213, respectively).

Conclusion: HFmrEF is a new category of HF. This observational data shows this cohort to have intermediate values for most parameters. However HFmrEF patients had similar in-hospital mortality and 1 year readmission rates to HFrEF and HFpEF patients.

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Differences in biomarkers and biochemical parameters between heart failure with severely depressed and mid range ejection fraction

S Del Prado Diaz[1]; G Alonso Salinas[1]; A Lorente[1]; M Abellas[1]; JM Vieitez[1]; A Pardo Sanz[1]; M Plaza Martin[1]; E Gonzalez[1]; S Fernandez Santos[1]; M Castillo Orive[1]; JL Zamorano[1]

[1]*University Hospital Ramon y Cajal de Madrid, Department of Cardiology, Madrid, Spain*

Introduction: The European Society of Cardiology guidelines recently published, defined a new heart failure classification based on left ventricular ejection fraction, including a new group, mid-range ejection fraction (40-49%).

Methods: In order to define the biochemical and biomarkers profile in heart failure with mid-range ejection fraction (HFmrEF), a consecutive series of heart failure patients followed in a Heart Failure Unit were evaluated.

Results: A total of 151 patients were included, 115 had severely reduced ejection fraction (76,2%) and 36 HFmrEF (23,8%). Analytic parameters were evaluated showing haemoglobin and haematocrit slightly higher in HFrEF. However creatinine was similar in both groups, urea was higher in HFrEF, as well as liver enzymes and bilirubin. Sodium and chloride values were lower in HFrEF. Osmolarity and uric acid was lower in HFmrEF. No one of parameters evaluated achieved statistically significant differences. BNP was lower in HFmrEF but this date did not achieve statistical significant.

Conclusion: HFmrEF group was related with lower BNP and liver parameters, as well as higher levels of chlorine and sodium. More studies are needed about this subgroup in order to confirm these differences.

Biochemical Parameterl

Biochemical Parameters	HFmrEF (40-49%)	HFrEF (<40%)
Haemoglobin	12.6	13.3
Creatinine	1.2	1.2
Urea	62.2	66.4
AST	23.7	25.1
ALT	21.7	22.1
GGT/Bilirubin	67.9/1.43	78.6/1.45
BNP	543	777
Sodium	139.6	138.8
Potassium	4.2	4.4
Chloride	102.6	99.1
Acid uric	7.7	7.8

P265

Right ventricular outflow tract fractional shortening in mid-range EF heart failure

M Tsverava[1]

[1]*Tbilisi State Medical University Iv.Javakhishvili (TSU), Internal Medicine, Tbilisi, Georgia Republic of*

According to 2016 ESCARDIO Guideline, Heart Failure was divided into 3 types: heart failure with reduced (HFrEF, EF <40%), with preserved (HFpEF,EF> = 50%) and middle range (HFmrEF, EF = 40-50%) ejection fraction. The last is less studied. Right ventricle (RV) plays important role in Heart Failure. Inflow and outflow tracts of this chamber are functionally and morphologically different. The inflow tract of RV was actively studied by different EchoCG methods in normal and pathologic state, but there is little information about RV outflow tract.

Aim: To investigate RV outflow tract with M-mode EchCG fractional shortening (FS%) in patients with HFmrEF.

Material and Methods: We studied 210 patients with HF, from which 47 had a HFmrEF (study group), and 190 healthy persons (control group). RVout M-mode EchCG was registered from parasternal short axis view. It was measured RV outflow diastolic (RVd) and systolic (RVs) diameters. RVout FS% was calculated by formula (RVd-RVs)/RVd)%.

Results: The RVd and RVs was significantly greater (30.6 ± 4.5mm versus 34.2 ± 5.5mm and 13.2 ± 2.9mm versus 21.5 ± 4.1mm respectively, p <0.001) and RV FS% was significantly lower (56.9 ± 5.8% versus 37.2 ± 7.0%, p <0.001) in patients with HFmfEF compared to normal persons. If we take for RV FS% <50% as reference point the sensitivity and specifity of this parameter in diagnosis of heart failure is 0.96 and 0.96 respectively.

Conclusion: There are prominent changes of systolic function of RV outflow tract in patients with HFmrEF. In patients with HFmrEF the RV outflow tract systolic, diastolic diameters and FS% was significantly different compared to normal persons, RV outflow tract FS <50% is sensitive and specific sign of heart failure.

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Screening of prespecified comorbidities in patients enrolled in Optimizing the Management of Heart Failure with Preserved Ejection Fraction in the Elderly by Targeting Comorbidities (OPTIMIZE-HFPEF)

V Goloskokova[1]; E Thunstrom[1]; C Ergatoudes[1]; D Morales[1]; K Makvandi[1]; M Fu[1]

[1]*Sahlgrenska Academy, Department of Molecular and Clinical Medicine, Gothenburg, Sweden*

On behalf of: OPTIMIZE-HFPEF study group

Background: Despite growing recognition of the importance of comorbidities in heart failure with preserved ejection fraction (HFPEF) identification of comorbidities are often challenging due to overlapping of symptoms. Therefore, it is difficult to obtain a complete picture of the comorbidities without screening. The aim of our study was to screen prespecified comorbidities in HFPEF.

Methods: OPTIMIZE-HFPEF is a pilot prospective, randomized intervention trial. Patients with HFPEF aged >60 years were randomized 1:1 to usual care or intervention arm. Patients must meet the following diagnostic criteria for HFPEF based

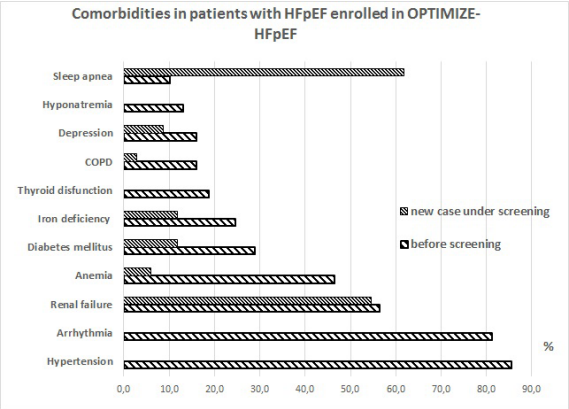

Figure 1

on the Guidelines of the European Society of Cardiology 2016 and N-terminal prohormone brain natriuretic peptide (NT-proBNP) >500 pg/ml (sinus rhythm) or >1000 pg/ml (atrial fibrillation). Comorbidity screening was based on a specified protocol including chronic obstructive pulmonary disease (COPD), Sleep disordered breathing (SDB), hypertension, diabetes mellitus, arrhythmia, hyponatremia, iron deficiency, anemia, thyroid disorders, renal dysfunction and depression.

Results: Up to now 69 consecutive patients have been enrolled in the study. Before screening, hypertension occurred in 85,5%, arrhythmia in 81,2%, renal failure in 56,5 %, anemia in 46,4%, diabetes mellitus in 29%, COPD in 15,9%, sleep apnea in 10,1%, iron deficiency in 24,6%, thyroid dysfunction in 18,8%, depression in 15,9%, hyponatremia in 13,0%. 36 patients were randomized to the intervention group e.g. screen for comorbidity according to the study protocol. Some comorbidities were completely identified before: hyponatremia, thyroid dysfunction, arrhythmia and hypertension. Other comorbidities were found to be more prevalent when screening was applied. New cases of renal failure (54,5%), diabetes mellitus (11,8%), iron deficiency (11,8%), depression (8,8%), anemia (5,9%) and COPD (2,9%) were identified. The striking finding relates to sleep apnea, where as many as 61,8% new cases were detected during the screening.

Conclusion: Screening of prespecified comorbidities is proven to be effective to identify comorbidities. Hypertension, arrhythmia, sleep apnea, renal failure and anemia are among five most common.

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Body mass index and all-cause mortality in heart failure patients with normal and reduced ventricular ejection fraction - a dose-response meta-analysis

J Zhang[1]; A Begley[1]; R Jackson[1]; M Harrison[1]; P Pellicori[2]; AL Clark[3]; JGF Cleland[2]

[1]Anglia Ruskin University, Faculty of Medical Science, Chelmsford, United Kingdom; *[2]University of Glasgow, Institute of Health & Wellbeing, Glasgow, United Kingdom*; *[3]University of Hull, Hull York Medical School, Hull, United Kingdom*

Background: Many reports suggest that patients with heart failure and a lower body mass index (BMI) have higher mortality rates compared to those with a higher BMI (obesity paradox) but this relationship may be U- or J-shaped both for patients with reduced (HFrEF) or preserved left ventricular ejection fraction (HFpEF). We sought to investigate this further in a dose-response meta-analysis.

Methods: PubMed and Embase were searched between June 1980 to April 2017 for prospective cohort studies evaluating associations between BMI and all-cause mortality in patients with HFrEF (LVEF < 45%) or HFpEF (LVEF >= 50%). Summary estimated effect sizes were obtained by using random effects models. Potential non-linear relationships were evaluated by using random effects restricted cubic spline models.

Results: Ten studies were identified including 96,424 patients of whom 59,263 had HFpEF (mean age 68 years of whom 50% were women) and 37,161 had HFrEF (mean age 60 years of whom 34% were women). For patients with HFpEF, the summary hazard ratio (HR) for all-cause mortality was: 0.93 (95%CI: 0.89-0.97) per 5 unit increase in BMI (I-squared = 75.8%, P-heterogeneity = 0.01; Begg's test, p = 1.0 and Egger's test, p = 0.29) but the association was U-shaped (p_nonlinearity < 0.01) with the nadir of risk at a BMI of 32-33 kg/m^2. For patients with HFrEF, the summary HR for all-cause mortality was: 0.96 (95%CI: 0.92-0.99) (I-squared = 95%, P-heterogeneity < 0.001 and Egger's test, p = 0.01, Begg's test, p = 0.45). The relationship was also U-shaped (p < 0.01), although 'flatter' than for HFpEF, with the nadir at a BMI of 33 kg/m^2.

Conclusions: For patients with heart failure, the relationships between BMI and mortality are U-shaped with a similar nadir of risk for HFpEF and HFrEF at a BMI of 32-33 kg/m^2. Beta-blockers increase BMI and reduce risk. Whether interventions to reduce high BMI reduce risk is unknown.

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The role of metabolically active obesity in chronic heart failure with preserved ejection fraction

Y Vasyuk[1]; E Shupenina[1]; E Nesterova[1]; E Golubkova[1]; V Nesvetov[1]

[1]Moscow State University of Medicine and Dentistry, Clinical Functional Diagnostics, Moscow, Russian Federation

The role of metabolically active obesity in chronic heart failure with preserved ejection fraction.

Background: Heart failure with preserved ejection fraction (HFpEF) currently accounts for more than 50% of all heart failure cases and its prevalence continues to rise at 1% per year. Large outcome trials revealed that HFpEF patients suffer from multiple comorbidities, mostly from obesity (84%). Metabolically active obesity (MAO) is characterized by visceral fat accumulation, presence of associated diseases and metabolic disorders. Visceral fat, such as epicardial, is the cause of systemic and local inflammation that can lead to endothelial dysfunction, myocardial fibrosis, decreased production and increased clearance of natriuretic peptides.

Purpose: The aim of the study was to reveal early signs of HFpEF in middle-aged patients with MAO.

Methods: We investigated 43 patients with MAO aged 35-55. All patients underwent physical examination, 12-lead electrocardiography, laboratory assessment, transthoracic echocardiography with speckle tracking technology, diastolic stress testing and cardiopulmonary exercise testing.

Results: All included patients were diagnosed with MAO based on increased waist circumference (117,5 ± 16,1 and 103,8 ± 13,1 cm), waist to hip ratio (0,99 ± 0,08 and 0,92 ± 0,08 in men and women, respectively). All patients had arterial hypertension 1-3 grade and metabolic disorders with increased total cholesterol (6,4 ± 0,7 mmol/l), triglycerides (2,1 ± 0,4 mmol/l) or high level of insulin resistance (3,4 ± 0,8). Most of patients (n = 32, 74%) had one symptom or sign of HF: dyspnea, fatigue or ankle oedema. But only 17 (40%) had several symptoms of HF and were diagnosed with diastolic dysfunction 1-2 grade by echocardiography at rest and during stress test. Patients with signs of HFpEF were older compared to others (52,9 ± 3,5 versus 46,3 ± 4,6). Degree of obesity determined by body mass index (BMI) didn't affect the presence of diastolic dysfunction, but patients with HFpEF had significantly more severe visceral adiposity determined by WC and epicardial fat (EF) thickness (0,87 ± 0,4 versus 0,66 ± 0,3 cm). Patients with HFpEF had early signs of systolic dysfunction determined by speckle tracking technology. Global longitudinal strain of left ventricle (LV) was significantly decreased in patients with HFpEF (-15,1 ± 1,1 versus -17,8 ± 1,7%). All included patients had reduced exercise capacity more severe in group with HFpEF, only 6 patients (35%) with HFpEF reached submaximal heart rate during the test. The main causes for end of test were dyspnea and exaggerated hypertensive response. Conclusion: MAO is one of the most common comorbidity of HFpEF. Visceral adipose tissue, including epicardial fat, can be the cause of systemic and local inflammation leading to myocardial fibrosis and diastolic dysfunction. EF thickness, not BMI, can be used as early biomarker of HFpEF in middle-aged patients.

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Design of the EMPERIAL-preserved trial of empagliflozin in patients with chronic heart failure with preserved ejection fraction

P Ponikowski[1]; W T Abraham[2]; J Lindenfeld[3]; C Zeller[4]; H Macesic[5]; M Brueckmann[6]; A Salsali[7]; S D Anker[8]

[1]Wroclaw Medical University, Wroclaw, Poland; *[2]The Ohio State University, Columbus, United States of America*; *[3]Vanderbilt University Medical Center, Nashville, Tennessee, United States of America*; *[4]Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach, Germany*; *[5]Boehringer Ingelheim (Canada) Ltd, Burlington, Ontario, Canada*; *[6]Boehringer Ingelheim GmbH & Co. KG, Ingelheim am Rhein, Germany*; *[7]Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, Connecticut, United States of America*; *[8]Charité University, Berlin, Germany*

Background and Purpose: In addition to increasing the risks of cardiovascular death and hospitalisation, chronic heart failure with preserved ejection fraction (HFpEF) is associated with considerable symptom burden and impaired physical functioning. Empagliflozin is a sodium-glucose cotransporter-2 inhibitor that was shown in the EMPA-REG OUTCOME trial to reduce the risk of cardiovascular events, hospitalisations and mortality in patients with type 2 diabetes and established cardiovascular disease. A Phase III trial, EMPERIAL–preserved, has been initiated to investigate the effects of empagliflozin on functional outcomes in patients with HFpEF.

Methods: EMPERIAL–preserved (Effect of EMPaglifozin on ExeRcise ability and heart failure symptoms, In patients with chronic heArt faiLure with preserved ejection

fraction) is a randomised, double-blind, placebo-controlled trial designed to evaluate the effect of empagliflozin on exercise capacity and HF symptoms in patients with HFpEF (left ventricular ejection fraction >40%). Inclusion criteria include 6-minute walk test (6MWT) distance of 100m to = 350 m, elevated N-terminal pro-brain natriuretic peptide (NT-proBNP) (>300 pg/mL or >600 pg/mL or for patients without or with atrial fibrillation, respectively) and the presence of structural heart disease (left atrial enlargement and/or left ventricular hypertrophy) documented by echocardiogram at screening and/or hospitalisation for heart failure within the previous 12 months. Patients must be on stable dose of diuretics for = 2 weeks prior to study entry. Approximately 300 patients will be randomised 1:1 to receive empagliflozin 10 mg or placebo once daily for 12 weeks. The primary endpoint is the change from baseline in 6MWT distance at week 12. Key secondary endpoints are changes from baseline in Kansas City Cardiomyopathy Questionnaire total symptom score and Chronic Heart Failure Questionnaire Self-Administered Standardised format dyspnoea score at week 12. Patient Global Impression of Change questionnaires and change from baseline in NT-proBNP at week 12 are other secondary endpoints.
Results: Recruitment for this trial will begin in 2018.
Conclusion: The findings of the EMPERIAL–preserved trial, together with those of the EMPERIAL–reduced trial that will be conducted in patients with chronic heart failure with reduced ejection fraction (HFrEF), will determine the effects of empagliflozin on symptoms, exercise capacity and patient reported outcome in patients with heart failure. The effects of empagliflozin on cardiovascular death and hospitalisation for heart failure in patients with chronic heart failure are being investigated in the EMPEROR–preserved and EMPEROR–reduced trials.

P270
Difference in effect of statin on prognosis in heart failure with preserved and reduced ejection fraction

SY Se Yong Jang[1]; DH Yang[1]; SC Chae[1]; BH Oh[2]; ES Jeon[3]; JJ Kim[4]; MC Cho[5]; SC Baek[6]; DJ Choi[7]; SM Kang[8]; BS Yoo[9]; KH Kim[10]
[1]Kyungpook National University Hospital, Daegu, Korea Republic of; *[2]Seoul National University Hospital, Seoul, Korea Republic of*; *[3]Samsung Medical Center, Seoul, Korea Republic of*; *[4]Asan Medical Center, Seoul, Korea Republic of*; *[5]Chungbuk National University Hospital, Cheongju, Korea Republic of*; *[6]The Catholic University of Korea, Seoul, Korea Republic of*; *[7]Seoul National University Bundang Hospital, Seongnam, Korea Republic of*; *[8]Severance Hospital, Seoul, Korea Republic of*; *[9]Wonju Christian Hospital, Wonju, Korea Republic of*; *[10]Chonnam National University Hospital, Gwangju, Korea Republic of*

On behalf of: KorAHF study investigators
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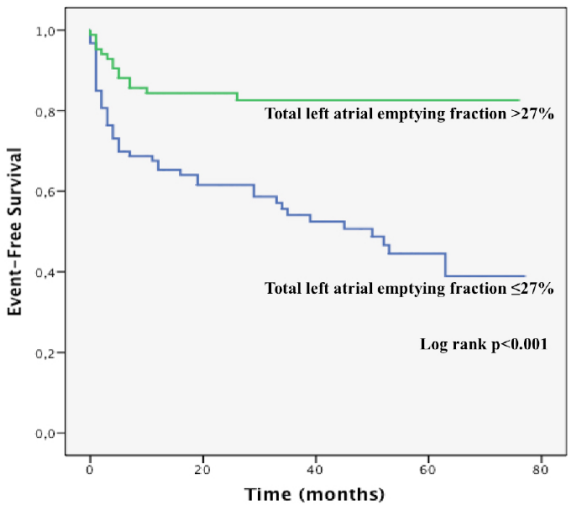
Background: Statin treatment in patients with reduced ejection fraction (HFrEF) has little evidence. Meanwhile, growing evidences are suggesting the benefit of statin in heart failure with preserved ejection fraction (HFpEF). We aimed to assess the effect of statin in HFpEF and compare them with that in HFrEF.
Methods: From Korean acute heart failure registry, 1085 patients with HFpEF and 2801 patients with HFrEF were included. A propensity-matched analysis was performed between the patients treated with and without statin in both groups of HFpEF and HFrEF.
Results: During 1-year follow-up, composite event of all-cause mortality and re-admission for heart failure was observed in 30.0% and 35.0% for HFpEF and HFrEF respectively. In HFpEF, the patients treated with statin was related to lower event rate than those without statin (24.7% vs 33.1%, log rank p = 0.006). Matched-population analysis also showed lower event rate in those with statin (28.1% vs 37.6%, log rank p = 0.026). There was no significant interaction between statin treatment and ischemic etiology of heart failure (p for interaction = 0.799). Matched analysis in HFrEF showed that statin treatment was also related to better outcomes; 31.3% vs 39.4% for those with and without statin (long rank p = 0.001). However, there was a significant interaction between statin treatment and ischemic etiology in HFrEF (p for interaction = 0.04); Hazard ratios of statin treatment in patients ischemic and non-ischemic etiology are 0.633 (0.502-0.798, p < 0.001) and 0.904 (0.707-1.156, p 0.422), respectively.
Conclusion: Statin treatment was related to better prognosis in patients with HFrEF. The effect of statin was not related to ischemic etiology, Whereas the benefit of statin treatment was markedly limited to ischemic etiology in patients with HFrEF. The results are suggesting that pathophysiology of benefit from statin in patients with HFpEF might beyond the anti-atherosclerosis effect.

P271
Left atrial function and atrial fibrillation in heart failure with preserved ejection fraction

R Schoenbauer[1]; AA Kammerlander[2]; F Duca[2]; S Aschauer[2]; C Binder[2]; C Zotter-Tufaro[2]; L Fiedler[1]; FX Roithinger[1]; C Loewe[3]; C Hengstenberg[2]; D Bondermann[2]; J Mascherbauer[2]
[1]Landesklinikum Wiener Neustadt, Cardiology, Wiener Neustadt, Austria; *[2]Medical University of Vienna, AKH - Vienna, Cardiology Clinic, Vienna, Austria*; *[3]Medical University of Vienna, Department of Bioimiging and Image-Guided Therapy, Vienna, Austria*

Background: Left atrial (LA) size and function have been shown to be associated with adverse events in heart failure with preserved ejection fraction (HFpEF).
Objectives: To study LA size and function and its impact on outcome in HFpEF patients in sinus rhythm versus atrial fibrillation (AF).
Methods and Results: 189 HFpEF patients were prospectively enrolled and underwent baseline clinical and echocardiographic assessment, cardiac magnetic resonance imaging (CMR) and invasive hemodynamic assessment. Coronary artery disease was ruled out by coronary angiography. 90 patients were in persistent AF, 24 in paroxysmal AF and 71 in sinus rhythm. LA size and function were assessed by CMR.
Patients in AF had significantly larger endsystolic LA volume indices (LAVI) (81 ± 27 vs. 55 ± 18ml/m2, p < 0.001), larger enddiastolic LAVI (68 ± 25 vs. 35 ± 17ml/m2, p < 0.001), lower total LA emptying volume (24 ± 11vs. 41 ± 14ml, p < 0.001) and fraction (16 ± 7 vs. 39 ± 11%, p < 0.001) as well as lower fraction of longitudinal shortening (5 ± 4 vs. 14 ± 7%, p < 0.001). Among patients in sinus rhythm passive LA emptying volume and fraction were 21 ± 10ml and 20 ± 7%. Active LA emptying volume and fraction were 21 ± 13ml and 20 ± 11%, respectively.
After 31 ± 24 months, 64 patients reached the combined endpoint defined as hospitalization for heart failure or cardiac death. By multivariate cox regression analysis including all LA parameters, only total reduced LA emptying fraction was significantly associated with adverse outcome (p < 0.001, HR 0.962, 95% CI 0.944-0.981). After adjustment for sex, age, presence of persistent AF, NTproBNP, right ventricular ejection fraction by CMR and pulmonary capillary wedge only elevated NTproBNP (p = 0.022, HR 1.078, 95% CI 1.011-1.150) and reduced total LA emptying fraction (p = 0.004, HR 0.969, 95% CI 0.949-0.990) were predictive for adverse events.
Conclusion: Impaired LA function plays a key role in HFpEF. Reduced total LA emptying fraction outperforms LA size and presence of persistent AF in prediction of adverse events in HFpEF.



Kaplan-Meier plot

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Potassium in heart failure with preserved ejection fraction - association with outcome and clinical parameters

B Begum Ozturk[1]; F Duca[1]; C Binder[1]; C Zotter-Tufaro[1]; C Nitsche[1]; AA Kammerlander[1]; S Aschauer[1]; L Schachner[1]; CDJ Capelle[1]; C Dona[1]; J Mascherbauer[1]; D Bonderman[1]
[1]*Medical University of Vienna, Internal Medicine II, Division of Cardiology, Vienna, Austria*

Background: Previous studies could demonstrate the prognostic significance of serum potassium levels in heart failure (HF) patients. However, studies investigating the association of serum potassium levels with prognosis or clinical parameters in patients with HF and preserved ejection fraction (HFpEF) have not been examined thus far.
Purpose: In the present study, we aimed to investigate the prognostic significance of baseline potassium levels and its correlation with clinical parameters in patients with HFpEF.
Methods: Consequtive HFpEF patients from a prospective registry were included into our study. Patients underwent clinical as well as laboratory assessment, 6-minute walk test, right heart catheterization, and cardiac magnetic resonance imaging. Patients were prospectively followed in 6-month invervals. The primary endpoint was a composite of cardiac death or HF hospitalization.
Results: Between December 2010 and May 2017, 263 HFpEF patients were included into our study. Median age of the study population was 72.0 years [Interquartile range (IQR): 67.0 - 77.0] , 185 (70.9%) were female, median N-terminal prohormone of brain natriuretic peptide levels were 1121 pg/mL (IQR: 455 - 2062) and 178 (68.0%) were in New York Heart Association class = III. Median level potassium was 4.2 mmol/L (IQR: 3.9 - 4.5). 13 (4.9%) patients had hypokalemia (< 3.5mmol/L), 24 (9.1%) had hyperkalemia (= 5.0 mmol/L) and 226 (86.0%) were normokalemic (= 3.5 - < 5.0 mmol/L). 97 (36.9%) patients experienced the combined endpoint.
Patients were grouped according to potassium tertiles (< 4.0 mmol/L, = 4.0 mmol/L - < 4.4 mmol/L and, = 4.4 mmol/L). Significant differences between the groups were detected with regards to estimated glomerular filtration rate [62.2 ml/min/1.73m2 (IQR: 49.2 - 74.2) versus 60.8 ml/min/1.73m2 (IQR: 45.1 - 79.3) versus 54.5 ml/min/1.73m2 (IQR: 40.5 - 66.8), p = 0.036], the combined endpoint [n = 42 (49.4%) versus n = 25 (28.4%) versus n = 30 (34.1%) p = 0.013)] and right ventricular EF (RVEF) [48.9% (IQR: 44.0 - 55.5) versus 56.5% (IQR: 44.8 - 64.0) versus 52.0% (IQR: 45.5 - 61.0), (p = 0.031)]. No differences with regards to concomitant medication were found between the groups.
The lowest potassium tertile was significantly associated with adverse outcome in univariable [hazard ratio (HR): 1.705, 95% confidence interval (CI): 1.137 – 2.555, p = 0.010] (Figure 1) as well as multivariable analyses (HR: 1.674, 95% CI: 1.089 - 2.574, p = 0.019).
Furthermore, a significant correlation between potassium and RVEF was found (R = 0.198, p = 0.016).
Conclusion: Low potassium levels (< 4.0mmol/L) are indenpendently associated with adverse outcome in HFpEF patients

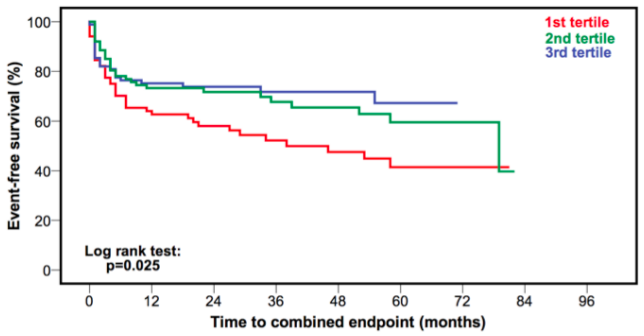


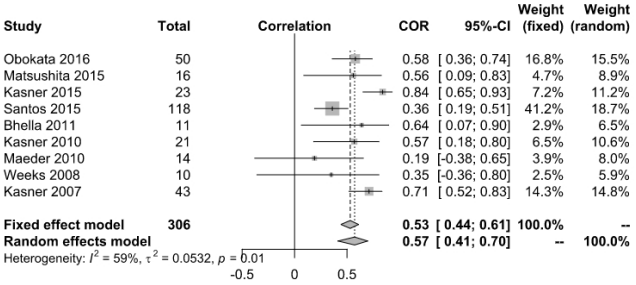
Figure 1

P273

What are the best echo parameters to diagnose HFpEF?

J F Jan Focko Nauta[1]; YM Hummel[1]; P Van Der Meer[1]; CSP Lam[1]; AA Voors[1]; JP Van Melle[1]
[1]*University Medical Center Groningen, Groningen, Netherlands*

Aims: Five echocardiographic parameters - left atrial volume index (LAVI), left ventricular mass index (LVMI), tricuspid regurgitation velocity (TRV), myocardial tissue velocity (e') and the ratio of early mitral inflow to tissue velocity of the mitral annulus (E/e') - are recommended in both the current ESC Heart Failure Guidelines and the ASE/EACVI recommendations for the evaluation of left ventricular diastolic function. We performed a systematic review of these echocardiographic parameters for their correlation with elevated left ventricular filling pressures and prognosis.
Methods and results: Nine studies reported the correlation between echocardiography and invasive hemodynamics, and 14 papers reported on the prognostic value of echocardiography in HFpEF. Among the parameters, the most data were reported for E/e'. The pooled correlation coefficient r was 0.57 for the relation between E/e' and invasively measured filling pressures. Higher E/e' resulted in increased hazard ratios for composite outcomes and mortality. In the largest study of 935 patients, E/e' >10 was associated with a hazard ratio of 2.36 for a composite outcome during median follow-up of 35 months. Other echo parameters were less strongly correlated with outcome. Diagnostic algorithms do increase the sensitivity and specificity of diagnosis of HFpEF over clinical examination and biomarkers alone.
Conclusion: Only a small number of studies provide rationale for the use of echocardiographic parameters in the diagnosis of HFpEF. The best established parameter appears to be E/e', but the existing data only show modest correlations of E/e' with invasive filling pressures and outcomes in HFpEF. More robust imaging techniques for diagnosing HFpEF and validation of current algorithms are therefore much needed.



P274

Renal oxygen consumption in chronic heart failure

J D Parker[1]; A Al-Hesayen[1]
[1]*University of Toronto, Toronto, Canada*

Background: The cardiorenal syndrome continues to be a major clinical problem for patients with both acute and chronic heart failure (CHF). The etiology of this syndrome remains unclear and is almost certainly multifactorial. The purpose of this study was to measure renal oxygen consumption in a group of patients with chronic CHF and reduced systolic function as compred to a group with normal ventruicular function and no history of heart failure.
Methods: We measured renal blood flow with para-aminohippurate and obtained samples of arterial and renal venous blood to measure oxygen saturatiions. Using standard calculations the oxygen content of arterial and renal venous blood was determined and renal oxygen consumption was calculated as (arterial O2 content - renal vein O2 content) x renal plasma flow. GFR was measured with inulin. Hemodynamics were asessed invasively with an arterial line and a right heart catherization using standard methodology. Renal blood was obtained using a Left Judkins catheter from the right femoral vein.
Results: The patients with CHF had a mean ejection fraction of 23 ± 2 percent and manifest lower systemic arterial pressure, higher cardiac filling pressures with relatively well preserved cardiac output. Those with normal ventricular function had normal hemodynamic parameters. Renal plasma flow was lower in patients with CHF than in those with normal ventricular function (447 ± 29 vs 585 ± 38 mls/min; P = 0.01). GFR was also lower in the CHF group (92 ± 6 mls/min vs 115 ± 10 mls/min). There was greater oxygen extraction across the kidney in patients with CHF. The AV difference of blood O2 content was 2.97 ± 0.25 vs 1.66 ± 0.91 mls; P < 0.002). Renal oxygen consumption was greater in those with CHF than in the group with normal ventricular function (1268 ± 79 vs 986 ± 78 mls/min; P < 0.03).

Conclusions: Therefore, despite lower filtration rates, patients with chronic heart fialure have increased renal oxygen consumption as compared to those with normal ventricular function. This may lead to relative renal ischemia and may contribute to the pathophysiology of the cardiorenal syndrome in chronic heart failure. Further, the response of renal oxygen consumption to therapy in the setting of heart failure should be explored.

Normal LV

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Trajectory of endothelial progenitor cells levels in heart failure patients undergoing heart transplantation

T Tomasz Rywik[1]; A Braniewska[2]; A Wojciechowska[1]; A Kasprzyk-Pawelec[1]; K Kozar-Kaminska[1]; M Firczuk[2]; M Sobieszczanska-Malek[1]; P Leszek[1]; P Rozentryt[3]; T Zielinski[1]

[1]National Institute of Cardiology, Warsaw, Poland; [2]Medical University of Warsaw, Warsaw, Poland; [3]Silesian Center for Heart Diseases (SCHD), Zabrze, Poland

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Introduction: Endothelium undergoes dynamic processes of degeneration and regeneration. Endothelial progenitor cells (EPC), have endothelial reparative properties and play an important role in this mechanism. In non-transplant settings high levels of EPC are associated with better cardiovascular outcomes. However in transplant physiology, due to persistent allograft antigenicity, this EPC homeostatic mechanism may become uncontrolled and pathological.Thus allograft rejection may be a consequence of defective EPC repair mechanisms. There is no data regarding prospective EPC changes in heart failure patients (pts) undergoing HT, which might influence their prognosis.

EPC changes in HT recipients

Variable1	Variable 2	n	Variable1	Variable2	Paired differences	
Median	Median	Median	P			
EPC_before_OHT	EPC_12_24h_OHT	12	64,3407	116,5774	49,2666	0,0122
EPC_12_24h_OHT	EPC_1_mo._post_OHT	27	225,1000	72,8303	-81,6341	0,0009
EPC_1_mo._post_OHT	EPC_3__mos._post_OHT	27	72,8303	88,2566	38,1000	0,0036
EPC_3__mos._post_OHT	EPC_6_mos._post_OHT	26	129,5312	132,3084	-57,8848	0,0263
EPC_1_mo._post_OHT	EPC_before_OHT	12	59,2657	64,3407	0,6588	0,6772

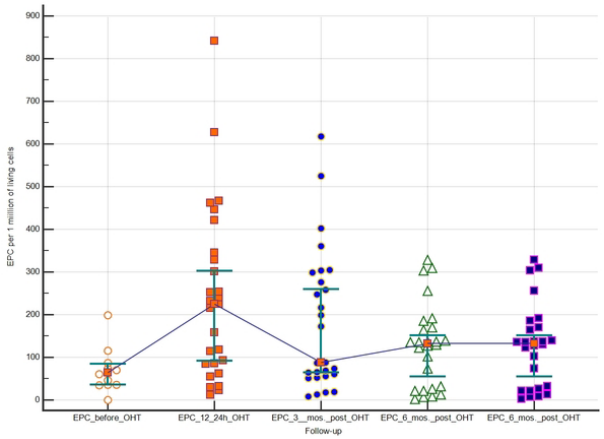
Data in medians; paired wilcoxon test

Purpose: Prospective evaluation of EPC in heart failure patients undergoing HT.

Methods: Study comprised 27 of pts undergoing HT due to severe heart failure (HF), 12 participants included into the study before HT and 15 included within 24 hours post HT. The circulating EPC count was detected by multicolor flow cytometry (FCM) in a single-tube panel as CD34+CD45dimVEGFR+. Subjects included before HT, had their first blood samples taken before operation. Testing for all subjects were done within 12-24 hours post HT, at 1 month post HT, at 3 and 6 months post HT.

Results: Majority of participants were males 77.7% and mean age was 50.1 ± 14.3 yrs.Nonischemic etiology was a dominant cause of HF (59.6%).Table and figure present data regarding EPC per 1 million living cells. Lowest values of EPC were recorded before HT. There was a noteworthy increase in EPC within 12-24 hours post HT, with subsequent drop at 1 month post HT. At 3 and 6 months post HT, we observed steady and mild increase in EPC levels. EPC levels, at different time-points differed significantly from the preceding test.

Conclusions: Within a few hours post HT, a significant increase in EPC levels is observed. At further observation, there is subsequent drop in EPC levels, with mild increase therafter. The significance of these findings needs further evaulation.



P276

Lack of improvement in autonomic cardiac tone after sacubitril/valsartan at lower than target doses

J Perez Copete[1]; M Navarro Penalver[1]; D Fernandez Vazquez[1]; DJ Vazquez Andres[1]; E Cabrera Romero[1]; A Martinez Lopez[1]; IP Garrido Bravo[1]; DA Pascual Figal[1]; A Garcia Arberola[1]; FJ Pastor Perez[1]

[1]Hospital Clínico Univeristario Virgen de la Arrixaca, Murcia, Spain

Background: Autonomic regulation plays a role in the progression of heart failure (HF) and is related with sudden death. Pharmacological and cardiac resynchronization therapy can improve this sympathovagal balance. The aim of the study was to evaluate the effect of Angiotensin-neprylisin inhibition (ARNI) compared to angiotensin inhibitors in the modulation of the autonomic tone in patients with HF in a RW population.

	Before ARNI	3 months after ARNI	p value
Time-domain measures			
SDNN, ms	42.1±11.5	38.3±12.3	n.s.
rMSSD, ms	22.2±8.2	23.3±11.6	n.s
pNN50, %	3.4 [2.0-5.7]	2.8 [1.4-6.3]	n.s
Frequency measures			
LF, ms	297 [187-450]	189 [119-388]	n.s.
HF, ms	117 [74-185]	109 [58-198]	n.s.
LF/HF	2.6 [1.7-4.1]	2.3 [1.7-3.3]	n.s
Detrended flucuation analysis			
$\alpha 1$	1.20± 0.2	1.16±0.2	n.s
$\alpha 2$	1.09±0.1	1.10±0.1	n.s.
Heart rate turbulence			
TO, %	-0.67 [-1.08-0.01]	-0.16 [-1.30-0.57]	n.s.
TS, ms/RR	3.36 [2.01-5.75]	2.89 [1.54-4.90]	n.s.
Ventricular extrasystoles/24h	449 [199-1502]	586 [51-2854]	n.s.

Methods: A 24-hour ambulatory ECG was performed at baseline (under angiotensin inhibitors) and after 3 months of maximum tolerated dose of ARNI to evaluate changes in autonomic tone using hear rate variability and heart rate turbulence parameters.

Results: We enrolled 21 HF patients in sinus rhythm (60.8 ± 13.1 years; LVEF 27 ± 4%). Angiotensin inhibitors dose was 70% of the target dose and it was changed to ARNI, to a maximum tolerated daily dose of 190 ± 102mg, representing 47.5% of the recommended dose. After 3 months of ARNI, no significant differences were found in NT-proBNP levels: 912 [643-1225] vs 845 [610-1200] pg/dl, p = 0.32. Mean blood pressure dropped from 107 ± 14 mmHg at baseline to 105 ± 14 mmHg after 3 months (p = 0.21). No significant differences were found the parameters after 3 months of ARNI (table 1).

Conclusions: ARNI use at lower than target doses did not improve autonomic cardiac tone evaluated with 24-hour holter monitoring.

Chronic Heart Failure - Epidemiology, Prognosis, Outcome

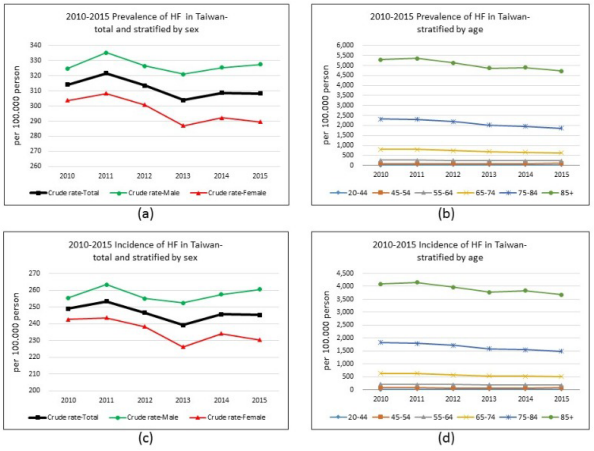
P277

Nationwide trends in prevalence and incidence of and 3-year mortality in hospitalized heart failure patients in Taiwan (2010-2015): lingering hazards remain

TD Wang[1]; ST Huang[2]; CY Wang[3]; FJ Lin[2]; SR Chen[4]; TH Ho[4]; FY Hsiao[2]
[1]National Taiwan University Hospital, Cardiovascular Center and Division of Cardiology, Department of Internal Medicine, Taipei, Taiwan ROC; *[2]National Taiwan University, Graduate Institute of Clinical Pharmacy, College of Medicine, Taipei, Taiwan ROC*; *[3]National Taiwan University, School of Pharmacy, College of Medicine, Taipei, Taiwan ROC*; *[4]Novartis (Taiwan) Co., Ltd, Taipei, Taiwan ROC*

Funding Acknowledgements: Novartis (Taiwan) Co., Ltd

Introduction: "Real-world" data on the secular trends and long-term outcomes of heart failure (HF) are scarce, especially in Asian populations. The objectives of this study were to estimate the annual prevalence, incidence, and mortality among patients hospitalized with HF in Taiwan from 2010 to 2015 using the National Health Insurance Research Database (NHIRD).



2010-2015 prevalence and incidence of HF

Methods: Patients aged 20 years or older and having been admitted for HF, defined as a hospitalization with a primary or first two secondary diagnosis of HF [ICD-9-CM codes: 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, 428,428.0, 428.1 and 428.9], between 2010 and 2015 were identified from Taiwan's NHIRD. Annual prevalence and incidence of HF hospitalization were reported as estimates per 100,000 person-years at risk. Sex- and age-stratified estimates of annual prevalence and incidence were also reported. For all identified incident hospitalized HF cases between 2010 and 2012, we further estimated their 30-day, 90-day, 180-day, 1-year, 2-year and 3-year mortality rates.

Results: The overall annual prevalence (ranged from 304 to 322 per 100,000 people) and incidence (ranged from 240 to 254 per 100,000 people) remained stable during the study period (Figure). Both the prevalence and incidence of HF were ~10% higher in men as compared to women. Between 2010 and 2015, age-stratified estimates showed that among patients over 55 years, the prevalence and incidence rates declined by between 10 and 20%.

For all identified incident hospitalized HF cases between 2010 and 2012 (n = 124,816; age 74.0 ± 13.9 years, 51.2% male, 33.7% ischemic heart disease, 37.1% diabetes mellitus, and 65.5% hypertension), the 30-day, 90-day, 180-day, 1-year, 2-year and 3-year all-cause mortality were 8.1, 14.5, 20.3, 28.4, 39.0 and 47.4%, respectively. The annual mortality remained ~10% in the 2nd and 3rd year irrespective of sex. Cardiovascular disease-related deaths accounted for nearly 40% of all-cause death among these patients.

Conclusion: Our study provides population-based "real-world" estimates regarding the annual prevalence, incidence, and mortality of hospitalized HF patients in Taiwan, which could serve as a reference for HF management in Asian populations. The remaining ~10% annual mortality following the first year of hospitalization in HF patients highlights the importance of optimized long-term medical care.

P278

Modes of death in cardiac amyloidosis

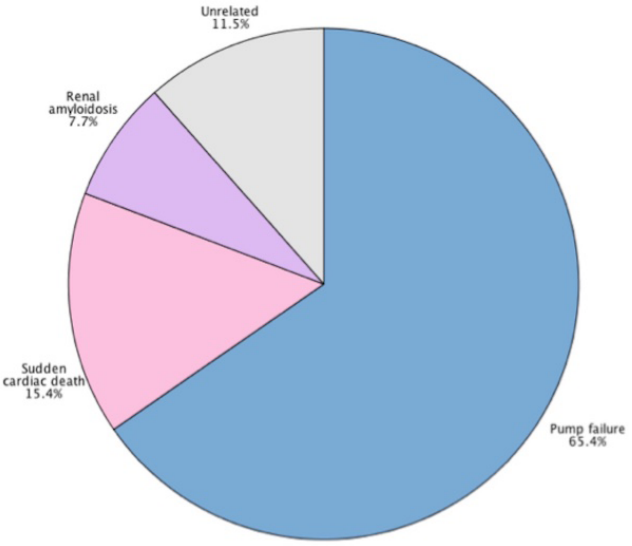
C Binder[1]; S Aschauer[1]; F Duca[1]; PD Stelzer[1]; H Agis[2]; R Kain[1]; AA Kammerlander[1]; C Hengstenberg[1]; J Mascherbauer[1]; D Bonderman[1]
[1]Medical University of Vienna, AKH - Vienna, Cardiology Clinic, Vienna, Austria; *[2]Medical University of Vienna, Oncology, Vienna, Austria*

Background: Cardiac Amyloidosis (CA) used to be seen as a very rare disease, however, it may not be as uncommon as previously perceived. With the help of modern imaging techniques and a rising awareness of this disease, cases of amyloidosis with cardiac involvement are being recognized more frequently. However, little is known about the clinical course of the disease, especially in the end-stages of this condition. Our aim was to characterize patients with CA and achieve a better understanding of the modes of death in this highly malignant condition.

Methods: Between March 2012 and September 2017 we included patients with light-chain amyloidosis (AL) or transthyretin amyloidosis (ATTR) into our prospective registry at the Vienna General Hospital, a university-affiliated tertiary care center. The diagnosis of CA was made by myocardial biopsy in most cases, or by the diagnostic algorithm recently proposed by Gillmore et al. for patients with ATTR. Cases of death were evaluated thoroughly and reviewed by at least two specialized physicians. Patient records, imaging modalities including echocardiography and cardiac magnetic resonance imaging, as well as N-terminal pro-brain natriuretic peptide levels were reviewed to understand the mode of death in each given patient.

Results: In total, 101 patients were enrolled in our registry. Fifty-five patients (54.4%) were diagnosed with AL- amyloidosis and 46 (45.5%) with either wild-type or familial ATTR. During a mean follow-up time of 57.03 ± 50.91 weeks, 29 patients (28.7%) reached the primary composite endpoint of death or heart-transplantation, Of the patients who passed away or received a new heart, 25 (86.2%) had been diagnosed with AL-amyloidosis and 4 with ATTR (13.8%). In most cases, patients died from cardiac causes (80.8%). Seventeen patients (65.4%) died from pump failure and 4 (15.4%) of sudden cardiac death. Other modes of death were myocardial infarction in 1 patient and failure of another involved organ or infection in 2 further patients. In the remaining subject, mode of death was primarily unrelated to amyloidosis or could not be evaluated due to a lack of documentation.

Conclusion: In our cohort, subjects with AL-amyloidosis had a worse prognosis than patients with ATTR. When cardiac involvement is present, more than half of patients die from heart failure.



MOD Piechart

P279

Liver-specific microRNA-122 as a prognostic biomarker in patients with chronic heart failure

S Stefan Stojkovic[1]; L Koller[1]; P Sulzgruber[1]; M Huelsmann[1]; J Wojta[1]; A Niessner[1]
[1]*Medical University of Vienna, Department of Internal Medicine II, Division of Cardiology, Vienna, Austria*

Funding Acknowledgements: Anniversary Fund of Austrian National Bank grant to Johann Wojta, OeNB grant number: AP15688ONB

Background. Several circulating microRNAs (miRs) have been proposed as potential diagnostic biomarkers in heart failure. However, studies investigating the prognostic value of circulating miRs in patients with chronic heart failure (CHF) are scarce.
Purpose: The aim of this study was to investigate the potential role of circulating miRs as prognostic biomarkers in patients with CHF.
Methods: A pathway-focused microRNA array was performed in pooled plasma samples of 40 patients with CHF who died during the follow-up and 40 age- and sex-matched survivors to screen for potential prognostic miR-candidates. In a second validation step, circulating levels of differentially expressed miRs were assessed using quantitative polymerase chain reaction in 234 patients with CHF admitted to our outpatient department for heart failure. Primary study endpoints were defined as all-cause and cardiovascular mortality.
Results: In the first phase, pathway-focused array analysis revealed differential expression of miR-122, miR-126 and miR-423 between CHF survivors and non-survivors. Circulating levels of these 3 miRs were then assessed in a large validation cohort of 234 patients. During a median follow-up time of 3.2 years, 76 patients (32.5%) died. miR-122 and miR-423 were strong, independent predictors of the primary endpoint even after comprehensive multivariable adjustment for age, sex, LVEF, NYHA class, renal function, CRP and BNP with respective HR per 1 increase of standard deviation (1-SD) of 1.16 (95% CI: 1.05-1.29, p = 0.005) and 1.24 (95% CI: 1.09-1.41, p = 0.001). In contrast, miR-126 showed no association with primary endpoint in univariate cox regression analysis (HR per 1-SD 1.01, 95% CI: 0.84-1.21, p = 0.915). Interestingly, adding miR-122 to multivariable model improved Harrell's C index from 0.78 (95% CI: 0.73-0.83) to 0.81 (95% CI: 0.76-0.86, p = 0.030), whereas no improvement was observed after adding miR-423 to the same model (C-index 0.79, 95% CI: 0.76-0.85, p = 0.259).
Conclusion: Circulating miR-122 and miR-423 are independent predictors of all-cause and cardiovascular mortality in CHF patients. Furthermore, miR-122 improves risk stratification in this vulnerable group of patients. Thus, miR-122 might be a new, valuable and easily accessible biomarker for enhanced risk assessment in CHF.

P280

Genetics in heart failure prognosis: does it make a difference?

A Ulitin[1]; V Tishkova[1]; A Kuular[1]; A Muraviev[1]; A Kozyreva[1]; E Lyasnikova[1]; A Kostareva[1]; M Sitnikova[1]
[1]*Federal Almazov Medical Research Centre, Saint Petersburg, Russian Federation*

Introduction: Heart failure (HF) is a multifactorial disease, which is the leading cause of morbidity and mortality worldwide. Severity, therapeutic response of HF and expectancy of life are variable among individuals, which may be related to genetic variation. The study of the genetic mechanisms of HF is important.
Purpose: The aim of this study to analyze relation between clinical and genetic markers including HSPB7 (rs1739843), FRMD4B (rs6787362), locus 15q22 (rs10519210) (genes associated with the HF syndrome as had been demonstrated by GWAS on a large sample of EU residents); MADD (rs10838692, rs2290149) polymorphisms (gene is participating in expression sarcomeric proteins) and 3-year follow-up in patients with ischemic HF.
Methods and Results: 506 men aged 30-65, who had MI more than 3 months ago, were evaluated. The index group consists of 260 patients with HFrEF (I - IV NYHA) LV EF (Sim) < 40% (?1 group). The reference group included 246 patients with no clinical signs of HF and LVEF (Sim)>55% (?2 group). The groups were comparable in the duration of AH (11.4 vs. 11.2 years) but different in the AH prevalence (68.5 and 83.3%; ? < 0.01) in the groups ? 1,2, respectively. Standard clinical, laboratory and instrumental, including ECHO with defining signs of the LV hypertrophy and dilatation, were performed. Investigation of gene polymorphisms was made using the real-time-PCR method. Control group consists of 257 healthy donors comparable in age. Prospective attendance was performed by phone calls. Intermediate FU was 3.3 years (3 to 5 yrs). After 3 yrs the survival of patients was 69.3% and 96.0%, contact was lost with 28% and 19% patients in the groups ? 1 and ? 2, respectively. CC genotype of gene polymorphism HSPB7 was detected more often in surviving patients compared to deceased patients both in the whole post-MI group and in the group ?2: 66% vs 39% (p = 0,002), 83% vs 50% (p = 0,037), respectively. CC genotypes of MADD polymorphisms (rs10838692) and (rs2290149) were more rarely seen, while TT genotype of MADD polymorphism (rs2290149) appeared more frequently seen in the post-MI group compared to healthy subjects: 9%vs18%(p = 0.0001); 1%vs7% (p = 0.03); 82%vs73% (p = 0.0001), respectively. Statistically significant associations with the prognosis and other polymorphic alleles of the studied genes during the 3-yrs FU were not obtained.
Conclusion: The contribution of genetic factors to the development of HF is unquestionable. On the other hand, remains still unclear, what makes a contribution more: genetic or another factor especially in ischemic HF. Investigation of candidate genes and genome-wide associations, including presented gene polymorphisms, their role in LV post-MI remodelling, development HF and prognosis may be interesting for further research.

P281

Economic impact of ivabradine use in the vulnerable phase: results from the ROCI registry

C I Clara Ines Saldarriaga[1]; G Gonzalez[2]; S Navarrete[3]; LE Echeverria[4]; M Novoa[5]; N Murrillo[6]; A Rivera[7]; MJ Rodriguez[4]; B Rolong[8]; G Trout[9]; C Martinez[1]; CV Arguello[10]; L Semanche[8]; E Contreras[8]; J Vanegas[8]
[1]*Cardiovascular Clinic Santa Maria, Universityof Antioquia cardiology department, Medellin, Colombia*; [2]*Fundacion Santa Fe de Bogota , Cardiology - heart failure, Bogota, Colombia*; [3]*Clinica Fundadores, Cardiology, Bogota, Colombia*; [4]*Fundacion cardiovascular , Heart failure, Bucaramanga, Colombia*; [5]*Clinica del Norte , Cardiology, medellin, Colombia*; [6]*Angiografia de occidente, cardiology, Cali, Colombia*; [7]*Clinica Rosales, Cardiology, Pereira, Colombia*; [8]*Sociedad Colombiana de cardiologia, Cardiology, Bogota, Colombia*; [9]*Universidad del Magdalena , Cardiology, Santa Marta, Colombia*; [10]*Clinica Leon XIII, Cardiology, medellin, Colombia*

On behalf of: Optimize Colombia Program
Funding Acknowledgements: This study was supported by Servier

Introduction: The ROCI registry included patients in the vulnerable phase of heart failure, who were treated according to the recommendations of the Optimize Colombia Program in order to reduce early outcomes, such as hospitalization and death. The patients were educated and involved in self-care and treated with all pharmacological treatments that provide benefits before hospital discharge: beta-blockers, ACEI or ARB, diuretic, ivabradine. This strategy reduced the 30-day readmission rate.
Objective: To simulate the economic impact and cost savings driven by the decrease in 30-day readmissions by the implementation of a strategy recommended by the Optimize Colombia Program and to compare the cost of patients treated with and without ivabradine.
Methods: Based on the results of ROCI registry, local epidemiological data, and Colombian hospitalization costs published in the scientific literature, we simulated the potential economic impact and cost savings of the widespread use of ivabradine in heart failure patients with reduced ejection fraction in the Colombian healthcare system for a 1-year period.
Results: In the ROCI registry, 436 patients were included, the mean ejection fraction was 32%, 94% of the population was on beta-blockers, and additionally 42% received ivabradine. The 30-day readmission rate was 8.6% in patients without ivabradine and 1.5% in those with ivabradine. The 30-day readmission rate reported in international registries is around 25%. The cost of a heart failure hospitalization in Colombia is €2062, and an estimated 647 853 patients have this diagnosis. The annual estimated cost of 30-day readmission in Colombia is therefore €134 090 337. With the implementation of the Optimize Colombia Program without ivabradine (58% of patients), this cost could be reduced to €42 908 908, and if 42% have an indication for ivabradine and are treated with it, the cost of hospitalization would be €3 218 168.
Conclusion: Our results suggest that the use of ivabradine from hospital discharge, as per the recommendations of the Optimize Colombia Program, will reduce the 30-day readmission rate and hence the cost to the health care system.

P282

What is the meaning of pericardial effusion in the general population? Results from the STAAB cohort study

M Breunig[1]; C Morbach[1]; G Gelbrich[2]; T Tiffe[2]; FA Eichner[2]; M Wagner[2]; PU Heuschmann[2]; S Stoerk[1]
[1]*University Hospital of Würzburg, Comprehensive Heart Failure Center and Dept. of Medicine I, Würzburg, Germany*; [2]*Insitute of Clinical Epidemiology and Biometry and Comprehensive Heart Failure Center, University Würzburg, Würzburg, Germany*

Funding Acknowledgements: BMBF 01EO1004 and 01EO1504

Background: Pericardial effusion (PE) is usually attributed to advanced cardiac disease, inflammation, or malignancy. Knowledge on prevalence and relevance of PE in the general population is scarce.

Purpose: To determine prevalence and determinants of PE in a population-based cohort.
Methods: We present data from the first planned interim analysis of the ongoing STAAB Cohort Study (Characteristics and Course of Heart Failure STAges A/B and Determinants of Progression), which recruits participants (30-79 years) free of symptomatic heart failure from a representative sample of the population of Würzburg. Participants undergo detailed clinical evaluation and transthoracic echocardiography including a dedicated evaluation of the prevalence of PE. Echocardiographic quality is closely monitored by the EchoCoreLab Würzburg.
Results: 2440 out of 2473 participants (98.7%) had valid information on PE. Of those, PE was prevalent in n = 66 (2.7%; 95%CI 2.0-3.5%). Individuals with PE were more often female (68% vs. 51%, p = 0.008), had higher NTproBNP values (75 [42-115] ng/L vs. 53 [26-99] ng/L, p = 0.016), and their body mass index was lower (23.5 ± 3.7 kg/m2 vs. 26.6 ± 5.1 kg/m2, sex-adjusted p < 0.001). There was no significant difference regarding age (55 ± 10 years vs. 54 ± 12 years, p = 0.88), C-reactive protein (0.8 [0.4-1.5] mg/dL vs. 0.9 [0.5-2.1] mg/dL, p = 0.26), leucocytes (5.6 ± 1.4 109/L vs. 5.9 ± 1.7 109/L, p = 0.14), glomerular filtration rate (85 ± 12 mL/min/1.73 m2 vs. 86 ± 15 mL/min/1.73 m2, p = 0.44), rheumatoid disease (2% vs. 4%, p = 0.52), malignoma (ever; 11% vs. 10%, p = 0.83), atherosclerotic disease (coronary disease, peripheral artery disease, stroke; 5% vs. 7%, p = 0.62), and left ventricular ejection fraction (LVEF; 60 ± 6% vs. 60 ± 5%, p = 0.91).
Conclusions: In a population-based cohort, about 3% of individuals exhibit a subclinical PE. These subjects are characterized by higher values of NTproBNP as a potential surrogate of incipient myocardial impairment. However, presence of PE was not associated with inflammation, malignancy, atherosclerotic disease, or LVEF. It remains unclear why particularly women with lower BMI were prone to PE; this aspect deserves further research.

P283

Outcomes are equally poor for patients with suspected heart failure and raised natriuretic peptides, regardless of whether heart failure is confirmed or excluded by a specialist

A Alice Zheng[1]; K Guha[1]; P Kalra[1]; G Morton[1]
[1]*Portsmouth Hospitals NHS Trust, Portsmouth, United Kingdom*

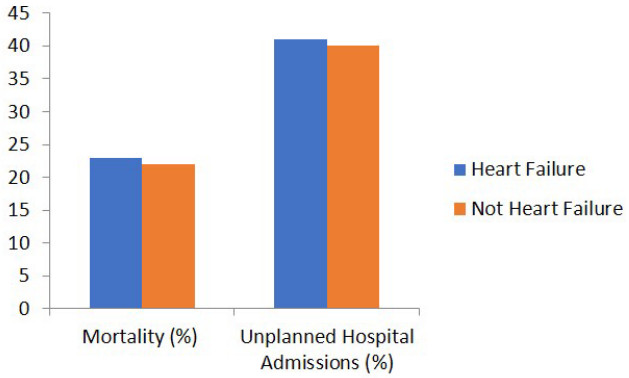
Introduction: Elevated natriuretic peptides in symptomatic patients identifies those with possible heart failure (HF) and predict prognosis. They are however non-specific, and there are few data on how prognosis compares based on whether HF is finally confirmed or excluded.

Table 1

	Heart Failure (n = 133)	Not Heart Failure (n = 102)	p value
Mean Age ±SD (Years)	79±10	80±9	0.37
Mean NTproBNP ±SD (pg/mL)	3749±4343	1542±2034	<0.0001
Male (%)	71 (53)	45 (44)	0.15
Atrial Fibrillation (AF) (%)	79 (59)	47 (46)	0.04
Hypertension (%)	93 (70)	65 (64)	0.32
Diabetes (%)	35 (26)	13 (13)	0.01

Table 1 - Baseline characteristics of patients.

Purpose: Compare outcomes in patients with suspected HF and raised natriuretic peptides, based on whether HF is confirmed or not after specialist assessment.
Evaluate the incidence of subsequent HF in the same population, where the diagnosis of HF is initially rejected.
Methods: All patients with suspected HF and raised NTproBNP (>400 pg/mL) referred to a single centre from March 2014-15 were included. Following echo and specialist assessment they were designated as HF or Not Heart Failure (NHF). All-cause unplanned hospitalisation and mortality data over a minimum follow up of 2 years were obtained from electronic records. Event rates were compared between HF and NHF groups. NHF patients who subsequently developed HF were also noted.
Results: 235 patients were included. Mean follow up was 29 ± 4 months. 133 (57%) were diagnosed with HF; 102 (43%) as NHF.
HF patients had much higher NTproBNP levels and higher rates of AF and diabetes (table 1). Despite this, there were no differences in either mortality (HF 23% [n = 31], NHF 22% [n = 22]; p = 0.75) or hospitalisations (HF 41% [n = 54], NHF 40% [n = 41]; p = 0.95) between the groups; figure 1.
7 (7%) of NHF patients were subsequently diagnosed with HF. Negative predictive value of a NHF diagnosis was 93%.
Conclusions: Patients with suspected HF and raised natriuretic peptides are at high risk of adverse outcomes regardless of their diagnosis after specialist evaluation. Prognosis in the HF group was no worse despite higher NTproBNP levels and rates of diabetes and AF. This may be due to the use of disease modifying therapies improving HF prognosis. The adverse outcome in NHF group is not explained by unrecognised HF at assessment as subsequent presentations with HF were uncommon. These findings should be taken into consideration when discussing prognosis with patients, regardless of their diagnosis.



Event rates between HF and NHF groups

P284

Heart failure with recovered ejection fraction in a colombian heart failure clinic

C I Clara Ines Saldarriaga[1]; QI Santana Fontalvo[1]; CV Gallego[1]; LA Fajardo[1]; AM Agudelo[1]
[1]*Cardiovascular Clinic Santa Maria, Universityof Antioquia cardiology department, Medellin, Colombia*

Background: Little is known about the characteristics, and outcomes of Heart failure recovered patients. Previous reports suggest that these patients might have a different clinical although this is not well understood.
Purpose: To identify the incidence of heart failure with recovered ejection fraction, in a structured Colombian heart failure clinic. The primary endpoint was the recovery of the ejection fraction (EF) to more than 40% after 1 year of follow up. The clinical variables were analysed in order to identify the predictors of the recovery
Methods: A retrospective cohort study was performed. Comprehensive multivariable analyses were performed including the covariates.
Results: 343 patients were included, the mean age was 67 +/- 13.3 years, ischaemic heart disease was the cause of heart failure in 49,3%, and diabetes was the most frequent comorbidity in 24,2% of the population. The initial EF was 25% , optimal medical therapy that included a beta blocker, ACE/ ARB and MRA was prescribed in 89.2% of the patients. After one year of follow up, 28.6% of the population presented a recovery in the EF (to more than 40%). The multivariable analysis is showed in table 1. Younger age OR: 0,97 (0,95-0,99) p = 0,038 and the use of optimal medical therapy OR 0,02 (0,004-0,09) p < 0,0001 were the best predictors of the recovery in the ejection fraction.
Conclusion: This retrospective cohort study showed that 1 of every 3 patients followed in a heart failure clinic can improve the ejection fraction after 1 year of follow up, younger patients treated with optimal medical therapy have the best chance to improve.

Predictors of recovery

characteristic	OR (CI 95%)	p value
Age	0,97 (0,95-0,99)	0,038
Male sex	1,53 (0,72-3,24)	0,264
Optimal medical therapy	0,02 (0,004-0,09)	<0,0001
CRT	0,89 (0,45-1,74)	0,732
Creatinine clearance	0,67 (0,28-1,61)	0,376
End sistolic left ventricular diameter cm/m2	0,75 (0,34-1,69)	0,496
End diastolic left vemtricular diameter cm/m2	0,63 (0,22-1,79)	0,392
Left ventricular mass index. g/m2	0,98 (0,97-1,003)	0,123

Multivariable analysis

P285

Sub-maximal cardiopulmonary exercise test in heart failure: which parameters should we trust?

A Valentim Goncalves[1]; R M Soares[1]; T Pereira-Da-Silva[1]; R Ilhao Moreira[1]; J Feliciano[1]; P Rio[1]; A Abreu[1]; T Mendonca[1]; M Coutinho Cruz[1]; S Aguiar Rosa[1]; R Cruz Ferreira[1]

[1]Hospital de Santa Marta, Lisbon, Portugal

Aims: Peak oxygen consumption (pVO2) is a major criterion for listing patients for heart transplantation but requires a maximal cardiopulmonary exercise test (CPET). In the event of a sub-maximal CPET (respiratory exchange ratio (RER) < 1.05), a ventilation equivalent of carbon dioxide (VE/VCO2) slope may be considered for risk stratification according to current guidelines, despite a low level of evidence.
Purpose: We aimed to evaluate the power of different CPET parameters to predict adverse events in patients achieving maximal and sub-maximal CPETs.
Methods: Ambulatory patients followed in our institution in NYHA class II-III with LVEF = 40%, underwent a prospective evaluation including a CPET. All patients were followed for 60 months and the combined endpoint was cardiac death and urgent heart transplantation.
The pVO2, pVO2(%) predicted, VE/VCO2 slope, oxygen uptake efficiency slope (OUES) and heart rate recovery in the first minute (HHR1) were analysed as potential predictors of the combined endpoint (Cox regression) and their predictive power was compared (area under the curve (AUC) analysis), in the subgroups of patients with achievement of RER <1.05 (G1) or = 1.05 (G2).
Results: In the 274 enrolled patients (98 in G1 and 176 in G2) the combined event rates were 27,6% and 35,8%, respectively (p = 0.164).
Age (p = 0.007) and body mass index (p = 0.003) were higher and diabetes mellitus (p = 0.01) and cardiac resynchronization therapy (p = 0.008) were more common in G1.
The discriminative power of each CPET parameter is presented in the Table. The VE/VCO2 slope was the most accurate parameter for risk stratification in both groups. No significant differences were found in the predictive power of pVO2, pVO2(%) predicted or VE/VCO2 slope between the 2 groups, despite a numerically lower AUC in G1. The HHR1 and OUES significantly lost discriminative power in G1.
Conclusions: VE/VCO2 slope seems to provide a discriminative power at least as good as pVO2 for predicting adverse events in both submaximal and maximal CPET. The discriminative power of HHR1 and OUES was lower in submaximal compared to maximal CPET.

	RER < 1,05	RER ≥ 1,05	Comparison of AUCs (p-value)
pVO_2	0,751	0,813	0,410
pVO_2 (%) predicted	0,762	0,818	0,440
V_E/V_{CO2} slope	0,767	0,860	0,161
OUES	0,654	0,829	0,017
HHR1	0,651	0,845	0,008
pV_{O2} vs V_E/V_{CO2} slope (RER < 1,05)			0,890

Discriminative power of CPET parameters

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Glycemic status in non diabetic elderly hypertensives with heart failure with preserved ejection fraction

L Livia Popescu[1]; H Balan[1]

[1]University of Medicine and Pharmacy Carol Davila , Bucharest, Romania

Background: Epidemiological evidence suggests increasing proportion of elderly people. Hypertension, which is worldwide spread and represents the leading cause of death and of heart failure with preserved ejection fraction (HFpEF), occurs in one half/two thirds of them. HFpEF is an important cause of disability and hospitalization and, unfortunately, until now, despite multiple randomized controlled trials, no disease-specific therapy exists to improve prognosis. The prevalence of glycemic disturbances increases with age.
Purpose: The aim of our study was to assess glycemic status in non diabetic elderly patients hospitalized with arterial hypertension and HFpEF in an Internal Medicine Department.
Methods: 168 consecutive elderly patients, 65-94 years old, with arterial hypertension and HFpEF with unknown diabetes were enrolled into the study. For each patient we recorded demographic and anthropometric data, blood pressure measurements, BMI, complete lipid profile, and cardiovascular complications (ischemic heart disease, MI, stroke, angina pectoris). Glycemic status was defined by standard oral glucose tolerance test in all non diabetic patients. Patients were divided into 4 groups: 1) normal glucose tolerance (n = 31), 2) impaired fasting glucose (IFG) (n = 60), 3) impaired glucose tolerance (IGT) (n = 32), 4) newly diagnosed diabetes mellitus (n = 45).
Results: Glucose intolerance was observed in 81.54% (n = 137) elderly with HFpEF previously non diabetic hypertensive patients. 35.71% of them had impaired fasting glucose, 19.05% had impaired glucose tolerance, and 26.78% had newly diagnosed diabetes mellitus. Newly diagnosed diabetes mellitus in elderly patients with hypertension, HFpEF, and cardiovascular complications was observed in 35%. In patients without cardiovascular complication only 14.7% had newly diagnosed diabetes mellitus. The difference was statistically significant (p <0,001). There were no statistically significant differences between groups with/without cardiovascular complications in impaired fasting glucose and impaired glucose tolerance.
Conclusions: Elderly hypertensive patients with HFpEF without previously diabetes mellitus had a high prevalence of glucose intolerance, with newly diagnosed diabetes mellitus affecting more than a fourth of them. Frequency of newly diagnosed diabetes mellitus was twice high in elderly hypertensive with cardiovascular complications than in those with uncomplicated arterial hypertension. Special attention should be given to this group of patients.

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Assessment of liver and cardiac iron overload using MRI in patients with chronic anemias in Latin American countries: Results from ASIMILA study

F Manzur[1]; R Cancado[2]; N Watman[3]; C Lobo[4]; Z Chona[5]; F Traina[6]; M Park[7]; G Drelichman[8]; J Zarate[9]; L Marfil[9]

[1]Centro de Investigaciones Biomédicas - Universidad de Cartagena, Facultad de Medicina, Cartagena, Colombia; *[2]Sao Paulo University Medical School, Department of Hematology/Oncology, Santa Casa of Sao Paulo Medical School, Sao Paulo, Brazil,, Sao Paulo, Brazil*; *[3]2Hospital General de Agudos Dr. Ramos Mejía, Buenos Aires, Argentina, Buenos Aires, Argentina*; *[4]Instituto Estadual de Hematologia Arthur de Siqueira Cavalcanti, Rio de Janeiro, Brazil*; *[5]Hospital Universitario de Caracas, Caracas, Venezuela*; *[6]6Haematology and Hemotherapy Center, University of Campinas/Hemocentro-Unicamp, Instituto Nacional d, Cartagena, Brazil*; *[7]Sao Paulo Hematology Center, Sao Paulo, Brazil*; *[8]Hospital de Niños Dr. R Gutierrez, Buenos Aires, Argentina*; *[9]9Novartis Pharmaceuticals Corporation, East Hanover, New Jersey, United States of America*

Objectives: A multicenter, noninterventional, observational study was conducted in the Latin American countries including Argentina, Brazil, Colombia, Mexico, and Venezuela to assess the prevalence of liver and cardiac iron overload using magnetic resonance imaging (MRI) in patients with chronic anemias except thalassemia.
Methods: Patients aged >10 years with transfusion-dependent anemias, except thalassemia, either with < 20 units of red blood cell (RBC) transfusions with serum ferritin (SF) levels >2000 ng/mL or with = 20 units of RBC transfusions regardless of SF level in their lifetime, were enrolled. Iron overload was assessed using MRI.
Results: Among 175 patients included, majority had sickle cell disease (SCD; 52%), followed by aplastic anemia (AA; 17.7%), myelodysplastic syndrome (MDS; 8.6%), Diamond-Blackfan anemia (DBA; 4%), pure red cell aplasia (1.1%), and others (16.6%). Liver iron overload was observed in 76.4% of patients, while cardiac iron overload was seen in only 19.2% when assessed by MRI. The prevalence of iron overload was 80.2% in patients with SCD, 73.3% in MDS, 77.4% in AA, 100% in pure red cell aplasia, 71.4% in DBA, and 68.9% in other transfusion-related disorders. A moderate correlation between liver iron concentration (LIC) and SF was observed in patients with SCD and MDS (r = 0.47 and r = 0.61, respectively). All adverse events reported were consistent with the published data for deferasirox or underlying disease.
Conclusion: A high prevalence of iron overload in this patient population seen in Latin American countries indicates that a better diagnosis and management of iron overload is required in these countries.

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Serial biomarkers activity determination during NT-proBNP-guided treatment and its association with long-term clinical outcomes in patients after heart failure decompensation

OY Narusov[1]; AA Skvortsov[1]; DE Protasova[2]; VN Protasov[1]; SN Nasonova[1]; TV Kuznetcova[1]; MD Muksinova[1]; VP Masenko[1]; SN Tereshchenko[1]

[1]Russian Cardiology Research and Production Complex, Moscow, Russian Federation; *[2]National Research Center for Preventive Medicine, Moscow, Russian Federation*

Purpose: To evaluate biomarkers activity changes during NT-proBNP-guided treatment and its association with clinical outcomes in pts after ADHF.Materials and methods. The study included 100 pts with ADHF III-IV FC NYHA due to CAD, arterial hypertension and dilated cardiomyopathy and LV EF < 40 %. After HF symptoms compensation, at discharge, high risk pts (discharge NT-proBNP?1400 pg/ml) were

randomized into group of therapy guided by NT-proBNP (NBGT - group1) and standard HF therapy (group2). Mean follow-up period was 10,5 ± 2,1 mts. At the end of study, an additional group 3 of high-risk pts who were noncompliant with the protocol was formed out of pts from these two groups (n = 10).Blood sampling to determine the biomarkers concentrations (sST2, copeptin, galektin-3, hsTrT,NGAL) were collected at discharge, 3,6 mts after. At discharge, median NT-proBNP was 3750.0 (2 224.0;6613.0) pg/ml in the NBGT group, 2 783.0 (2021.5;4827.5) pg/ml in the group 2, and 2162.0 (1684.5;5750.0)pg/ml in the group 3 (? = 0.315).
Results: All pts in study received the triple combination of iACE/ARB+bb+MRA (100%). Over the treatment period, NT-proBNP decreased by 53.0 % (? = 0.001) in the NBGT group and by 10.2%(p = 0.024) in the standard therapy group (? = 0.001). More pronounced biomarkers activity reduction at the end of the follow-up were also found in group 1 pts, especially for sST2 (?% =-37,1%) and copeptin (?% =-29,9%) concentration. ?% NT-proBNP, ?% sST2 and ?% copeptin closely and significantly correlated with ?% E/E' (relatively r = 0,67; r = 0,63 and r = 0,7, p < 0.01 for all). At the end of the study CV mortality rate in group 2 was significantly higher than in NBGT group 1 (34% vs 13%, p = 0.025), as well as the rate of the first and total HF hospitalization (34% vs 13%, p = 0.028 and 54%vs13%,p = 0.02,respectively). Instead of revealed lowest NT-proBNP discharge values at randomization, the highest rate of CV mortality and HF hospitalization was found in group 3 pts (20% and 80% , respectively), witch correlated with increased activity of all investigated biomarkers at the end of the protocol. This fact may be explained by pts noncompliance protocol demands (pts missed>20% of planned visits and had lowest doses of iACE/ARB+bb+MRA in our study). But, this group of pts also had significantly highest admission, discharge and follow-up median sST2 values - another powerful prognostic factor for worse outcomes. sST2 in group 1 vs group 2 vs group 3: 37,7(23,9;58,2) vs 39,7(28,7;51,3) vs 54,8(35,8;68,2)ng/ml at discharge and 22,9(12,7;30,4)vs30,9(30,2;47,3) vs 70,8(48,3;82,2)ng/ml at 6 mts of follow-up (p < 0.05 between groups 1-2 and 3).
Conclusion: The NT-proBNP-guided therapy of high-risk pts after ADHF associates with significantly more pronounced reduction of biomarkers activity during long-term follow-up compared with the standard therapy. sST2 increases opportunities additionally to NT-proBNP in pts long-term risk stratification after ADHF.

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Albumin as a prognostic marker in patients with chronic heart failure and reduced ejection fraction

M Marta Ferreira Fonseca[1]; J Farinha[1]; S Goncalves[1]; C Sa[1]; T Duarte[1]; R Marinheiro[1]; R Rodrigues[1]; R Caria[1]
[1]Hospital Center of Setubal, Cardiology, Setubal, Portugal

Introduction: Hypoalbuminemia is common in the presence of certain chronic diseases, usually associated with a worse prognosis. Although low levels of albumin are commonly found in patients with heart failure (HF), the relationship between them isn't totally defined.
Purpose: To determine the prognostic value of hypoalbuminemia in patients with heart failure and reduced ejection fraction (HFrEF).
Methods: We evaluated 167 patients with HFrEF, followed in a heart failure centre. The level of albumin was determined in the beginning of follow-up. Patients whose value of albumin was not determined initially were excluded. The population was characterized according to their clinical, laboratorial and echocardiographic characteristics. Patients were divided in two groups, based on the presence (or not) of hypoalbuminemia (= 3,4g/dL). The adverse events considered were the occurrence of hospitalizations (total or caused by HF) or death.
Results: We studied 167 patients (61% were males) with a mean age of 68 ± 11 years and a median left ventricle ejection fraction (LVEF) of 31 ± 8%. The mean value of albumin was 3,5 ± 0,6g/dL and 41% of the patients presented with hypoalbuminemia. Body mass index (BMI) was lower in patients with lower values of albumin (19kg/m2 vs 24kg/m2). The group of patients with hypoalbuminemia had more hospitalizations (total or caused by HF) and death (see table). Hypoalbuminemia was a predictor of total and HF hospitalizations, in multivariate analysis, independently of BMI (OR: 2,37 CI 95% 1,1-5,0; OR: 2,4 CI 95% 1,1-5,0, respectively). It was a predictor as well of death by any cause (OR: 9,5 CI 95% 1,9-47,8).
Conclusion: Hypoalbuminemia is common in HFrEF and is a marker of worse prognosis, independently of BMI. Additional investigation is needed to enhance our comprehension of the mechanism by which hypoalbuminemia correlates with the prognosis of these patients.

	Albumin≤3,4g/dL (n = 68)	Albumin>3,4g/dL (n = 99)	p
Total hospitalizations	39 (57%)	41 (41%)	0,03
HF hospitalizations	34 (50%)	36 (36%)	0,05
Death	14 (21%)	4 (4%)	0,001

Hypoalbuminemia and clinical outcomes

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The target degree of sST2 and NT-proBNP values decrease during biomarker-guided treatment for long-term patients outcomes improvement after heart failure decompensation

AA Skvortsov[1]; VN Protasov[1]; OY Narusov[1]; DE Protasova[2]; MD Muksinova[3]; AV Sychev[3]; VP Masenko[3]; SN Tereshchenko[3]
[1]Russian Cardiology Research Center, Moscow, Russian Federation; *[2]National Research Center for Preventive Medicine, Moscow, Russian Federation*; *[3]Russian Cardiology Research and Production Complex, Moscow, Russian Federation*

Purpose: To evaluate target degree of sST2 and NT-proBNP values decrease during biomarker-guided treatment for long-term patients outcomes improvement after heart failure decompensation (ADHF).Materials and methods. The study included 100 patients with ADHF III-IV FC NYHA and LV systolic dysfunction due to coronary artery disease, arterial hypertension and dilated cardiomyopathy and LV EF < 40 %. After HF symptoms compensation, at discharge, high risk pts (discharge NT-proBNP ? 1400 pg/ml) were randomized into group of therapy guided by NT-proBNP (monthly) (NBGT - group 1) and standard HF therapy (group 2). The goal of treatment was to reduce NT-proBNP concentration < 1000 pg/ml, or at least 50% of the initial. Mean follow-up period was 10,5 ± 2,1 months. Blood sampling to determine the biomarkers concentrations (sST2, copeptin, galektin-3, highly sensitive Troponin T and NGAL) were collected at discharge from the hospital, 3 and 6 months after. At the time of discharge from the hospital, median NT-proBNP concentration was 3750.0 (2 224.0; 6 613.0) pg / ml in the NBGT group and 2 783.0 (2021.5; 4 827.5) pg/ml in the group 2 (? = 0.315).
Results: All patients in our study received the triple combination of iACE/ARB+beta-blocker+MRA (100%). Over the treatment period, NT-proBNP concentration decreased by 53.0 % (? = 0.001) in the NBGT group and by 10.2 % (p = 0.024) in the standard therapy group (? = 0.001 between groups). The goal of treatment (decreasing the NT-proBNP concentration to below 1000 pg / ml and / or = 50 % from baseline) achieved by 74% of pts in NBGT group. More pronounced biomarkers activity reduction at the end of the follow-up were also found in group 1 pts, especially for sST2 (?% =-37,1%) and copeptin (?% =-29,9%) concentration. ?% NT-proBNP, ?% sST2 and ?% copeptin closely and significantly correlated with ?% E/E' (relatively r = 0,67; r = 0,63 and r = 0,7, p < 0.01 for all).At the end of the study CV mortality rate in group 2 was significantly higher than in NBGT group 1 (34% vs 13%, p = 0.025), as well as the rate of the first and total HF hospitalization (34% vs 13%, p = 0.028 and 54% vs 13%, p = 0.02, respectively).Pts risk for CVevents (CV death, repeated decompensation, and hospitalization for CHF) during long-term follow-up decreased only when we achieved NT-proBNP or sST2 concentration reduction more than = 40,0% or = 24,9% from discharge values respectively [OR at 95 % CI = 0.08 (0.02-0.36), p < 0.0001 for NT-proBNP and = 0.1(0.02-0.5), p = 0.004) for sST2].
Conclusion: During NTproBNP-guided therapy high-risk patients after ADHF, reduction of CV death, repeated decompensation and hospitalization for HF may be achieved only in pts with NT-proBNP or sST2 concentration reduction more than = 40,0% or = 24,9% from discharge values

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Causes of decompensation of heart failure in patients attended in primary care

J M Jose Maria Verdu[1]; L Gril[2]; J Woebkenberg[3]; L Glynn[4]; H Vaillant-Rousell[5]; J Demurtas[6]; P Torsza[7]; R Asenova[8]; H Thulesius[9]; D Lazic[10]; R Abellana[1]; MA Munoz[1]
[1]Primary Care Research Institute (IDIAP), Barcelona, Spain; *[2]University Medical Centre Maribor, Maribor, Slovenia*; *[3]Hannover Medical School, Hannover, Germany*; *[4]University of Limerick, limerick, Ireland*; *[5]Universite Clermond Auvergne, Clermond Ferran, France*; *[6]VERONA, VERONA, Italy*; *[7]Semmelweis University, Budapest, Hungary*; *[8]Medical University Plovdiv, Plovdiv, Bulgaria*; *[9]Lund University, Lund, Sweden*; *[10]University of Zagreb School of Medicine, Zagreb, Croatia*

On behalf of: HEFESTOS GROUP
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Background: Information about factors that contribute to decompensation of the heart failure patients attended in primary care is scarce.
Purpose: To determine the distribution and importance of factors, especially the preventable ones, that contribute to heart failure decompensation in patients attended in primary care
Methodology: HEFESTOS is a cohort study aimed at knowing the main triggers and the prognosis of some factors related with the heart failure decompensations attended in primary care setting.
The following variables were collected: age, sex, heart rate, blood pressure, NYHA class, days since the onset of symptoms, oxygen saturation, diuretic dose, crackles

, ankle oedemas, paroxistic dispnea, pathological weight gain, orthopnea, hospital admission in the last year, causative factor of decompensation, comorbidity and ejection fraction. The main outcome was hospitalization or death in the month following the inclusion.
Results: Consecutive sample of 425 patients attended in primary care for decompensation of pre-existing heart failure (from 1st, March 2015 to 31st December 2017) were included. Women were 55.8%. Mean (SD) age was 81.5 (9.1) years. Hospitalization or death in the month following the inclusion occurred in 133 (31.3%) patients. Potential causative factors for decompensated heart failure were identified in 83.1% of patients. More than one factor was identified in 34.9% of patients. Non compliance with fluid or salt restriction was the most commonly identified factor (30.3%), followed by respiratory infection (30.2%),non-compliance with drugs treatment (21.4%), worsening of atrial fibrillation(12.2%),contraindicated drugs (9.7%), worsening of renal function (4.7%), anemia(4.5%) and coronary ischaemia (3.8). Respiratory infection, worsening of atrial fibrillation, worsening of renal function and coronary isquaemia were related with more probability of hospitalizacion or dead.
Conclusions: Non compliance with fluid or salt restriction and respiratory infection Were the most frequent causes of decompensation of HF in patients attended in primary care. More than half of the causes could have been prevented

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One-year prognosis of patients with chronic heart failure, depending on AHEAD score and renal function (creatinine and NGAL).

K Karel Labr[1]; J Spinar[2]; J Parenica[2]; L Spinarova[1]; F Malek[3]; M Spinarova[1]; O Ludka[2]; J Jarkovsky[4]; K Benesova[4]; J Tomandl[5]; M Tomandlova[5]; R Labrova[2]
[1]St. Ann university hospital and Masaryk university, Brno, Czech Republic; *[2]University hospital Brno and Masaryk university, Brno, Czech Republic*; *[3]Na Homolce Hospital, Prague, Czech Republic*; *[4]Institute of Biostatistics and Analyses of Masaryk University, Brno, Czech Republic*; *[5]Masaryk University, Department of Biochemistry, Brno, Czech Republic*

Background and Purpose: The incidence of renal insufficiency is increasing with an increasing number of patients with heart failure. Therefore, it is important to detect and predict renal failure. Neutrophil gelatinase-associated lipocalin (NGAL) is an early marker of renal impairment and is associated with the prognosis of heart failure patients.
Methods and Results: 547 patients from the multicenter registry of FARmacology and NeuroHumoraL activation (FAR NHL) were included, who had available data on follow-up hospitalizations, mortality, and biomarker levels. Patients with heart failure with a lower left ventricular ejection fraction below 50% who were at least one month stable (80.3% of men, median age 66 years). The etiology of heart failure was 54% ischemic heart disease, in 40% dilatated cardiomyopathy. 69% of patients were in New York Heart Associaton (NYHA) functional class II. In the first year of follow-up, 76 events (13.9%) occurred, including all-cause deaths (3.8%), hospitalization for acute heart failure (10.1%), and left ventricle assist device (LVAD) implantation or orthotopic heart transplantation (OHT, 2.0%). In patients with AHEAD score (atrial fibrillation, anemia, old age, renal insufficiency, diabetes mellitus; 1 point for each), 0-1, the incidence of events was 11.9%, AHEAD 2-3 in 16.2%, and AHEAD 4-5 in 18.0% of patients. The best predictive power of NGAL and creatinine was in patients with AHEAD score 2-3, when NGAL at a cut-off value of 61.3 ng / mL (according to ROC analysis) has a sensitivity of 73.3% and a specificity of 50.6% (p = 0.032). For creatinine at 119.5 µmol / L, the sensitivity was 52.6% and the specificity was 65.3% (p = 0.035).
Conclusion: According to FAR NHL registry, renal functions expressed by creatinine and NGAL have the best ability to predict occurrence of events in moderately ill patients.

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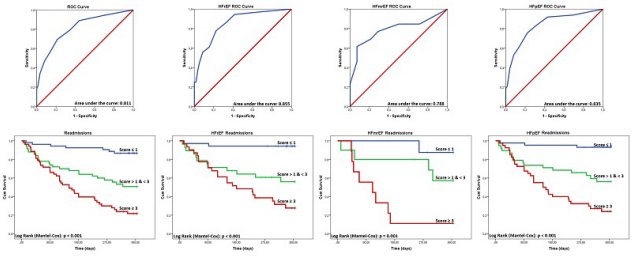
Predicting readmissions in patients with heart failure: a novel and easy-to-apply scoring model

J Ribeiro Agostinho[1]; J Rigueira[1]; A Nunes-Ferreira[1]; I Aguiar-Ricardo[1]; T Guimaraes[1]; I Goncalves[1]; R Pires[2]; F Veiga[1]; M Mendes Pedro[1]; FJ Pinto[1]; D Brito[1]
[1]Cardiology Department, Santa Maria Hospital, CHLN, CCUL, Lisbon University, Lisbon, Portugal; *[2]Faculty of Psychology, CINEICC, University of Coimbra, Coimbra, Portugal*

On behalf of: RICA-HFTeam

Introduction: Readmission (reH) rates are particularly high in patients (pts) admitted for acute/decompensated chronic heart failure, being a relevant cause of impaired quality of life, and a main negative prognostic determinant. Therefore, the identification of pts at a higher risk of reH is at utmost relevance.
Objective: Development of an easy-to-apply score, useful for prediction of all-cause reH during the first year after discharge.
Methods: Retrospective study with prospective data registry of consecutive pts discharged after an index-hospitalization due to acute HF. All pts were submitted to clinical, laboratorial, electrocardiographic and echocardiographic evaluations. Cox Regression was used to ascertain predictors of readmission; ROC curve method, and Kaplan-Meier survival analysis were used to evaluate score efficacy.
Results: 156 pts were included (mean age:68.1 ± 12.4years, 60.1% males). The mean left ventricular ejection fraction (LVEF) was 36.4 ± 15.9% (LVEF < 40% in 60.3%). Seventy (44.8%) pts were discharged in NYHA I functional class, 51.9% in class II and 3.2% in class III. Mean follow-up time was 11.1 ± 2.6 months. The reH rate during follow-up was 46.2% and the mortality rate was 10.3%. Previous ischemic stroke (iS) (HR = 2.3, CI = 1.3-4.1, p = 0.004), history of malignancy (hNeo) (HR = 2.6, CI = 1.4-4.9, p = 0.025), on-admission values of hemoglobin (Hb) < 12g/dL (HR = 2.3, CI = 1.4-3.6, p = 0.001), total bilirubin (TBil) >1.2mg/dL (HR = 2.1, CI = 1.2-3.5, p = 0.007), alkaline phosphatase (ALP) >105U/L (HR = 2.0, CI = 1.2-3.3, p = 0.027) and thyroid-stimulating hormone (TSH) >4.1uU/mL (HR = 2.3, CI = 1.4-3.6, p = 0.003) and a length of stay (LOS) > 17days (HR = 2.1, CI = 1.2-3.4, p = 0.028) and NTproBNP>4250pg/mL (HR = 2.1, CI = 1.1-4.1, p = 0.011) and blood nitrogen urea (BUN) >67mg/dL (HR = 3.3, CI = 2.0-5.6, p = 0.004) at-discharge were independent predictors of reH. According to the Hazar Ratio, was attributed 1 point to iS, Hb < 12g/dL, TBil>1.2mg/dL, ALP>105U/L, TSH>4.1uU/mL, NTproBNP>4250pg/mL and LOS>17days; and 1.5 points to BUN>67mg/dL and hNeo, with a maximum score of 10 points in total. This model showed a good accuracy to predict reH during the first year after discharge [area under de ROC curve (AUC) = 0.81]. Based on tercile distribution the population was classified as low-risk (score = 1; reH rate:13.2%), intermediate-risk (score>1 and < 3; reH rate:48%) and high-risk (score = 3; reH rate:77.4%). The model showed the best accuracy for pts with either a reduced LVEF (AUC = 0.86), or a preserved LVEF (AUC = 0.84), and showed fair accuracy when applied to pts with HF and LVEF in the midrange (AUC = 0.79).
Conclusion: This new scoring model showed good accuracy in predicting all-cause readmissions during the first year after discharge when applied to patients hospitalized for acute HF. As it is based on clinical and laboratorial standard parameters, it may be a useful and easy-to-apply tool for the identification of HF patients requiring a closer follow-up after discharge.



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Long-term clinical outcome in patients with heart failure and pacemakers: a single-center cohort study

M Martin Riesenhuber[1]; A Spannbauer[1]; F Rauscha[1]; H Schmidinger[1]; T Pezawas[1]; C Schukro[1]; M Gwechenberger[1]; C Khazen[2]; G Stix[1]; T Wrba[3]; C Hengstenberg[1]; D Traxler[1]; C Muller[1]; M Gyongyosi[1]
[1]Medical University of Vienna, Department of Cardiology, Vienna, Austria; *[2]Medical University of Vienna, Department of Cardiac Surgery, Vienna, Austria*; *[3]Medical University of Vienna, Center for Medical Statistics, Informatics and Intelligent Systems, Vienna, Austria*

Background: Clinical and pacemaker (PM) data were retrospectively analyzed and combined with survival in a 10-year follow-up.
Purpose: Aim was to identify differences in patients with/without heart failure (HF).
Methods: Patients with all available clinical (age at the time of first implantation, diagnosis of heart disease, survival data) and PM data were included (N = 1969 women, N = 3129 men). Survival was retrieved from the Federal Institute "Statistics Austria".
Results: HF was diagnosed in 2149 of 5098 PM patients (42.2%): less female (N = 671/34.1%) than male (N = 1478/47.2%) had HF (P < 0.001). Patients with HF had similar age at the first PM implantation as compared to patients without HF (73.2years ± 16 IQR vs 72.5 ± 15 with HF, n.s.). Equal implantation rates of dual-chamber PM were found in HF/non-HF-patients (Table). Patients with HF had significant worse 10-years survival than patients without HF (Figure), with

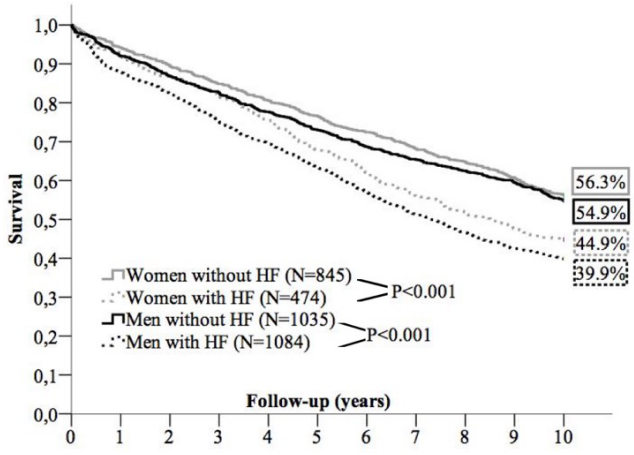
more cardiovascular deaths. Lead impedance of the PM was significantly lower in HF-patients, while pacing thresholds was not different.

Outcome parameters.

	HF N = 2149	Non-HF N = 2949	P Value
Device type			
— Single-chamber PM	624 (31.8%)	867 (31.9%)	n.s.
— Dual-chamber PM	1340 (68.2%)	1848 (68.1%)	n.s.
10-year survival N = 3438	41.4%	55.5%	<0.001
Cause of death			
— Total deaths	1209 (56.3%)	1221 (41.4%)	<0.001
— Cardiovascular death	668 (31.1%)	613 (20.8%)	<0.001
— Malign death	149 (6.9%)	194 (6.6%)	n.s.
— Other death	392 (18.2%)	414 (14.0%)	<0.001
Parameters			
— Atrial PT (V)	0.6±0.5	0.7±0.5	n.s.
— Ventricular PT (V)	0.5±0.4	0.5±0.3	n.s.
— Atrial LI (Ohm)	495±139	507±150	0.007
— Ventricular LI (Ohm)	650±210	671±194	<0.001

PT: Pacing threshold; LI: Lead impedance

Conclusion: PM-patients with HF had worse clinical outcome and higher cardiovascular mortality. Lead impedance was decreased in HF and might be a predictor of fluid overload.



Kaplan-Meier: 10-year survival

P295

QRS duration is associated with outcome in symptomatic HF patients. What about ACCF/AHA stages A and B? Data from the DAVID-Berg study

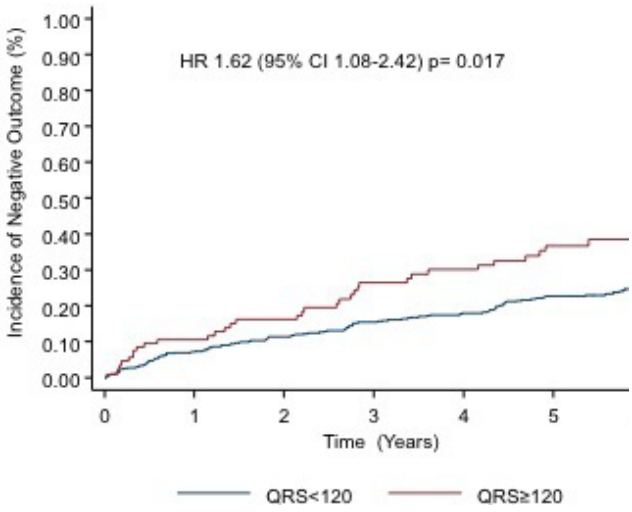
A Andrea Pozzi[1]; M Gori[2]; A Iorio[2]; A Iacovoni[2]; A Grosu[2]; A Fontana[2]; P Canova[2]; A Calabrese[2]; P Ferrari[2]; A Gavazzi[3]; M Senni[2]

[1]Cardiovascular Research Centre of Glasgow, Glasgow, United Kingdom; [2]Ospedale Papa Giovanni XXIII, Cardiology, Bergamo, Italy; [3]Ospedale Papa Giovanni XXIII, FROM Fondazione per la Ricerca, Bergamo, Italy

On behalf of: DAVID-Berg

Background: QRS duration is associated with poor outcome in symptomatic heart failure (HF), irrespective of ventricular function. However, no data are available in asymptomatic patients with HF ACCF/AHA classes A and B. Our aim was to assess whether QRS duration may predict outcome in a HF preclinical setting.

Methods: The DAVID-Berg study prospectively enrolled 614 outpatients at increased risk for HF, but asymptomatic. All patients underwent a protocol consisting of history, physical examination, blood chemistry, NT-proBNP testing, 12-lead ECG, and echocardiogram. ECGs were coded according to Minnesota coding system blinded to clinical information. QRS duration was considered both as continuous and as cathegorical variable (cut-off= 120 ms). The endpoint of interest was a composite of HF onset, cardiovascular (CV) hospitalization (stroke, TIA, myocardial infarction, and myocardial revascularization), and all cause death.



KM cumulative incidence of outcome

Results: Mean age of the population was 69 ± 7, 56% were male, mean LV ejection fraction (LVEF) was 58%, mean QRS duration was 97 ± 21 ms, and 18% (n = 109) had QRS duration = 120 ms. During a median follow-up of 5.7 years, there were 149 adverse events. At Cox regression analysis QRS duration was associated with increased risk of the composite outcome, even accounting for demographics, CV risk factors, LVEF, diastolic function, NT-proBNP, and other ECG abnormalities (HR 1.01, 95% CI 1.00-1.02, adjusted p = 0.038). Considering QRS as categorical variable, patients with wider QRS (= 120 ms) were more likely to have worst outcome (HR 1.62, 95% CI 1.09-2.42, adjusted p = 0.017; Fig 1).

Conclusions: In patients with HF ACCF/AHA stages A and B, QRS duration is related with increased risk of HF onset, CV hospitalization and all cause of death.

P296

A method for predicting the survival of patients with heart failure

LV Prokopova[1]; MYU Sitnikova[1]; EV Shlyakhto[1]

[1]Almazov National Medical Research Centre, Department for Heart Failure, Saint Petersburg, Russian Federation

To determine the tactics of management in a patient with heart failure, it is important to accurately qualitatively evaluate the patient's survival within 1 year.

Goal. Creation of a method for qualitative assessment of the survival prognosis of a patient with systolic heart failure.

Materials and methods: A prospective study of 212 II-IVF patients with "non-valvular etiology" of HF with an LV ejection fraction (Simpson) = 35% at the age of 18-70 years. Of these, 176 men (83%) and 36 women (17%). Design work: hospitalization of patients in the department, specialized in the treatment of heart failure; selection of therapy and stabilization of patients; assessment of status, performance of laboratory and instrumental studies; observation, telephone contacts, correction of therapy and hospitalization during decompensation; filling the database of 200 indicators. After 12 months, the endpoints were recorded.

Results: Within 12 months, 64% of patients (135 people) survived, 2% (5 people) had an implant system EXCOR, 10% (21 people) had cardiac transplantation, 24% of cases (51 people) were lethal. The end points reached 77 people. Later, a multiple logistic regression analysis was carried out. A method for qualitative assessment of the survival prognosis was obtained, which includes the following predictors: the age of debut of heart failure, the frequency of respiratory movements, systolic blood pressure, orthostasis measured at 3-5 minutes, lymphocyte count and erythrocytes distribution by volume in serum ($p < 0.05$). Survival is calculated by the formula including these predictors with the corresponding coefficients. If a patient with a survival prediction is less than 1 year old, he should be sent to the selection committee at a major cardiac center in the shortest time to resolve the issue of heart transplantation or mechanical support of blood circulation. With the expected prognosis of survival over 1 year, further outpatient monitoring and the resolution of the ICD question are indicated.

Conclusions: 1. The method of qualitative assessment of the prognosis of survival of a patient with systolic heart failure allows one to evaluate the patient's survival in the coming year using simple indicators.

3. Using the method of qualitative assessment of the patient's survival forecast, the doctor can adjust the tactics of the patient's management and determine the indications for high-tech medical care.

P297
Predictors of mid-term rehospitalization and mortality rates in Bulgarian patients with heart failure and mid-range ejection fraction: a single-center study

R Pancheva[1]; N Runev[1]; E Manov[1]; B Stoimenov[1]; E Dimchovski[2]; D Vassilev[3]
[1]University Hospital Alexandrovska, Cardiology Clinic, Department of Propaedeutics of Internal Diseases , Sofia, Bulgaria; *[2]Medical Institute of Ministry of Interior, Department Cardiology, Sofia, Bulgaria*; *[3]University Hospital Alexandrovska, Department Cardiology, Sofia, Bulgaria*

Background: Chronic heart failure (CHF) is a major cause of death and recurrent rehospitalization. Heart failure with midrange ejection fraction (HFmrEF) is a new category of heart failure (HF), inbetween HF with reduced ejection fraction (HFrEF) and HF with preserved ejection fraction (HFpEF). Limited data exist on the epidemiology, treatment and short or longterm prognosis of patients with HFmrEF.
Purpose: The aim of this study was to analyse baseline characteristics and outcome of patients with HFmrEF.
Methods: An observational study of patients with decompensated HFmrEF, admitted at our Department between January 2012 and June 2013, was conducted. Among the risk factors, co-morbidities, clinical, echocardiographic and hemodynamic indicators, predictors of their mortality and rehospitalization rates were investigated.
Results: A total of 135 patients, mean age 68.6 ± 11.1 years, were studied. The demographic characteristics were as follows: 89.6% had arterial hypertension (AH) (1.5% stage I; 47.4% stage II; 40.7% stage III); 33% type 2 diabetes mellitus (DM); 32.6% suffered from coronary artery disease (CAD), of whom 13.3% with previous myocardial infarction (MI); 49.5% had valvular heart disease (VHD) (of whom 21.5% with mitral valve disease (MVD); 4.4% with aortic valve disease (AVD); 8.9% with combined mitral and aortic valve disease (MVD+AVD) and 11.1% with prostetic heart valve/s); 75.6% had atrial fibrillation (AF) (of whom 2.2% with de novo AF; 11.9% with paroxysmal AF; 3,0% with persistent AF and 58,5% with permanent AF); and 51.1% elevated pulmonary artery systolic pressure (PASP) (<40 mmHg). In the follow-up period with average duration of 5 years, 68 patients (50.4%) died. For independent predictors of the 5-year mortality in our HFmrEF group, the following were found: age>67 years (OR 2.42; 95% CI, 1.19-4.92; $p < 0.05$), mitral valve disease (MVD) and combined mitral and aortic valve disease (AVD) (OR 3.29; 95% CI, 1.49-7.26; $p < 0.01$), PASP >44 mmHg (OR 4.79; 95% CI, 1.92-11.98; $p < 0.01$), CHA2DS2VASc >4 points (OR 2.80; 95% CI, 1.29-6.10; $p < 0.01$).
In the clinical follow-up period with average duration of 1 year, 19 patients (14.1%) experienced rehospitalization because of an exacerbation of congestive HF. Using a multivariate logistic regression analysis, the following independent predictors of rehospitalization were found: AH stage III (OR 3.76; 95% CI, 1.33-10.65; $p < 0.05$) and permanent AF (OR 3.38; 95% CI, 1.95-5.86; $p < 0.01$).
Conclusion: Because of the lack of data regarding patients with HFmrEF in Bulgaria, we performed this single-center study. The analysis has revealed that the 5 year mortality rate is predicted mainly by the advanced age (<67 years), presence of MVD and combined MVD + AVD, pulmonary hypertension and high CHA2DS2VASc score. The 1 year rehospitalization rate has been found to be highly dependent on AH stage III and permanent AF.

P298
Clinical presentation of heart failure in female patients-results from CRO-HF Registry

D Glavas[1]; K Novak[1]; D Milicic[2]; J Borovac[1]; B Jurcevic Zidar[1]
[1]Split University Hospital, Split, Croatia; *[2]University of Zagreb-School of Medicine, Zagreb, Croatia*

Introduction: Heart failure (HF) could be different in specific population. The aim of the study was to analyse clinical presentation of HF in female patients according to results from CRO-HF Registry.
Methods and Results: We analysed 2203 hospital HF patients (data based on CRO-HF Registry): 1175 (53.3%) males (m) and 1028 (46.7%) females (f); median age 76 y. One third patients suffered of acute HF. Preserved left ventricular function (LVEF = 50%) was recorded in 37.8% patients. Females had frequently preserved LVEF (= 50%) (f-49.3%, m-29.3%, $p < 0.001$) and males reduced LVEF (< 50%) (m-70.7%, f-50.7%).
History of hypertension (AH) had 67.5% patients, diabetes 34.4%, myocardial infarction 22.7%, renal failure 19.2%, COPD 17.3%, stroke 16.5% and atrial fibrillation 53.7% patients. In males, comparative to females, important disease was COPD (m-19.7%, f-14.7%, $p = 0.009$), renal failure (m-23%, f-14.8%, $p < 0.001$), diabetes (m-36.1%, 32.6%, $P = 0.08$), stroke (m-17.1%, f-15.9%, $P = 0.547$) and smoking habit (m-14.8%, f-6.4%, p= < 0.001).
The frequently precipitating factors of HF were: arrhytmiae (m-56.1, f-58.3), valvular diseses (m-67.3%, f-67%) and infections (m-18.7, f-20.4%). Important "trigger" in females was hypertension (f-58.7%, m-52.7%, $P = 0.009$), arrhytmiae (f-58.3%, m-56.1%), infections (f-20.4%, m-18.7%), and acute coronary syndrome (ACS) in males (m-22.1%, f-17%, $P = 0.010$). Females had often atrial arrhytmiae (f-92.2%, m-87.6, $P = 0.010$)
Lower values of haemoglobin was recorded in 51.9% patients, higher creatinine had 46.8%, ALT 29.8%, cholesterol 32.7%, triglycerides 31.9%, uric acid 79.3%, and hyperglycaemia 99.8% patients. In females, we recorded higher values of ALT (f-33%, m-27%, $P = 0.012$, $C = 0.066$), cholesterol (f-36.8%, m-29.1%, $P = 0.009$), triglycerides (f-36.1%, m-28.3%, $P = 0.014$), uric acid (f-82.9%, m-76.4%, $P = 0.007$), and males lower haemoglobin levels (m-58%, f-44.8%, $p = 0.001$)
Hospital mortality was lower in males than in females (m-12.6%, f-14.4%).
There were no significant differences in HF treatment according to gender.
Conclusion: Clinical presentation of HF could be different in female patients, according to CRO-HF Registry
Results: Females have frequently preserved LVEF, higher values of ALT, cholesterol, tryglicerides and uric acid, and males have lower values of LVEF and haemoglobin. Hypertension is important "trigger" of HF in females and ACS in males. HF treatment should be adapted to clinical presentations of HF according to gender.

P299
Heart failure and chronic obstructive pulmonary disease: outcome predictors

VM Violetta Gazizianova[1]; OV Bulashova[1]; EV Khazova[1]
[1]Kazan State Medical University, Kazan, Russian Federation

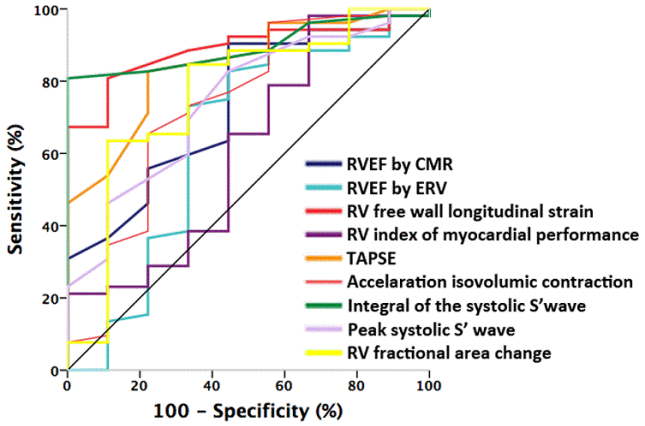
Introduction: It is well known that coexistence of heart failure (HF) and chronic obstructive pulmonary disease (COPD) increases amount of cardiovascular and pulmonary events. There is information about prognostic factors in HF and COPD, however there is little data about prognostic factors in HF associated with COPD.
Purpose of the study was to analyze the one year outcomes in HF patients concominant COPD and to indicate prognostic factors of cardiovascular and pulmonary events.
Methods: Clinical assessment, spirometry, echocardiography were performed in 105 patients with stable HF concominant COPD (mean age 65,09 ± 10,74 years, ischaemic aetiology 92,3%, NYHA class I-II 42%, III-IV 58%). Forced expiratory volume in 1 s (FEV1) and forced vital capacity (FVC) were assessed according to American Thoracic Society/European respiratory society Guidelines. All cardiovascular events (cardiovascular death, non-fatal myocardial infarction and stroke, tromboemboli complications, acute heart failure decompensation) were assessed as combine outcome. Amount of cardiopulmonary events (summary of all cardiovascular and pulmonary events) was assessed independently. The median follow up time was 1 year. Cox logistic regression was performed with using Statistica 10.0 software for analysis, p value of < 0,05 was taken as significant.
Results: The 98 patients were followed up for a period one year which included cardiovascular and pulmonary outcomes. After one year follow up the cardiovascular events structure was following: cardiovascular death was found in 6,1%, non-fatal myocardial infarction in 9,2%, non-fatal stroke in 6,1%, acute decompensation of chronic heart failure in 38,8%, tromboemboli complication in 5,1%. Combine outcome (cardiovascular events) was noted in 62,2%, cardiopulmonary outcomes in 98,0%. The combine outcome was associated with 6 minute walking distance < 300 meters (OR = 2,832; 95% CI 1.97-4.06, $p < 0,001$), FEV1 < 50% (OR = 2,155; 95% CI 1.569-2.959, $p < 0,001$), FVC < 70% (OR = 2,074; 1.496-2.876, $p = 0,004$). Cardiopulmonary outcome predictors were the same: walking test less than 300 meters (OR = 2,063; 95% CI 1.596-2.665, $p < 0,001$), FEV1 < 50% (OR = 1,875; 95% CI 1,477-2,381, $p < 0,001$), FVC < 70% (OR = 1,442; 1,158-1,797, $p = 0,049$). Conclusion. Our study showed a strong association of 6 minute walking distance < 300 meters, FEV < 50%, FVC < 70% with combine outcome (cardiovascular events) and cardiopulmonary outcome in HF patients concominant with COPD.

Chronic Heart Failure - Diagnostic Methods

P300
What is the best imaging technique to explore right ventricular function at the time of multimodality cardiovascular imaging?

S Stephanie Cazalbou[1]; V Chong Fah Shen[1]; A Petermann[2]; D Eyharts[1]; P Fournier[1]; E Cariou[1]; Y Lavie-Badie[1]; D Carrie[1]; M Galinier[1]; I Berry[3]; O Lairez[1]
[1]Toulouse Rangueil University Hospital (CHU), Department of Cardiology, Toulouse, France; *[2]Toulouse Rangueil University Hospital (CHU), Department of Radiology, Toulouse, France*; *[3]Toulouse Rangueil University Hospital (CHU), Department of Nuclear Medicine, Toulouse, France*

Background: - Right ventricular (RV) function is a powerful independent predictor of adverse heart failure outcomes. Several RV imaging parameters have been



ROC curves for the prediction of MACE

proposed to detect patients at risk new-onset acute heart failure. The objective our study was to compare the predictive value of main RV systolic parameters for outcomes.

Methods: One hundred and one patients underwent comprehensive cardiovascular imaging modalities including transthoracic echocardiography (TTE), cardiac magnetic resonance imaging (CMR) and tomographic equilibrium radionuclide ventriculography (ERV) for the assessment of RV function. The composite primary endpoint was the occurrence of a major adverse cardiac event (MACE), i.e., death, heart transplantation, or new-onset acute heart failure defined as hospital admission for diuretic treatment optimization.

Results: Mean NYHA class and left ventricular ejection fraction were 1.7 ± 0.9 and 46 ± 18%, respectively. During a mean follow-up of 10 ± 9 months, 16 (16%) patients reached the composite primary endpoint. The areas under the receiver operator characteristic curves for the prediction of MACE were 0.894 (P < 0.001), 0.890 (P < 0.001), 0.844 (P = 0.001), 0.765 (P = 0.012), 0.745 (P = 0.020), 0,735 (P = 0.025), 0.734 (P = 0.026), 0.643 (P = 0.173) and 0.613 (P = 0.281) for integral of the systolic S' wave of tricuspid annulus, RV free wall longitudinal strain, tricuspid annular plane systolic excursion, RV fractional area change, peak systolic S' wave velocity of tricuspid annulus, RV ejection fraction by CMR, RV index of myocardial performance, RV ejection fraction by ERV and acceleration of the RV myocardium during isovolumic contraction, respectively (Figure).

Conclusion: Among comprehensive cardiovascular imaging modalities allowing the assessment of RV function, echocardiographic parameters, and particularly integral of the systolic S' wave of tricuspid annulus and RV free wall longitudinal strain, have the best prognostic performance.

P301

The assessment of myocardial deformation in patients with acute decompensation of ischemic heart failure with reduced ejection fraction by 2d-speckle tracking technology

EV Kruchinkina[1]; TR Ryabova[1]; VV Ryabov[2]
[1]Cardiology Research Institute, Tomsk National Research Medical Center, Tomsk, Russian Federation; *[2]National Research Tomsk State University, Tomsk, Russian Federation*

Background: Ischemic heart disease is a common cause of chronic heart failure (CHF). Despite significant advances in study of the pathogenesis of CHF and the introduction of effective medical therapy for CHF patients, the incidence of hospitalizations for acute decompensated heart failure (ADHF) remains high. An important component in the pathogenesis of CHF and ADHF is myocardial inflammation. A left ventricular (LV) remodeling causes the development of heart failure, and directly correlates with the left ventricular ejection fraction (LVEF), but does not represent the myocardial contractility. 2D-speckle tracking echocardiography allows determining the deformation of the LV and the prognosis of CHF, in contrast to standard echocardiography.

The purpose of study was to assess the deformation of the LV in patients with ADHF of ischemic etiology depending on the presence or absence of diagnosed myocardial inflammation.

Materials and Methods: The analysis included 25 patients (84% men, LVEF 29.17 ± 9.4%) with ADHF of ischemic etiology. Patients were divided into groups according to the classification of ADHF: warm-dry (58%), warm-wet (4%), cold-dry (8%), cold-wet (30%). The average age of the patients was 60.12 ± 9.3years. All the patients underwent an echocardiography including 2D-speckle tracking technique to assess LV deformation. A coronary angiography was performed to exclude ischemic etiology of ADHF. An endomyocardial biopsy with following immunohistological examination was performed to diagnose the presence of myocardial inflammation. Patients were divided into 2 groups depending on the presence or absence of myocardial inflammation.

Results: We have revealed a statistically significant decrease in apical rotation by 49% (p = 0.0286) and apical rotation rate (S) by 44% (p = 0.0382) in the group with diagnosed myocardial inflammation upon admission. We did not notice the difference in apical rotation between 2 groups of patients in a year. However, we have observed the increase of global longitudinal strain in the group of patients with the presence of myocardial inflammation (p = 0.0431).

Conclusion: We observed significant decrease in apical rotation in the group of patients with diagnosed myocardial inflammation, while there were not statistically significant differences in basal rotation characteristics between 2 groups. This fact could be the marker of the presence of inflammatory, not the ischemic, myocardial damage. Thus, 2D-speckle tracking is a promising non-invasive method for diagnostics of myocardial inflammation.

P302

Low Levels of CA125 and Risk of Short-term Events after an Episode of Acute Heart Failure

M Amiguet Comins[1]; G Minana[1]; E Santas[1]; E Valero[1]; R De La Espriella[1]; FJ Chorro[1]; I Cardells[1]; J Gonzalez D'gregorio[1]; A Mollar[2]; J Sanchis[1]; R Heredia[1]; A Paya[1]; A Bayes-Genis[3]; J Lupon[3]; J Nunez[1]
[1]University Hospital Clinic of Valencia, Cardiology, Valencia, Spain; *[2]Research Foundation Hospital of Valencia (INCLIVA), Valencia, Spain*; *[3]Germans Trias i Pujol University Hospital, Badalona, Spain*

Funding Acknowledgements: CIBER CV 16/11/00420, 16/11/00403; FEDER and PIE15/00013.

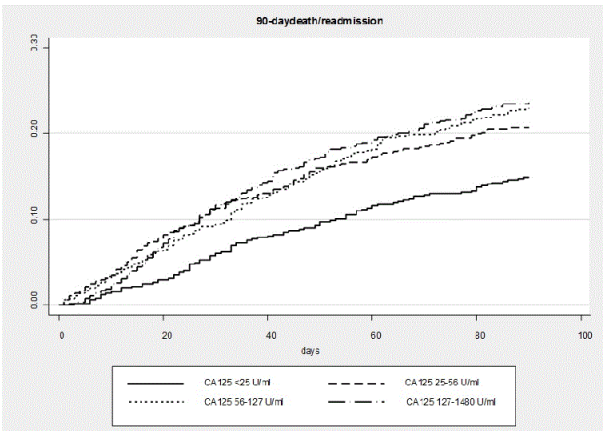
Backgroud: After an episode of acute heart failure (AHF) the risk of early adverse events, specially readmission, remains very high. Unfortunately, there are not well-established risk factors to tailor this risk. Plasma levels of Antigen Carbohydrate 125 (CA125) have emerged as a reliable biomarker of congestion and higher values have been consistently related with higher risk of mortality in AHF. In this work, we sought to evaluate the relationship between this biomarker and the composite of 90-day death and/or HF-readmission.

Methods: We included 2244 patients consecutively with AHF. CA125 was measured during early admission. The association between the composite of 90-day death and/or HF-readmission was assessed using COX regression analysis.

Results: Mean age was 73 ± 11years, 711 (31.7%), 336 (15%) and 1197 (53.3%) patients displayed reduced, intermediate and preserved ejection fraction, respectively. Median CA125 plasma levels were 56 U/ml (25-127). At 90 days, 439 events (19.6%) were registered.

Patients in the inferior quartile (Q1 < 25 U/ml) showed the lowest cumulative risk of events, as it is depicted in the figure below (p < 0.01).

After multivariable adjustment this association persisted. Compared to patients in the upper quartile (Q4), patients belonging to Q1 exhibited a significant decrease of risk (HR = 0.63; CI95: 0.47-0.84, p = 0.002). Conversely, patients in the medium quartiles (Q2, Q3) showed similar risk.



90-day death and/or readmission

Conclusion: In patients admitted with AHF, low plasma levels of CA125 identify a subset of patients at lower risk of the composite of 90-day death and/or readmission.

P303
Incremental value of intact fibroblast Growth factor 23 to natriuretic peptides for long-term risk estimation of heart failure patientsg

D Damien Gruson[1]; S Ahn[1]; MF Rousseau[1]
[1]*Saint-Luc University Clinics, Brussels, Belgium*

Background: Fibroblast growth factor 23 (FGF-23), a key hormone for the regulation of the phosphorus homeostasis, has also several direct effects on cardiac function. In heart failure (HF), the increase of FGF-23 could stimulate cardiac hypertrophy and remodeling.
Purpose: To determine intact FGF-23, the biologically active hormone, in HF patients with reduced ejection fraction (HFrEF) and assess its prognosis value for cardiovascular death over a long-term follow-up.
Methods: One hundred twenty chronic HF patients (females n = 25; males n = 95; NYHA II-IV; mean age: 66 years; etiology: ischemic n = 83, dilated cardiomyopathy n = 37; mean EF: 23 %) were included. The primary outcome was cardiovascular death. Levels of iFGF-23 and N-terminal proBNP (NT proBNP) were measured with fully automated and sensitive immunoassays.
Results: Median levels of iFGF-23 were equivalent in women (78.2 pg/mL) and men (75.1 pg/mL; p = 0.81). The concentrations of iFGF-23 were not statistically different between ischemic cardiomyopathies (79.4 pg/mL) and dilated cardiomyopathies (68.0 pg/mL; p = 0.29). As for NT proBNP, iFGF-23 levels were significantly related to New York Heart Association (NYHA) functional classes (p < 0.001). Intact FGF-23 levels were significantly correlated to age (? = 0.17, p = 0.04), eGFR (? = -0.64, p < 0.001) and NT-proBNP (? = 0.20, p = 0.03). Over a mean time of follow-up of 4.2 years, the primary outcome was reported in 76 HF patients. In univariate COX survival analysis, FGF-23 levels were significantly related to long-term cardiovascular death (p < 0.01). The area under the receiver operating characteristic curve, criteria defined as cardiovascular death at the end of the follow-up, was 0.66 (95% confident interval (CI): 0.57 to 0.75) for iFGF-23 and 0.73 (0.64 to 0.80) for NT-proBNP. When iFGF-23 and NT-proBNP were integrated in multimarker strategy, the rate of CV death at the end of the follow-up was 41% in HF patients with both biomarkers below than the median values (n = 34), 65% in HF patients with only one of the biomarker higher than their median value (n = 52); and raise to 82% in HF patients with both iFGF-23 and BNP higher than their median values (n = 34).
Conclusions: Circulating concentrations of intact FGF-23 are related to mortality in patients with HFrEF. Furthermore, measurement of iFGF-23 could provide added value to NT-proBNP for the prognostication of HFrEF.

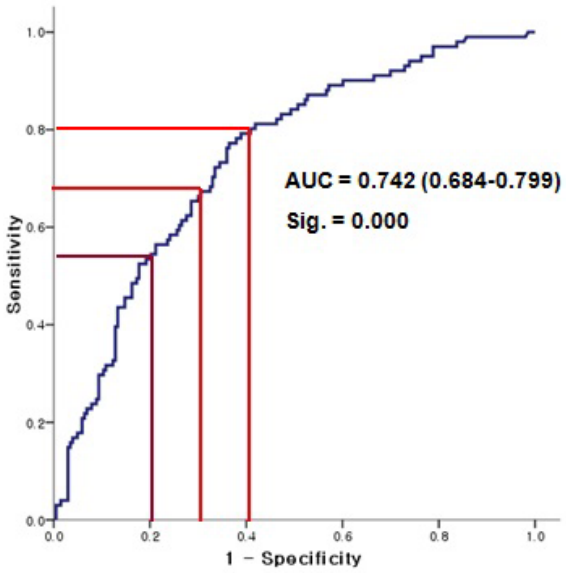
P304
N-terminal pro-B type natriuretic peptide imply left ventricular diastolic function but is a low sensitivity marker

H Hanul Choi[1]; M Shin[1]; W Chung[1]
[1]*Gil Hospital, Department of Cardiology, Gachon University, Gil Medical center, Incheon, Korea Republic of*

Background: Correlations between NT-proBNP with diastolic echocardiographic parameters were not analyzed precisely. We sought to evaluate the clinical implication of NT-proBNP on the LV diastolic function in large scale databases.

Multivariate analysis predictingNTproBNP

Variables	B-Coefficient	P-Value
Age	0.015	0.119
LVEF (vol)	-0.035	0.004
LVmi	0.004	0.229
LAVi	0.042	0.000
RVsP	0.027	0.306
E/E' ratio	0.042	0.000
BSA	-0.198	0.778



ROC curves of NT-proBNP predicting E/E'

Methods: NT-proBNP(n = 23,029) and echocardiography databases(n = 48,750) were collected. Cases measured within 24 hours were enrolled and increased serum creatinine level(>2.0 pg/ml) or acute coronary syndrome were excluded. Finally, echocardiographic parameters were compared with serum NT-proBNP levels in 1,852 patients.
Results: Among patients (54% female, mean age 63.0 ± 0.3), 460 patients (24.8%) showed preserved LV systolic functions (LVEF = 40%, 53.5 ± 0.4%). NT-proBNP levels were significantly correlated with LVEF(r=-0.52, p = 0.01), LA volume index(r = 0.50, p = 0.01), E/E'(r = 0.44, p = 0.01), RV systolic pressure (r = 0.43, p = 0.01) and LV mass index(r = 0.40, p = 0.01). NT-proBNP showed low sensitivities to determine E/E' ratio above 15 and LAVI above 27 on cut-off values of the ROC curve with specificity of 80% (51.7% at 686.6 ng/L, 58.7% at 643.1 ng/L). Interestingly, in patients with preserved systolic function (55.9% male, mean age 61.2 ± 0.7), NT-proBNP showed slightly high sensitivity than in total study group (53.5% at 717.0 ng/L, 60.9% at 443.3 ng/L).
Conclusions: Although NT-proBNP was proved as a useful parameter for assessing LV diastolic function as well as systolic function, it showed relatively low sensitivity to determining LV diastolic function. Therefore, NT-proBNP may imply LV diastolic function but should be interpreted with combining clinical informations.

P305
Increase of high molecular weight adiponectin in heart failure patients with reduced ejection fraction.

D Damien Gruson[1]; B Ferracin[1]; S Ahn[1]; MF Rousseau[1]
[1]*Saint-Luc University Clinics, Brussels, Belgium*

Background: Adiponectin is secreted by the adipose tissue and is an important regulator of insulin sensitivity, lipid metabolism and inflammation. Adiponectin has also complex roles in cardiovascular diseases and is considered cardioprotective by reducing oxidative stress, hypertrophy, and inflammation. In heart failure (HF), the increase of circulating adiponectin has been observed. However, several circulating forms of adiponectin exist and a comprehensive evaluation of high-molecular-weight (HMW), the active form of the hormone, remains to be performed in HF.
Purpose: To determine circulating levels of HMW adiponectin in HF patients with reduced ejection fraction (HFrEF) and assess the relationships with other cardiac biomarkers.
Methods: Forty four chronic HF patients (females n = 11; males n = 33; NYHA II-IV; mean age: 71 years; etiology: ischemic n = 32, dilated cardiomyopathy n = 12; mean EF: 23 %) were included. Twenty healthy volunteers were also included in our study. Levels HMW adiponectin was quantified on a fully-automated chemiluminescence-based enzyme immunoanalyzer (Lumipulse, Fujirebio). Circulating levels of other biomarkers, B-type natriuretic peptide (BNP), N-terminal pro-B-type natriuretic peptide (NT-proBNP), Galectin-3 and soluble ST2 (sST2) were also measured.
Results: The mean level of HMW adiponectin in healthy volunteers was 4.32 µg/mL and the reference interval was 1.2 to 7.4 µg/mL. The circulating HMW adiponectin levels were significantly increased in HFrEF (mean: 7.8 µg/mL; p = 0.03). As for

natriuretic peptides, HMW adiponectin levels were significantly related to New York Heart Association (NYHA) functional classes (p = 0.03). The concentrations of HMW adiponectin were not statistically different between ischemic cardiomyopathies (7.4 μg/mL) and dilated cardiomyopathies (8.8 μg/mL; p = 0.38). HMW adiponectin levels were significantly correlated to eGFR (? = -0.37, p = 0.02), NT-proBNP (? = 0.34, p = 0.05), BNP (? = 0.50, p <0.01), Galectin-3 (? = 0.36, p = 0.02) and sST2 (? = 0.45, p <0.01). Over a mean time of follow-up of 4.2 years, 35 HF patients died of a cardiovascular event. Concentration of HMW adiponectin was significantly higher in HF patients who died in comparison to survivors (8.3 vs 5.9 μg/mL).
Conclusions: Our results demonstrate that circulating HMW adiponectin, the active form of the hormone, is significantly increased in HFrEF patients and correlates with biomarkers related to HF severity.

P306

High-sensitivity cardiac troponin I in heart failure patients with preserved ejection fraction

E Eiji Miyajima[1]; N Fujii[1]; C Yajima[1]; K Hashiguchi[1]; Y Tashiro[1]; Y Takanami[1]; H Hirose[1]; H Yonezawa[1]
[1]*Yokohama City University Medical Center, Yokohama, Japan*

Objectives: High-sensitivity cardiac troponin I (hs-cTnI) is known to be increased in heart failure (HF) patients with decreased ejection fraction (EF), but for HF patients with preserved EF, less is known. Therefore, we examined serum concentrations of hs-cTnI and the relationship between serum concentrations of hs-cTnI and echocardiographic indexes in patients with preserved EF.
Methods: Echocardiography was performed on patients at HF clinic, and 144 patients with preserved EF were enrolled for this study (67 ± 14 years old, 52% male). Mean EF was 70 ± 9% (6 HFmrEF, 138 HFpEF). The 99th percentile cut-off value of the hs-cTnI assay used was 18.3 ng/L, total imprecision was 4.4 % at 18.3 ng/L, and LoD was 0.7 ng/L. During echocardiography, brachial blood pressures (BPs) were measured and echocardiographic indicators, such as left ventricular mass index (LVMI, g/m^2) and E/e' as an indicator of LV diastolic function, were also calculated. Estimated glomerular filtration rate (eGFR (mL/min/1.73 m^2)) was also calculated by converting serum creatinine value.
Results: In all patients, hs-cTnI was detected, in other words greater than LOD, and in 13 % of these patients, the level of hs-cTnI was greater than the 99th percentile value; mean hs-cTnI was 11.6 ± 10.0 (2.2 - 65.2) ng/L. hs-cTnI was significantly correlated with left atrial dimension (LAD), mean E/e', LVMI, and eGFR, but not with BPs, EF. We also applied stepwise regression for multivariate analysis of data for hs-cTnI and for echocardiographic indicators, BP, and eGFR, and found both E/e' and LVMI to be significant (p less than 0.001) variables to predict levels of hs-cTnI, but not eGFR nor EF.
Conclusion: hs-cTnI was detected in HF patients with preserved EF, and correlated with both E/e' and LVMI. Because HF with preserved EF has a poor prognosis, comparable with that of reduced EF, hs-cTnI may be a good clinical indicator for the assessment of treatment, which could improve LV diastolic function and regress LV hypertrophy.

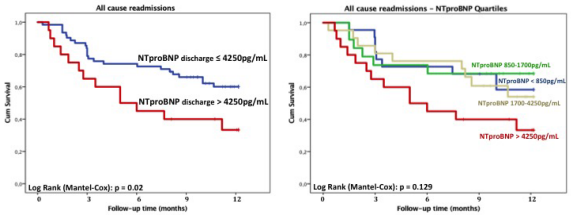
P307

NTproBNP in acute heart failure: which values to rely on to estimate long-term prognosis?

A Nunes-Ferreira[1]; JR Agostinho[1]; J Rigueira[1]; I Aguiar-Ricardo[1]; R Santos[1]; I Santos Goncalves[1]; T Guimaraes[1]; R Placido[1]; T Rodrigues[1]; N Cunha[1]; M Mendes-Pedro[1]; F Veiga[1]; FJ Pinto[1]; D Brito[1]
[1]*Cardiology Department, Santa Maria Hospital, CHLN, CCUL, Lisbon University, Lisbon, Portugal*

On behalf of: RICA-HFTeam

Background: Hospitalizations remain a main cause of morbidity and mortality in heart failure (HF) patients (pts), and readmission rate is still unacceptably high. NTproBNP is widely used as a tool in establishing the diagnosis of HF and as a marker of decompensation. However its efficacy in predicting readmissions is not well established.
Aim: To evaluate the efficacy of NTproBNP in predicting all-cause hospital readmissions during the first year after discharge (index-hospitalization for acute HF).
Methods: Retrospective study with prospective data registry of consecutive pts discharged after hospitalization for acute HF. All pts were submitted to clinical, laboratorial, electrocardiographic and echocardiographic evaluations, including NTproBNP on admission and at discharge. Multivariate Cox regression and Kaplan-Meier survival analysis were used to evaluate NTproBNP utility as a predictor of readmissions.
Results: One hundred and fifty six pts were included (mean age: 68.1 ± 12.4 years, 60.1% males). The mean left ventricular ejection fraction (LVEF) was 36.4 ± 15.9% (LVEF < 40% in 60.3%). Patients were discharged in NYHA functional class I (44.8%), in class II (51.9%), and in class III (3.2%). During a mean follow-up time of 11.1 ± 2.6 months, the readmission rate was 46.2%, and the mortality rate was 10.3%.
The median NTproBNP values were 4222 (IQ: 1981-9715) pg/mL on admission, and 1717 (IQ: 858-4249) pg/mL at discharge. In 92.5% of pts there was a decrease of NTproBNP during hospitalization, and the average descent rate was 48.1 ± 31.9%.
The presence of preserved LVEF (p = 0.011) and worse functional class at discharge (p = 0.005) were associated with readmissions during follow up. NTproBNP at discharge (p = 0.036), particularly if values > 4250pg/mL (4th quartile) were also linked to higher probability of readmission (p = 0.024).
By multivariate analysis (age-adjusted) discharge NTproBNP > 4250pg/mL was established as an independent factor to predict readmissions (HR = 2.6, CI = 1.2-6.0, p = 0.022).
There was no association between admission NTproBNP or the magnitude of decrease during hospitalization and the rate of readmission during follow up (p = NS). Additionally, an increase of NTproBNP during hospitalization did not predicted readmissions as well (p = NS).
Conclusions: NTproBNP at discharge is an important biomarker to predict one-year hospital readmissions. However, contrary to expectations, the absolute value of NTproBNP at discharge, mainly in the presence of higher biomarker levels, seems to be more important than its variation (decrease or increase) during hospitalization for acute HF.



NTproBNP values at discharge

P308

ST2 at time of hospitalisation for heart failure-considerable prognostic value over time

J J Dalal[1]; A Digrajkar[1]; B Das[1]
[1]*Kokilaben Dhirubhai Ambani Hospital, cardiology, Mumbai, India*

Aim: Ability to judge prognosis in patients with heart failure would be of considerable benefit, and the aim of the study was to evaluate the role of ST2 biomarker to predict prognosis in patients hospitalised for chronic heart failure.
Method: 150 patients hospitalised for heart failure and confirmed by NTProBNP had an ST2 measurement during their hospitalisation. All patients were followed for period of two years. They were divided into two groups (1) Normal ST2 (2) Elevated ST2 (above 35 ng/mL)
Result: There were 48 patients in the Normal Group (mean age 65 years, 58% diabetics and 71% hypertensives) and 102 in the Elevated Group (mean age 69 years, 56% diabetics and 79% hypertensives)
At the end of two years there were 2 deaths in the Normal Group and 22 deaths in the Elevated Group.
Conclusion: An elevated ST2 at time of hospitalisation for heart failure was associated with a ten fold increase in mortality over a two year period. This is of considerable clinical value in terms of patient and family understanding of the problem. It will also allow cardiologists to pay greater attention to maximise guideline therapy, and early consideration for devises and cardiac transplantation. We suggest that all patients hospitalised with heart failure should have at least one measurement of ST2 biomarker to separate patients at high or low risk of death.

HEART FAILURE	NUMBER OF PATIENTS	DEATHS AT TWO YEARS
NORMAL ST2	48	2
ELEVATED ST2	102	22

Ten fold higher mortality at two years with elevated ST2

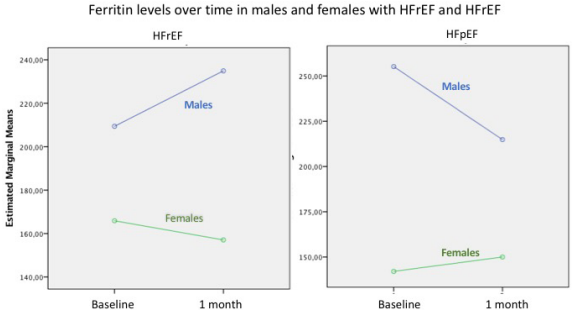
P309

Sex differences in biomarkers over time - covering the HFrEF, HFmrEF and HFpEF spectrum

S Sandra Van Wijk[1]; AMA Barandiaran Aizpurua[1]; M Maeder[2]; V Van Empel[1]; HP Brunner-La Rocca[1]
[1]*Maastricht University Medical Center, Department of Cardiology, Maastricht, Netherlands*; [2]*Kantonsspital St. Gallen, Department of Cardiology, St. Gallen, Switzerland*

On behalf of: TIME-CHF investigators
Funding Acknowledgements: Horten Research Foundation, Roche diagnostics

Background: Despite known sex differences in disease presentation and in biomarkers in heart failure (HF), it is unknown if biomarker sex differences have a similar fashion in HFpEF, HFrEF and HFmREF. Nor is it known how biomarkers change over time in males vs females.



Ferritin levels over time by sex

Purpose: investigate biomarkers over time in males vs females covering the spectrum of HFrEF, HFmrEF and HFpEF.
Methods: Biomarker levels and their changes from baseline to 1 month were compared between males and females in 622 HF patients in TIME-CHF, aged> = 65 years, included as outpatients. 459 had HFrEF (LVEF < = 40; 67% male), 52 HFmrEF (LVEF41-49; 46% male) and 112 HFpEF (LVEF > = 50; 36% male). Investigated biomarkers are NT-proBNP, hsTnT, hsCRP, Hb, creatinine, urea, cystatin-C, ferritin, sTFR, IL-6, GDF-15, Gal-3, ST2, tP1NP, PLGF, sFlt.
Results: In HFrEF, females had lower Hb, lower creatinine, higher tP1NP, lower ferritin, higher sTFR, lower hsTnT, lower GDF-15, and lower ST2. In HFpEF, females had lower creatinine, lower urea, lower ferritin, lower hsTnT. In HFmrEF, females had lower Hb and higher PLGF. The other biomarkers did not differ between males and females in neither of the HF-subtypes.
In the first month, ferritin increased in HFrEF-males but decreased in HFrEF-females (P-interaction = 0.02, figure). In HFpEF, ferritin decreased in males and slightly increased in females (P-int = 0.15). Hs-CRP and hsTnT decreased equally in males and females of all HF-subtypes. NT-proBNP decreased in HFrEF females but remained stable in HFrEF-males (P-int < 0.001). In HFpEF, NT-proBNP decreased in both sexes equally.
Conclusion: Sex-differences in changes over time of ferritin and NT-proBNP are dependent on the HF-subtype, whereas hsTnT and hsCRP decrease over time in males and females of all HF-subtypes equally. This proposes a potential for differential therapeutic strategies in males vs females in different subtypes of HF.

P310

Dynamic changes of sST2 and NT-proBNP levels in responders and non-responders to cardiac resynchronization and cardiac contractility modulation therapies

A Armenui Gasparyan[1]; NB Shlevkov[1]; TV Sharf[1]; VN Shitov[1]; SYU Kashtanova[1]; MD Utsumueva[1]; NA Mironova[1]; VP Masenko[1]; AA Skvortsov[1]
[1]*Cardiology Research and Production Center, department of heart rhythm disturbances, Moscow, Russian Federation*

On behalf of: Gasparyan AZh, Shlevkov NB, Sharf TV, Shitov VN, Kashtanova SYu, Utsumueva MD, Mironova NA, Masenko VP, Skvortsov AA

Background: Use of cardiac contractility modulators (CCM) and cardiac resynchronization therapy (CRT) known to improve clinical course of chronic heart failure (CHF). The influence of these devices on the levels of neurohormonal markers sST2 and NT-proBNP is poorly studied.
Aim: To investigate the changes in the sST2 and NT-proBNP levels in CHF patients in relation to efficacy of cardiac contractility modulaton and cardiac resynchronization therapies.

Methods: Twenty three consecutive patients (16 males / 7 females, mean age = 59 ± 9 years) with medically resistant NYHA class II-III CHF were prospectively studied after CRT (n = 11) and CCM (n = 12) implantation. Six-minute walk test distance (6MWD), echocardiography (ECHO) parameters and levels of neurohormonal markers were evaluated initially and also 6 and 12 months after implantation of the devices. Patients were considered responders to device therapy if end-systolic volume of left ventricle decreases by at least 15% according to repeated ECHO.
Results: Based on the results of observation, signs of a positive response to device therapy ('Responders' group) were registered in 6 of 12 (50%) patients with CCM and in 7 of 11 (64%) with CRT devices, the remaining patients (n = 10) were grouped together as "Non-responders". Initially the groups did not differ significantly according to 6MWD, ECHO parameters, sST2 and NT-proBNP levels. Marked differences between groups were identified after device therapy (see table) with highest relative diagnostic value for sST2 by ROC-analysis.
?onclusion: Dynamic changes in sST2 level are at greatest diagnostic value for the detection of CHF patients with clinical response of either CRT or CCM therapies.

Results of the study by groups

Parameters	'Responders' (n = 13)	'Non-responders' (n = 10)
The level of sST2 ng/ml The area under the ROC-curve = 0,806	21 (19,3-26,3)	40,4 (25,2-40,9)
The level of NT-proBNP, pg/ml The area under the ROC-curve =0,759	362 (71-867)	895 (609-1486)
6-minute walk test distance, m The area under the ROC-curve =0,704	500 (480-540)	464 (340-498)
The LVEF, % (by ECHO)	45 (42-48)	29 (25-34)

P311

Circulating miR-489 as a useful biomarker for DCM

T Tomoya Ishiguro[1]; M Hayashi[1]; W Fujiwara[1]; H Izawa[1]; S Okumura[1]; Y Sugishita[1]; M Yoshinaga[1]; R Yamada[1]
[1]*Fujita Health University Second Hospital, Nagoya, Japan*

Background: : MicroRNAs (miRNA) are functional RNAs that have emerged as pivotal gene expression regulators in any cardiac disease. Although several cardiomyocyte miRNAs have been proven to play roles in the progression of heart failure among patients with idiopathic dilated cardiomyopathy (DCM), the role of circulating miRNAs has not been well-examined.
Methods and Results: After total RNA extraction from peripheral blood samples of three controls and six patients with DCM, miRNA profiling was performed using miRNA arrays. Based on the results of an initial screening, a quantitative analysis of blood samples from an increased number of matched patients (DCM, n = 20; controls, n = 5) was performed using RT-PCR. Finally, the correlation between specific miRNA expression levels and hemodynamic parameters was analyzed.
A primary screening of 2325 miRNAs resulted in the identification of 12 miRNA candidates. Quantitative RT-PCR results revealed significantly increased miR-489 expression levels in the DCM group. Moreover, a significant positive correlation was observed between miR-489 expression level and left ventricular ejection fraction. [Conclusions] Our results suggest that circulating miR-489 could be a potential noninvasive diagnostic biomarker for DCM. Moreover, quantification of circulating miR-489 could have potential prognostic value for patients with DCM, given its positive correlation with left ventricular ejection fraction.

P312

Multibiomarker approach in the assessment of disease severity in patients with stable chronic heart failure

TA Andreasova[1]; F Malek[1]; DV Vondrakova[1]; L Sedlackova[2]; J Dvorak[3]; L Taborsky[2]; P Neuzil[1]
[1]*Na Homolce Hospital, Department of Cardiology, Prague, Czech Republic*; [2]*Na Homolce Hospital, Clinical biochemistry, hematologa and immunology, Prague, Czech Republic*; [3]*National Institute of Public Health, Prague, Czech Republic*

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Background: Novel CHF biomarkers have additive role in prognostic stratification, their role in the assessment of disease severity has not been established.

Study objective: to assess the role of single value of novel CHF biomarkers in the evaluation of the severity of cardiac dysfunction and other organs dysfunction in patients with stable CHF

Patients and method: NT-pro BNP together with galectin-3, sST2, GDF-15, cystatin C, TIMP-1 and ceruloplasmin were analysed together with other laboratory parameters and parameters of systolic and diastolic cardiac function in 160 consecutive stable CHF patients of a tertiary care CHF clinic. Patients cohort comprised od 123 males and 37 females with mean age 65 years, ischemic etiology had 47 % subjects, of 39% had ICD and 36% CRT-D, patients were on optimal medical therapy including BB 98%, ACEI/ARB 84%, MRA 69%. Median NYHA was 2.

Results: median NT-proBNP was 121 pmol/l (1023 pg/ml), mean LV EF 32%, E/A ratio was 1,3 and E/E ' ratio 11. NT-proBNP correlated with novel biomarkers except of galectin-3 (correlation coeficient r from 0,281 to 0,514, p < 0,001). NT-proBNP corellated signficantly with: Na, urea, creatinine, bilirubin, hemoglobin and eGFR and with LV EF, LV EDD, ESD, LA, RV, E/A, E/E'ratios, and estimated pulmonary artery pressure PAP (r from -0,259 to 0,392, p value from < 0,001 to < 0,05). Significant correlation of NT-proBNP and novel biomarkers with laboratory a echocardiografic parameters shown in tabel.

Conclusion: NT-proBNP remains golden standard in the assessment of disease severity in patients with stable chronic heart failure. Role of other biomarkers is limited.

Significant correlation of NT-proBNP and

Biomarker	Laboratory parametr	Echocardiografic parameter	Level of signifikance p
NT-proBNP	Na, urea, creatinine, bilirubin, hemoglobin, eGFR	LV EF, EDD, ESD, LA,RV, E/A, E/E´,PAP	from < 0,001 to < 0,05
Galectin 3	Na, K, urea, creatinine, eGFR		from < 0,001 to < 0,05
sST2	Na, urea, creatinine, eGFR, bilirubin	RV, PAP	from < 0,001 to < 0,05
GDF-15	Hemoglobin, eFGR, urea, creatinin, bili	LA, RV, E/E´ , PAP	from < 0,001 to < 0,05
Cystatin C	Hemoglobin, eGFR, urea, creatinin,	LA, E/A, PAP	from < 0,001 to < 0,05
TIMP-1	Urea, bilirubin	LA, PK, PAP	from < 0,001 to < 0,05
ceruloplasmin	Hemoglobin, Na, K	E/A	from < 0,001 to < 0,05

GDF 15- growth differentiation factorTIMP-1 tissue type inhibitor of matrix metalloproteinaseseGFR - estimated glomerula filtration rate, LV left ventrikle, EF ejection fraction, LA left atrium, RV right ventrikle, EDD enddiastolic diameter, ESD endsystolic diameter, PAP estimated pulmonary artery preassure, E/A filling velocities ratio

P313

A comparative analysis of novel cardiac biomarkers (sST2, GDF-15, Galectin-3, suPAR, H-FABP and Fetuin-A) in patients with heart failure, STEMI and controls without cardiovascular disease

P Jirak[1]; M Lichtenauer[1]; B Wernly[1]; V Paar[1]; I Rohm[2]; C Jung[3]; A Yilmaz[4]; UC Hoppe[1]; PC Schulze[2]; R Pistulli[2]; D Kretzschmar[2]

[1]Paracelsus Private Medical University, Internal Medicine II, Cardiology, Salzburg, Austria; *[2]University Hospital of Jena, Clinic of Internal Medicine I, Jena, Germany*; *[3]Medical Faculty, University Duesseldorf, Division of Cardiology, Pulmonology, and Vascular Medicine, Duesseldorf, Germany*; *[4]Elisabeth Klinikum Schmalkalden, Clinic of Internal Medicine II, Schmalkalden, Germany*

Background: Heart failure and myocardial infarction constitute a major therapeutic challenge in cardiology, leading to a considerable impact on morbidity, hospitalisation rates and health-care costs. Cardiac biomarkers represent an important tool for diagnosis, risk stratification and monitoring in these disease entities, with gaining clinical significance over the last years.

Purpose: The aim of this analysis was to investigate the role of six novel cardiovascular biomarkers, namely sST2, GDF15, Galectin-3, suPAR, H-FABP and Fetuin-A in patients suffering from heart failure (ICM and DCM) and ST-elevation myocardial infarction (STEMI)

Methods: A total of 260 patients were enrolled in this current study. 123 patients were diagnosed with ischaemic or dilative cardiomyopathy and 61 patients were diagnosed with STEMI. 76 patients without coronary artery disease (excluded by coronary angiography) or signs of acute or chronic heart failure were enrolled as control group. Plasma samples were drawn within the first hours of presentation (STEMI patients) or follow-up visits (controls, HF patients) and analyzed for sST2 (hemodynamics and inflammation), GDF-15 (injury, remodelling), Galectin-3 (fibrosis, remodelling), suPAR (inflammation), H-FABP (ischemia) and Fetuin-A (vascular calcification) by using ELISA.

Results: Levels of sST2, GDF-15, suPAR and H-FABP were significantly higher in HF and also STEMI patients compared to the control group (p < 0.0001). Galectin-3 (1792 vs. 2795 pg/ml, p < 0.0001) and Fetuin-A levels (76.8 vs. 116.6 ng/ml, p = 0.001) evidenced lower levels in HF patients compared to controls. Significantly higher levels of sST2 (13211 vs. 8169 pg/ml, p < 0.0001), GDF-15 (818.8 vs. 666.9 pg/ml, p = 0.004) and H-FABP (5.78 vs. 1.89 ng/ml, p < 0.0001) were found in STEMI patients compared to HF patients. suPAR levels showed comparable levels in HF patients and those presenting with STEMI (3614 vs. 3461 pg/ml, p = 0.6). Galactin-3 levels showed lower levels in HF patients compared to control and STEMI patients (HF: 1792 pg/ml vs. 2795 in controls and 2626 pg/ml in STEMI, p= 0.004 and < 0.0001).

Conclusion: By combining the information of different pathophysiological processes, novel cardiac biomarkers represent a promising tool for a more precise diagnosis, risk stratification and therapy monitoring. Furthermore, multimarker analysis could facilitate an easier discrimination of different cardiovascular disease entities.

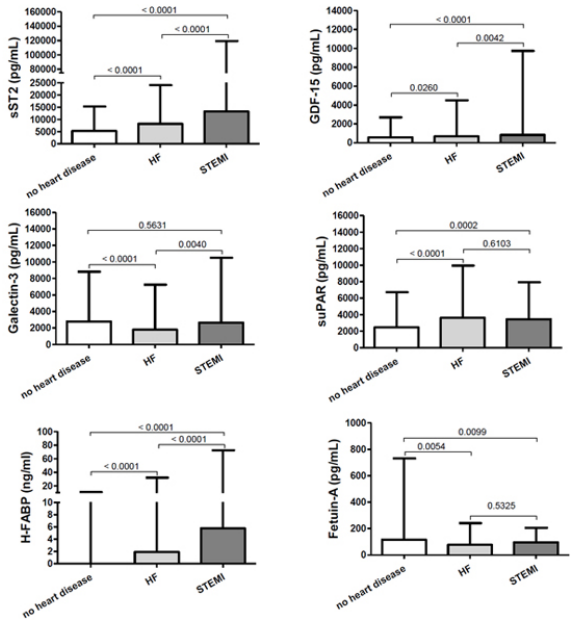


Figure 1

P314

Role of global longitudinal strain in cardiotoxicity monitoring of breast cancer patients initially assessed with MUGA

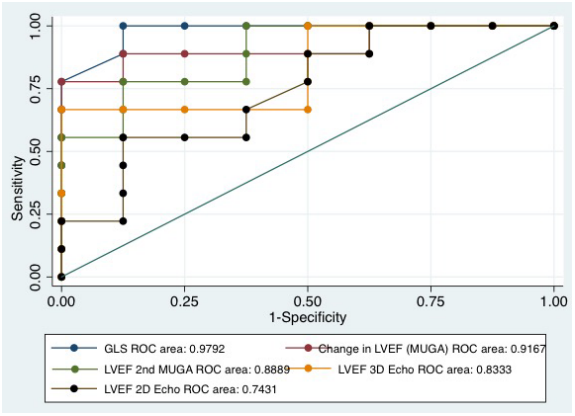
O Oscar Calvillo Arguelles[1]; JF Fritche Salazar[1]; HG Rodriguez Zanella[1]; JD Sierra-Lara Martinez[1]; DF Flores Diaz[2]; CH Arce Salinas[2]; LA Cota Apodaca[3]; M Herrera[3]; BE Dominguez Mendez[1]; K Balderas Munoz[1]; G Melendez[1]; LL Rodriguez Chavez[1]; J Cossio Aranda[1]; JA Arias Godinez[1]

[1]National Institute of Cardiology Ignacio Chavez, Mexico City, Mexico; *[2]National Cancer Institute (INCAN), Mexico City, Mexico*; *[3]Breast Cancer Foundation (FUCAM, A.C.), Mexico City, Mexico*

Background: Different imaging modalities can be used for cardiotoxicity monitoring of breast cancer patients receiving anthracyclines (AC) or trastuzumab (T). Although guidelines recommend using the same imaging technique for each assessment, patients who are found to have a drop in LVEF when initially assessed with MUGA are sometimes referred for an echocardiographic evaluation. The prognostic role of global longitudinal strain (GLS) in this setting is unknown.

Purpose: The aim of this study was to assess whether GLS measurements after initial MUGA assessment can predict clinical events related to cardiotoxicity

Methods: This is a prospective longitudinal pilot study including breast cancer patients who received AC within 12 months of enrollment and/or were receiving T at the time of initial assessment. Patients who had at least 2 LVEF measurements with MUGA before referral were eligible. Standard 2- dimensional echocardiography measurements, 3D LVEF, and speckle-tracking GLS from 3-, 4-, and 2- chamber views were obtained. Patients were followed up for the occurrence of a combined outcome (CO) of development of HF symptoms (= NYHA 2), HF admission, or T interruption. The clinical and echocardiographic characteristics of patients who developed the CO and patients without an event where compared. ROC curves were generated to determine the optimal GLS value to discriminate between the occurrence of the CO and no events.
Results: Between January and October, 2017, 30 eligible patients with a mean age of 48 ± 11 years and mean baseline LVEF 62.9% ± 4.1 were referred to the echocardiography laboratory of a tertiary care center. The main reason for referral was a = 5% LVEF drop in a subsequent MUGA in 18 (60%) patients. In total, 28 patients were receiving T (18 had previously received AC), and 2 patients received AC without T. Within a mean follow up of 6.7 ± 3.1 months, 13 (43%) patients reached the CO (8 had HF symptoms and 2 had HF admissions). Between patients who developed the CO and those who did not, no significant difference was observed regarding radiotherapy, mean AC dose, exposure to T (months), BMI, smoking history and dyslipidemia. The prevalence of diabetes (38.4% vs 5.8%, p = 0.027) and hypertension (61.5 vs 23.5, p = 0.035) was higher in patients with a CO. The mean change in LVEF (MUGA) was 14.7% (11.9-21) in the CO patients, and 3.1% (1.3-5) in patients without events (p < 0.001). Three- dimensional LVEF was higher in patients who did not had an event (58.7% ± 6.2 vs 45.6% ± 7.8, p < 0.001). Lower absolute measurements of GLS were observed in patients with a CO (-13.6 ± 3 vs -20.5 ± 2.3). A GLS value of -16.8%, yielded the highest accuracy with a sensitivity of 92.3% and specificity of 94.1% for a CO prediction.
Conclusions: The sequential use of different imaging modalities for cardiotoxicity monitoring can be feasible. GLS appears to have a prognostic role in this setting, which needs to be tested in a larger population.



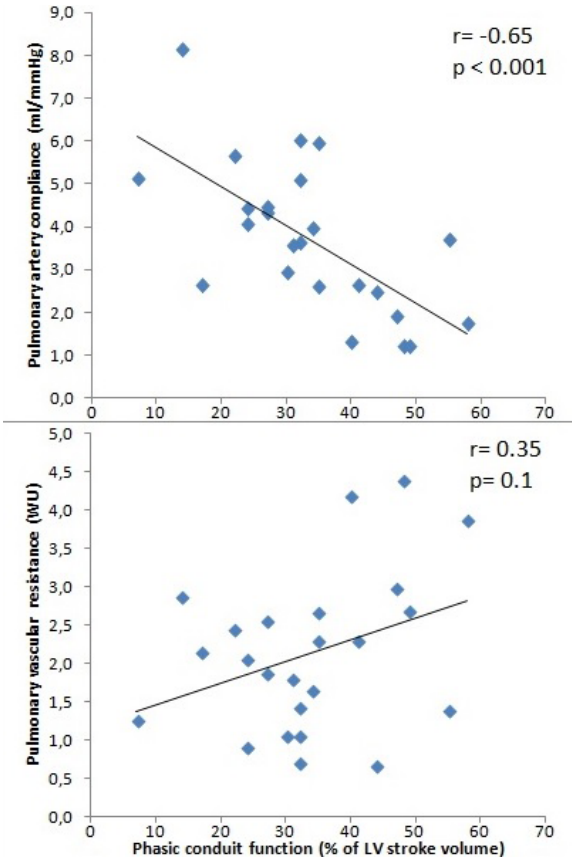
ROC curves for combined outcome

P315

The pulsatile component of right ventricular afterload is modulated by left atrial conduit function in heart failure patients

J Jacopo Zanaboni[1]; G Binda[1]; A Giubertoni[1]; C Piccinino[1]; P Marino[1]
[1]*University of Eastern Piedmont, Cardiology, Novara, Italy*

Background: Right ventricular (RV) dysfunction is an important cause of death in heart failure patients, with RV afterload contributed by a steady component (indexed by pulmonary vascular resistances [PVRs]) and a pulsatile component, assumed to be represented by pulmonary artery compliance (PAC). Left atrial (LA) properties should contribute to the pulsatile component given that atrial pulsatility is directly related to LA stiffness.
Purpose: Aim of the study was to assess if and to what extent the LA phasic conduit function (PCF), a surrogate of LA stiffness, can describe the pulsatile component of RV afterload.
Methods: 24 heart failure patients (16 males, mean age 69 ± 11 years, ejection fraction 46 ± 12%) underwent routine transthoracic echocardiographic evaluation plus real time 3D acquisitions analyzed with a dedicated echo software package. Computation of PCF was made by simultaneous gathering of real time 3D multibeat (6 cycles) LA and left ventricular (LV) volumes, using the formula proposed by Bauman & Kovacs (2004), with PCF as: PCF(time) = [LV(time)-LV minimum] - [LAmaximum - LA(time)] and expressed as % of LV stroke volume. PAC was assessed as the ratio between right ventricular stroke volume (computed as pulmonary velocity time integral*pulmonary valve annulus area measured by 3D echo) and noninvasively estimated pulse pressure, as obtained from pulmonary and tricuspid regurgitant envelopes. PVRs were obtained by the pulmonary velocity time integral using the formula: -0.156+1.154*[(pre ejection period / acceleration time) / total systolic time] as proposed by the group of Giannuzzi (2001). PAC and PVRs measures were validated invasively in 3 patients. LA stiffness was computed as the ratio between E/E' and LA integral strain.
Results: All patients were in sinus rhythm. Diastolic LV volumes averaged 135 ± 48 ml, while LA maximal and minimal volumes were 67 ± 24 ml and 40 ± 24 ml, respectively. PCF ranged from 7% to 58%, exhibiting a significant direct relation with LA stiffness (? = 0.7, p = 0.05). We found a significant reverse relationship (r = -0.65; p < 0.001) between PCF (mean 34 ± 13%) and PAC (mean 3.7 ± 1.8 ml/mmHg). On the contrary, there was no relation (r = 0.35; p = 0.1) between PCF and PVRs (mean 2.1 ± 1.0 WU).
Conclusion: The reverse relationship that we found between PCF and PAC suggests that conduit reflects the oscillatory component, but not the steady component of RV afterload. Given that PAC is a strong prognostic indicator in heart failure patients, even when PVRs are normal, our results suggest that PCF is an important parameter to be generated and taken into account in order to better stratify the early risk and to throughly quantify the global hemodynamic burden in heart failure patients.



Phasic conduit function vs PAC and PVR

P316

Ultrasound parameters associated with lower systolic blood pressure in patients with acute dyspnea

D Dovydas Verikas[1]; R Norvilaite[1]; G Ziubryte[1]; A Rimkus[2]; K Cerlinskaite[3]; A Krivickiene[4]; J Motiejunaite[4]; V Juknevicius[3]; J Simonavicius[3]; D Zaliaduonyte-Peksiene[4]; A Mebazaa[5]; A Kavoliuniene[4]; J Celutkiene[3]
[1]*Lithuanian University of Health Sciences, Kaunas, Lithuania*; [2]*Vilnius University, Faculty of Medicine, Vilnius, Lithuania*; [3]*Vilnius University, Clinic of Cardiac and Vascular diseases, Center of Cardiology and Angiology, Vilnius, Lithuania*; [4]*Lithuanian University of Health Sciences, Department of Cardiology, Kaunas, Lithuania*; [5]*Hospital Lariboisiere, Paris, France*

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Introduction: The association of echocardiography parameters and systolic blood pressure (SBP) in acute settings is not well characterized.
Purpose: To determine the association between SBP and echocardiographic parameters in acute dyspneapatients.
Methods: Prospective multicentre observational cohort study enrolled consecutive patients with acute dyspnea due to acute heart failure (AHF) and other conditions. Conventional and right ventricle (RV) focused echocardiography was performed in 482 patients in the first 48 hours of admission and included, among others, the following parameters: tricuspid annular plane systolic excursion (TAPSE), velocity of the tricuspid annular systolic motion (RV S'), fractional area change (FAC), RV basal diameter and global longitudinal strain, left atrium volume index (LAVI), left ventricle (LV) end diastolic diameter (LVEDD), interventricular septum (IVS) and LV ejection fraction (LVEF).The current study included 446 (92.5%) patients (mean age 68.5 ± 12.9) whose clinical and echocardiographic parameters were available. Measurements of SBP were divided into two groups at the threshold of 140 mmHg. For statistical analysis univariate and multivariate logistic regressions were used.
Results: 56.9% of patients had AHF. The multivariate regression model is given in Table 1. When analysing echocardiographic parameters in univariate logistic regression, both LV and RV echocardiographic parameters had predictive value for SBP. In the multivariate stepwise regression model, TAPSE, LVEDD and IVS were significantly associated with higher SBP.
Conclusions: Progressing LV dilatation, thinner LV walls and impaired longitudinal RV function are independently associated with lower SBP in patients with acute dyspnea.

Predictors for SBP

Variable	Univariate analysis for lower SBP	Multivariate stepwise analysis for lower SBP		
	OR	95% CI	OR	95% CI
IVS, per 1 mm.	0.87*	0.79;0.96	0.87*	0.78;0.99
LVEDD, per 1 mm.	1.02*	1.00;1.04	1.03*	1.01;1.06
LAVI, per 1 mL/m^2	1.02*	1.01;1.03		
RV basal diameter, per 1 mm.	1.04*	1.01;1.06		
TAPSE, per 1 mm.	0.92*	0.89;0.97	0.93*	0.89;0.98
RV S', per 1 cm/s	0.91*	0.85;0.97		
FAC, per 1 %	0.97*	0.96;0.98		
RV Strain global longitudinal, per 1%	1.10*	1.02;1.18		
LVEF, per 1 %	0.96*	0.94;0.97		

* $p < 0.05$

P317
Left atrial volume and left ventricular mass index - do they associate with established heart failure related parameters in HFpEF?

C Gehlken[1]; EM Screever[1]; MHL Van Der Wal[1]; A Koops[1]; KS Dijk[1]; J Warink-Riemersma[1]; P Van Der Meer[1]; JE Coster[1]; DJ Van Veldhuisen[1]; RA De Boer[1]; WC Meijers[1]
[1]*University Medical Center Groningen, Cardiology, Groningen, Netherlands*

Introduction: Heart failure with preserved ejection fraction (HFpEF) is currently a condition that is difficult to define. Key echocardiographic parameters mentioned in the guidelines are Left Atrial Volume index (LAVi) and Left Ventricular (LV) Mass Index (LVMi). We investigated whether patients' characteristics, biomarkers or comorbidities are associated with these parameters and whether this differs in HFpEF or heart failure with reduced ejection fraction (HFrEF).
Methods: In a tertiary referral academic hospital, we consecutively enrolled 842 outpatients with a diagnosis of heart failure (HF). As part of the standardized work-up, all patients underwent baseline characterization, laboratory measurements, as well as echocardiography to assess LV function. Several co-morbidities were recorded, such as coronary artery disease, arterial hypertension, diabetes mellitus, obesity (expressed as Body Mass Index, BMI), renal disease (eGFR < 60 ml/min), and atrial fibrillation (AF). Galectin-3 and NT-proBNP were measured. Patients were optimally treated according to ESC guidelines, with ACE-inhibitors or ARBs, ß-blockers, mineralocorticoid receptor antagonists (MRAs), unless not tolerated, and implantable defibrillators when indicated. We categorized patients based upon LV Ejection Fraction (LVEF), LVEF < 40% and LVEF>50% were defined as either HFrEF and HFpEF.
Results: Mean age was 68 years (+/- 14), 63% of the patients were male, and mean BMI was 28 kg/m2, mean blood pressure was 120/72 mm Hg. Of the 842 patients, 517 had HFrEF and 183 HFpEF. In HFrEF, both LVMi and LAVi were significantly associated with age (LV: ß 0.100; P = 0.030/ LA: ß 0.295; P < 0.001), diastolic blood pressure (LV: ß -0.114; P = 0.015/ LA: ß -0.136; P = 0.006), galectin-3 (LV: ß 0.102; P = 0.028/ LA: ß 0.247; P < 0.001), NT-proBNP (LV: ß 0.183; P < 0.001/ LA: ß 0.371; P < 0.001) and renal disease (LV: ß 0.120; P = 0.009/ LA: ß 0.189; P < 0.001). LVMi was more associated with CAD, HT and male gender, whereas LAVi was more stronger associated with BMI, systolic blood pressure, and AF. In HFpEF patients however, only AF (LV: ß -0.178; P = 0.025/ LA: ß 0.373; P < 0.001) was associated with both LVMi and LAVi. LVMi was only associated with BMI and sysolic blood pressure, and LAVi only with age and NT-proBNP.
Conclusions: Although LVMi and LAVi are primarily suggested as diagnostic parameters for HFpEF, they do not correlate with multiple established HF parameters. In contrast, in HFrEF patients, LVMi and LAVi relate strongly to several other HF parameters. These findings underscore the complex pathophysiology of HFpEF.

P318
Subclinical heart failure with right ventricular apical pacing assessed by speckle tracking echocardiography

N Nikolay Poroyliev[1]; D Markov[1]; E Kinova[1]; A Goudev[1]
[1]*University Hospital Tsaritsa Yoanna, Cardiology, Sofia, Bulgaria*

Introduction: Permanent pacing is the only effective treatment for patients with symptomatic sinus node disease (SND) and atrioventricular block (AVB). Speckle tracking echocardiography (STE) provides direct information on LV (left ventricle) and RV (right ventricle) contractile performance, which may serve as a more sensitive measurement of ventricular systolic function than LVEF.
Purpose: Assess ventricular function during short term RV apical pacing.
Methods: We included 53 consecutive patients. LV and RV function were assessed with 2D echocardiography, TDI and STE. The patients were divided according to the percentage of cumulative ventricular pacing < 40% (Group 1) n = 20 (38%) or >40% (Group 2) n = 33 (62%).
Results: In Group 1 patients there was decline in RV global -22.00% to -18.58% (p = .009) and RV free wall strain -21.66% to -19.11% (p = .034) but no significant change in GLS LV and LVEF. In Group 2 we observed significant decline in GLS LV strain -20.37% to -17.49% (p = .027), RV global -20.01% to -18.34% (p = .048) and RV free wall strain -22.73% to -19.04% (p = .049), without worsening of LVEF (p=.104). In Group1 the ratio of E/e'm increased from 10.68 to 14.31 (p=.002) and in Group2 increased from 13.5 to 16.6 (p=.014), without significant increase of the RV filling pressures. There was a significant decline in TAPSE (21.65mm to 19.12mm, p=.001) and S' (17.88cm/s to 12.33cm/s, p=.007) in patients from Group 1. The results in Group 2 were similar. We found significant decrease in TAPSE (21.7mm to 19.5mm, p=.004) and S' (13.6cm/s to 12.1cm/s, p=.029). There was no significant correlation between parameters at baseline and follow-up in Group 1 except for a negative correlation between LVEF and GLS LV in Group 2 patients (r=-.767; p=.000).
Conclusion: Permanent pacing caused subclinical worsening of LV and RV during short-term follow-up.

P319
Prognostic value of right ventricular speckle tracking imaging in patients with heart failure with preserved left ejection fraction evaluated with echocardiography

J Jean-Jacques Von Hunolstein[1]; A Lawson[1]; T Caspar[1]; B Marchandot[1]; H Petit-Eisenmann[1]; A Trinh[1]; S Hess[1]; N Messas[1]; U Crimizade[1]; G Roul[1]; O Morel[1]; P Olmhann[1]
[1]*University Hospital of Strasbourg, Cardiology Departement, Strasbourg, France*

Introduction: Heart failure with preserved ejection fraction (HFpEF) is a major cause of disability and represents an important cause of cardiovascular morbidity and mortality. We investigated the prognostic value of RV strain in patients admitted for HFpEF.
Methods: we prospectively included between April 2015 and April 2017, 62 HFpEF patients. Standard echocardiographic variables of the left and right ventricles were acquired. RV strain parameters were calculated off-line: RV-global longitudinal strain (RV-GLS) and RV-free wall longitudinal strain (RV-fwLS). Clinical follow-up for mortality and readmission for heart failure was conducted at one year.
Results: HFpEF patients were 83.2 ± 6.6 years old, 63% were female and 84% have a history of hypertension. During a mean follow-up of 392 ± 39 days, 21 patients died (34%). Clinical characteristics and left ventricular echocardiographic parameters were not statistically different between survivors and non-survivors. However, RVfw-LS and RV-GLS were significantly altered in non-survivors (-17,8% ± 7.8 vs. -23,1% ± 6,1; p 0.005) and (-14,9% ± 6.1 vs. -19,2% ± 4,6; p 0.003) respectively as well as TAPSE and S'DTI (14,5 ± 5.8 vs. 19,1 ± 5,2; p 0.003 and 10,2 ± 4,1 vs. 12,8 ± 2,6; p 0.004 respectively). RVfw-LS and RV-GLS were associated with all-cause mortality: RV-GLS (OR 2.97, CI 1.08-8.2; p 0.035), RVfw-LS (OR 2.53, CI 1.03-6.2; p 0.043). The optimal threshold for RV-GLS was -17.5% (sensitivity 71,4%:

specificity 61,5%) and for RVfw-LS was -20% (sensitivity 67%, specificity 72%). Of note, the RV systolic parameters TAPSE and SDTi were also related to mortality (OR 4.6 ,CI 1.69-12.6; p = 0.003) and 5.79 ,CI 2.3-14.4; p = 0.0001 respectively). No relationship could be shown between RV strain and the rate of readmission at follow-up.
Conclusion: our results show that RV-GLS and RV-fwLS are significantly associated with mortality in patients presenting with HFpEF. RV strain parameters provide an additional tool to identify higher risk patients.

P320
Presence and evolution of multiple pulmonary nodules with halo sign detected by computerized tomography in advanced heart failure.

R Raquel Lopez Vilella[1]; C Munoz Nunez[2]; I Sanchez Lazaro[1]; L Almenar Bonet[1]
[1]Hospital Universitario y Politécnico La Fe, Heart Failure and Transplant Unit. Cardiology Department, Valencia, Spain; *[2]Hospital Universitario y Politécnico La Fe, Radiology Department, Valencia, Spain*

Background and obkective: A radiographic finding not described in heart failure (HF) is the presence of pulmonary nodules with halo sign. The objective of this article is to describe and analyze the evolution of a series of cases of patients with advanced HF and multiple pulmonary nodules with halo sign identified by thoracic computerized tomography (CT).
Material and methods: We enrolled patients with advanced HF who underwent thoracic CT as part of the study for heart transplantation or ventricular assistant device implantation, in which pulmonary nodules with halo sign were found. The study was performed using high resolution multidetector CT with iodinated contrast, with 1 mm transverse reconstructions with mediastinal and lung filter. A nodule was defined as a rounded or irregular opacity = 3 cm in diameter. Two CTs were performed for diagnosis and follow-up (around 3 months). The patients gave their informed consent.
Results: The total number of patients with the radiological image described was 3. All males, mean age 59 years. All the patients were in an advanced functional situation (INTERMACS 4), with repeated admissions due to decompensation. Table 1 describes the characteristics of the 3 patients.
Conclusions: Nodules with a halo sign may correspond to a finding related to advanced HF that has not yet been described. Arriving at the definitive diagnosis or, at least, excluding the infectious and neoplastic cause is especially important in these patients in whom the option of performing a heart transplant is evaluated.

	Patient 1	Patient 2	Patient 3
Sex / Age (years)	Male / 53	Male / 58	Male / 58
Basal cardiopathy	DCM	Ischemic DCM	Ischemic DCM
Initial CT	Two nodules: 7 mm (in RUL) and 4 mm (in RLL)	Multiple nodules of 10-18 mm	Multiple nodules of 10-20 mm
Follow up CT (3 months)	Disappearance of all pulmonary nodules	Disappearance of all pulmonary nodules	Disappearance of all pulmonary nodules
Follow up	Urgent heart transplant with left ventricular assist device (Levitronix Centrimag®). No incidents.	Urgent heart transplant with biventricular assist device (ECMO). PGF, ECMO had to be manteined for 4 days.	Elective heart transplant. No incidents.

DCM: Dilated cardiomyopathy ; RUL: Right upper lobe; RLL: Right lower lob; ECMO: ExtraCorporeal Membrane Oxygenation; PGF: Primary graft failure.

P321
Caval index derived parameters and inspiratory IVC diameter are strictly related to non invasive estimation of right atrial pressure by semi-automated tracking of IVC in resting respiration patients

S Stefano Albani[1]; L Mesin[2]; M De Scordilli[1]; B Pinamonti[1]; C Gregorio[3]; G Barbati[3]; P Geri[4]; A Perkan[1]; C Daneluzzi[1]; G Sinagra[1]
[1]Postgraduate School in Cardiovascular Sciences, Cardiovascular Department, University Hospital of Trieste, Trieste, Italy; *[2]Politecnico di Torino, Mathematical Biology and Physiology - Department of Electronics and Telecommunications, Turin, Italy*; *[3]University of Trieste, Department of Medical Science, Surgery and Health (DCSMCS), Trieste, Italy*; *[4]University of Trieste, Department of Pneumology and Respiratory Intermediate Care Unit, ASUITS, Trieste, Italy*

Background: Inspiratory collapse of the inferior vena cava (IVC) and the measurement of its diameters are validated as indirect indexes for the non invasive estimation of the right atrial pressure (RAP). However, there are some critical issues about the actual reliability and reproducibility of the measurement, especially of those with intermediate values of RAP. At this regard, the use of a software able to highlight in semi-automatic mode the edges of the vessel and measure the diameter in each site could help to standardize the measurement of the IVC accurately documenting even slight variations in the caliber of the vein.
Objective of the study:
The aim of this study is to assess the usefulness and the performance in term of precision of the estimation of RAP of the semi-automated tracking technique previous

	Low-RAP group	Intermediate-RAP group	High-RAP group
N° of patients	7	11	15
Mean age	56.14 (± 15.08)	62.45 (± 15.44)	67.80 (± 13.87)
Mean weight (kg)	77.43 (± 12.93)	71.45 (± 15.31)	73.60 (± 15.66)
Mean BSA (m^2)	1.89 (± 0.19)	1.81 (± 0.22)	1.85 (± 0.22)
FE (%)	40.29 (± 21.20)	52.91 (± 20.30)	48.40 (± 22.16)
Right ventricle disfunction (n°)	4 (57.14%)	5 (45.45%)	9 (60%)
Pulmonary hypertension (n°)	6 (85.71%)	8 (72.73%)	15 (100%)
Mean central venous pressure (mmHg)	3.71 (± 0.49)	7,36 (± 1.03)	15,67 (± 3.83)
Mean max IVC diameter (manual) (mm)	20,14 (± 2.54)	19,18 (± 6.51)	24,3 (± 4.48)
Mean min IVC diameter (manual) (mm)	14,86 (± 4.14)	12,64 (± 5.80)	20,2 (± 4.51)
Mean collapsability index (manual) (%)	0,27 (± 0.14)	0,37 (± 0.11)	0,17 (± 0.07)
Mean estimated RAP (manual) (mmHg)	9.29 (± 4.31)	10.45 (± 5.50)	13.67 (± 2.29)
Mean max IVC diameter (automated) (mm)	20,93 (± 7.85)	18,6 (± 6.54)	25,57 (± 9.02)
Mean min IVC diameter (automated) (mm)	10,94 (± 4.69)	11,34 (± 6.25)	19,04 (± 7.22)
Mean collapsability index (automated) (%)	0,45 (± 0.21)	0,43 (± 0.16)	0,25 (± 0.11)
Mean estimated RAP (automated mean diameters) (mmHg)	8,24 (± 2.76)	7,9 (± 2.62)	11,61 (± 5.16)
Mean estimated RAP (automated algorithm) (mmHg)	6,93 (± 2.37)	8,84 (± 2.92)	12,71 (± 3.62)

RHC and echo parameters

described against the standard estimation of RAP in 2 D mode echocardiography by measuring IVC diameters variations. We used RAP measurement obtained by human right heart catheterization (RHC) as gold standard technique.
Materials and Methods: We prospectively enrolled from 1/12/2015 to 1/9/2017 a total on number of 88 patients undergoing RHC catheterization for all clinical indications Subsequently all patients underwent complete echocardiographic assessment in the next 6 hours after the invasive assessment. All the echocardiographic video clip used to estimate non invasively the RAP were analyzed by L. M using the tracking software that can highlight in semi- automatic mode the vein's edges, measure the diameters at different sites in a wide IVC region and then define a multiparameter algorithm to predict with high accuracy even small changes of the diameters of the vessel to predict RAP. In addition to standard IVC parameters (such as expiratory and inspiratory diameters and caval index) other parameters were obtained: caval index max (CImax) was obtained averaging the pulsatility in the 3 distal diameters and respiratory caval index (RCI) was obtained using dedicated filters.
Results: 88 patients were enrolled, 53 patients were excluded for technical reason mainly to low quality post processing imaging. 33 patients were finally included in the study (19 males and 15 females; mean ± std: age 63.2 ± 15.2 years, weight 71.5 ± 14.6 kg, height 168.0 ± 9.1 cm). The mean estimation error of the best model when using the automated approach is 2,11 mmHg from data collected by RHC and the final algorithm included CImax, RCI and IVC inspiratory diameter.
Conclusions: The semi-automated tracking of the IVC in resting respiration is a promising technique able to correctly estimate RAP with high precision degree (mean error +/-2,11mmHg). The stronger parameters associated to RAP are the inspiratory IVC diameter and derived collapsibility indexes.

P322

Right ventricular versus left ventricular systolic and diastolic parameters using tissue Doppler echocardiography in hypertensive patients

ALI Hasan Ali Farhan Al Alfarhan[1]; M A Zahid[1]
[1]*Baghdad Medical City, Cardiology, Baghdad, Iraq*

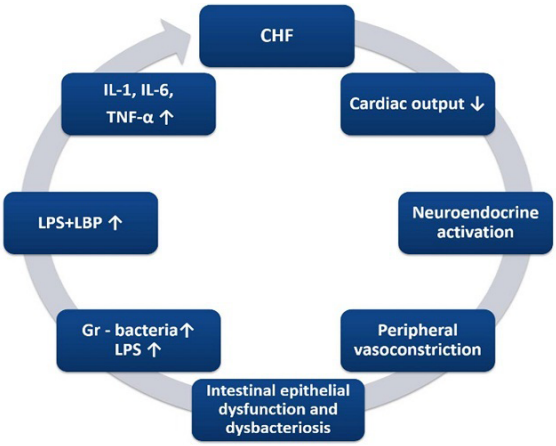
Background: Hypertension (HT) may determine impairment of both left ventricular (LV) diastolic and systolic function, due to increased afterload and changes of LV geometry and structure producing LV remodelling and hypertrophy (LVH). Also the right ventricle (RV) might be involved in this process by structural and functional abnormalities. RV chamber diastolic dysfunction has been shown in uncomplicated HT. To date, little information is available about functional changes of RV walls in HT. This issue is crucial to better understanding of the mechanisms underlying RV involvement in the hypertensive heart. Pulsed tissue Doppler has been used to analyze myocardial LV wall motion abnormalities in several cardiac pathologies and also appears suitable for assessing changes of RV longitudinal function due to HT
Purpose: To evaluate RV and LV functional and morphological changes in treated hypertensive patients using selected conventional and tissue Doppler echocardiographic methods, and to study the relationship between changes in both right and left ventricles of heart
Methods: One hundred and two treated hypertensive patients were selected in this study (group 1) in addition to 100 healthy age- and gender- matched patients for control (group 2), both study groups underwent echocardiographic examination using 2D, M Mode, Pulsed Doppler and Tissue Doppler imaging. Examination involved LV septal and posterior wall thicknesses, internal dimensions, left atrial area, ejection fraction (EF) and LV mass, also Tissue Doppler derived waves' velocities S', e', a' and e'\a' ratio. RV internal basal diastolic dimension, free wall thickness in diastole, right atrial area, TAPSE, PASP, fractional area change (FAC), PW tricuspid inflow waves' velocities e, a, and e\a ratio, Tissue Doppler derived myocardial performance index (MPI), S', e', a', and e'\a' ratio
Results: Hypertensive patients had higher measurements than control patients in: LV walls' thicknesses, end diastolic dimension, LV mass, left atrial area, peak velocity S', a', RV free wall thickness, Tricuspid inflow TV a wave velocity, right atrial area, PASP, TDI S' and a' waves velocities. Lower values than control patients in LV TDI peak velocity of e' wave and e'\a' ratio. Systolic function of both ventricles was not reduced. Diastolic function of both left and right ventricles were impaired, the Tissue Doppler derived e'\a' ratios were strongly correlated in both ventricles. There was a strong correlation between LVH and both Tissue Doppler derived RV & LV diastolic dysfunction.
Conclusions: HT causes morphological and functional changes in both ventricles, initially systolic function of LV and RV are not affected; diastolic dysfunction in LV is considered as one of the earliest functional changes, studying RV revealed diastolic dysfunction which was strongly correlated with LV diastolic dysfunction by using Tissue Doppler imaging, also with LVH were highly correlated with disease duration

P323

Intestinal dysbiosis-induced systemic inflammation in heart failure

BI Narziev[1]; AG Gadaev[1]; ME Rakhimova[1]; AA Razikov[1]
[1]*Tashkent Medical Academy, Cardiology, Tashkent, Uzbekistan*

Background: Intestinal dysbiosis plays a crucial role in the progression of chronic heart failure (CHF) and together with other pathologic processes demonstrates a vicious cycle of chronic heart failure progression (Figure 1).
Purpose: Evaluate the relationship between markers of inflammation and altered intestinal microbiome in patients with CHF.
Methods: In total 38 CHF patients with were examined. 11 patients (29%) were in functional classes III-IV (NYHA) and others 27 (71%) were in functional classes I-II (NYHA). The following laboratory test methods conducted: TNF-alpha in the blood and IL-6 in the blood by using ELISA (enzyme-linked immunosorbent assay). All patients were tested on bacteria in stool. Microbiological study of feces was carried out on the crop nutrient in the dilutions -1, -3, -5, and -7. After 48-hour incubation at 370C, estimate
Results: Microorganisms were identified by enzyme activity, as well as by microscopic examination of smears stained by Gram.
Results: There was correlation between levels of TNF-alpha and IL-6 and E. coli ($p < 0.01$), due to the growth of pathologic bacteria marked mainly by E. coli - 106 CFU / g (I-II FC HF), against 109 CFU / g (III-IV CHF FC) ($p < 0.0005$). In patients with chronic heart failure FC III-IV by NYHA, the level of IL-6 was 11.5 ± 0.3 U/L, where in FC I-II, it was 4.6 ± 0.3 IU / L. TNF-alpha in FC III-IV was 6.6 ± 0.4 U/L against 3.7 ± 0.4 IU / L in patients with FC I-II.
Conclusion: Altered intestinal function creates a condition to growing Gramm negative bacteria. Organism is contaminated either bacteria or bacteria's vital products as lipopolysaccharide (also known as endotoxin), and immune cells produce pro-inflammatory cytokines. Systemic inflammation worsens clinical course of CHF.



Cardio-intestinal syndrome

P324

Impact of body mass index on device measured diagnostic sensor measurements in ambulatory heart failure patients

J Boehmer[1]; G Mark[2]; G Wen[3]; P Thakur[3]; GZ Duray[4]
[1]*Penn State Hershey Medical Center, Hershey, United States of America*; [2]*Cooper University Hospital, Camden, United States of America*; [3]*Boston Scientific, St. Paul, United States of America*; [4]*Military Hospital, Budapest, Hungary*

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Background: Prior studies have reported a link between obesity and the development and progression of heart failure (HF). A device based multi-sensor algorithm was recently shown to detect impending worsening HF events with high sensitivity. The objective of this analysis was to characterize the relationship between sensor measurements and body mass index (BMI) of HF patients.
Methods: The MultiSENSE trial followed 900 patients implanted with a COGNIS CRT-D for 1 year. Device software was modified to permit collection of sensor data: heart sounds (S1 and S3), respiration, thoracic impedance (TI), heart rate (HR) and activity. Sensor data were combined into a multi-sensor alert algorithm (HeartLogic). Patients (N = 892) were classified into four categories of BMI (kg/m2): Underweight/Normal (BMI < 25, N = 193), Overweight (25 = BMI < 30, N = 285), Obesity I (30 = BMI < 35, N = 229) and Obesity II/III (BMI>35, N = 185). Correlations between sensor data and patients' BMI were computed, and average sensor data across BMI categories were compared using a one-way ANOVA.

Sensor Values across BMI categories

Daily Trend	Underweight/ Normal	Overweight	Obesity I	Obesity II/III	p value
S1 (mG)	2.68±1.01	2.53±0.85	2.53±0.93	2.48±0.97	0.172
S3 (mG)	0.98±0.34	0.98±0.34	0.93±0.28	0.98±0.33	0.350
Thoracic Impedance (Ohm)	48.20±9.15	49.37±8.40	50.35±8.71	50.25±8.24	0.046
Daytime RSBI (br/min/Ohm)	8.31±2.87	8.10±2.40	8.60±2.56	8.77±2.59	0.029
Night Heart Rate (bpm)	70.12±7.89	70.11±7.51	70.91±8.54	72.19±8.40	0.030
Respiratory Rate (median, br/min)	18.09±2.50	17.67±2.40	17.78±2.35	17.88±2.53	0.311
Activity (hours)	2.22±2.14	2.26±2.05	2.27±2.01	2.14±1.93	0.917
HeartLogic Index	6.53±5.33	6.99±5.46	6.60±4.92	6.66±4.94	0.759

BMI = Body Mass Index, RSBI = Rapid Shallow Breathing Index, S1, S3 = 1st, 3rd heart sound, Day = 6am to 12am, Night = 12am to 6am

Results: Poor correlations between sensor measurements and BMI were observed (|r| < 0.4) for all the sensor trends. On average, obese patients had higher TI, higher day-time Rapid Shallow Breathing Index (RSBI), and higher night HR than the other patients (Table). No statistical differences across the four BMI categories were detected in the other four sensor trends (S1, S3, Respiratory Rate, Activity), and the resulting HeartLogic index. With Bonferroni correction for multiple comparisons, none of the sensor trends were statistically different across the BMI categories.
Conclusion: There are significant differences across patients in different BMI categories in TI, day-time RSBI and night HR, although the overall predictive HeartLogic Index did not vary across these groups.

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Indicators of humoral regulation of the circulatory system in obese patients.

T Zaletova[1]; A Bogdanov[1]; I Shevchenko[2]; T Feofanova[1]; S Derbeneva[1]; A Bogdanova[3]
[1]Research Institute of Nutrition of Russian Academy of Medical Sciences, Moscow, Russian Federation; *[2]Gazprom Transgas Diagnostic and Rehabilitation Center, Internal Medicine, Moscow, Russian Federation*; *[3]N.I. Pirogov City Clinical Hospital No.1, Moscow, Russian Federation*

Introduction: The leading cause of CHF development is an excessive activation of neurohormonal systems, primarily renin-angiotensin-aldosterone (RAAS) and sympathoadrenal ones.
Objective: To study indicators of humoral regulation of circulatory system in obese patients as predictors of CHF development.
Methods: In the studied population of obese patients two groups of 40 patients were formed: the first group consisted of patients with initial obesity (grades 1 or 2) with BMI of up to 40 kg/m2, the second group included patients with severe obesity (grade 3 obesity) with BMI of over 40 kg/m2. None of the selected patients had a history of cardiovascular events (myocardial infarction or acute cerebrovascular event). The concentration value of renin-angiotensin-aldosterone system components was determined (renin, results expressed in pg/ml, angiotensin II, results expressed in ng/ml), aldosterone, the result expressed in pg/ml). The level of N-terminal pro B-type natriuretic peptide (NT-pro-BNP) was determined by immunoassay analysis.
Results: Studying aldosterone plasma level showed that for most obese patients, it is hyperaldosteronism that can induce heart failure. It was shown that a higher obesity grade is associated with higher aldosterone level. Aldosterone level in grade 1-2 obese patients was close to normal upper border, which was 58.9 [54.9; 73.8] pg/ml (normal range is 10-60 pg/ml), while in patients with grade 3 obesity it was 79.5 [64.5; 90.1], which is 25.9% higher than in patients of the first group and 24.5% higher above the normal level (for p <0.05). Detailed data analysis showed that these two groups are significantly different not only in average plasma aldosterone level, but in absolute number of patients with hyperaldosteronism, whose number increases from 46,2% in grades 1 or 2 obese patients to 85.7% among patients with grade 3 obesity. Plasma renin level in both groups was within the normal range. The median value in patients with obesity grades 1 or 2 was 23.2 [10.9; 51.8] pg/ml, in patients with grade 3 - 22.4 [11.2; 39.8] pg/ml (lab reference values 4.0 - 37.5 pg / ml). The differences between these values were insignificant (p> 0.05). No significant differences in angiotensin II levels were demonstrated in patients of the compared groups: the average value in grades 1 or 2 obesity patients 17.95 [1.58; 18,53] pg/ml, and in patients with grade 3 obesity - 18,54 [18,25, 18,83] pg/ml. NT-proBNP level in the first group was 23.7 [10.6; 23,6] pg/ml, in the second group - 138,0 [121,5; 145.9] pg/ml, which is 5.8 times higher (p = 0.001). Correlation analysis showed that aldosterone and NT-proBNP levels are closely related (r = 0.74, p <0.05).
Conclusions: This study shows that aldosterone level can be used as a predictor of HF. An increase in aldosterone activity may cause lung congestion and peripheral edema, which together with left ventricular dysfunction make up a clinical syndrome of CHF in obese patients.

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Using ballistocardiography measurements to assess diuretic effects in patients with heart failure

MMH Shandhi[1]; J Fan[2]; S Dowling[2]; OT Inan[1]; LIVIU Klein[2]
[1]Georgia Institute of Technology , School of Electric and Computer Engineering, Atlanta, United States of America; *[2]University of California San Francisco, Cardiology, San Francisco, United States of America*

Funding Acknowledgements: National Institutes of Health, USA

Background: Measuring hemodynamic responses to medications in heart failure (HF) patients can potentially enable caregivers and physicians a means of ensuring that patients are correctly following the prescribed dosage and timing of medication delivery (e.g. diuretics or vasodilators). In our previous studies, we have shown that weighing-scale-based measurements of ballistocardiogram (BCG) signals - the measurement of body vibrations in response to cardiac ejection - can accurately quantify cardiac contractility changes [pre-ejection period (PEP)/ Heart Beat Period (RR interval)]. This non-invasive measure can track hemodynamics in the hospital and at home for patients with HF.
Purpose: In this study, we quantified the impact of diuretic use on patients' BCG signals and associated cardiac parameters, paving the way for future studies aimed at assessing medication usage based on BCG measurements at home.
Methods: We enrolled 12 patients with HF and reduced ejection fraction (HFrEF). BCG and electrocardiogram (ECG) signals were simultaneously recorded using a previously validated modified weighing scale (Fig. 1A) at, or close to, the day of hospital admission, daily during the hospitalization, at hospital discharge, and then daily at home for 30 days following discharge. For the current analysis, we focused on the specific recording days when diuretic dosages were changed while all other medications (neurohormonal antagonists and vasodilators) were unchanged for at least two days. The BCG features were averaged for two days before and after a change in diuretics. For one subject, we have compared these features with changes in thoracic impedance, obtained from the commercially available SensiVest device.
Results: For 89% of readings, PEP/RR increases with increase in diuretic dose and vice versa (Fig. 1B). Within patient parameters show higher correlation for percent changes in PEP/RR with percent changes in diuretics compared to global model across all patients. Percent changes in thoracic impedance showed negative correlation with percent changes in diuretics (R2 = 0.74) as well as with percent changes in PEP/RR (R2 = 0.93).
Conclusion: Using a modified weighing scale we can monitor the effects of diuretics on cardiac hemodynamics in patients with HF. Further expanding this technology to other medications and more subjects can potentially allow for algorithms to be trained to determine whether the correct dosage of medications has been taken by patients at home.

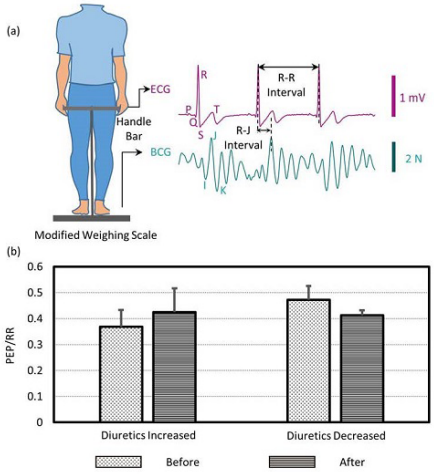

Figure 1: (a) Experimental setup with representative ECG and BCG signals. The RJ interval is a surrogate for pre-ejection period (PEP). (b) Changes in PEP/RR due to changes in diuretics doses.

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Structure and functional predictors of left atrial pressure in patients with end-stage heart failure

F Ferdinando Loiacono[1]; FM Righini[1]; A Dokollari[2]; CG Sassi[2]; S Bernazzali[2]; M Maccherini[2]; S Mondillo[1]; M Henein[3]; M Cameli[1]
[1]University of Siena, Department of Cardiovascular Diseases, Siena, Italy; *[2]Polyclinic Santa Maria alle Scotte, Department of Cardiac Surgery, Siena, Italy*; *[3]Umea University, Department of Public Health and Clinical Medicine, Umea, Sweden*

Background: End-stage heart failure (HF) is characterized by variable degrees of left ventricular (LV) dysfunction, myocardial fibrosis and raised filling pressures, leading to atrial enlargement and impaired function. Global peak atrial longitudinal strain (PALS) assessed through speckle tracking echocardiography (STE) is a non-invasive index of left atrial (LA) function which correlates closely with LV end-diastolic pressure. An independent but highly valuable predictor of LV dysfunction is myocardial fibrosis, which cause poor contractile and elastic properties of the myocardium, resulting in increased preload and filling pressures.

Purpose: Aim of this study was to investigate the relationship between increased filling pressure and LA function, assessed by STE and specifically global PALS, LV ejection fraction (EF) and fibrosis in patients with end-stage HF undergoing heart transplantation.
Methods: We consecutively enrolled 64 patients with end-stage HF who underwent heart transplantation into this study. Demographic, pre-transplant invasive intracardiac pressures, and echocardiographic comprehensive offline speckle tracking analysis were collected. After transplantation, specimens from explanted hearts were collected in order to quantify the degree of LV myocardial fibrosis which was defined as (fibrosis area-total area)×100. An average value of the extent of LV fibrosis was obtained from the seven samples.
Results: Patients were 56.3 ± 8.4 years old and mean NYHA class was 2.95 ± 0.7. Mean LV EF was 26.7 ± 4.3%. They presented mild LA enlargement (mean LA area 27.1 ± 9.6 cm2 and mean LA indexed volume 35.1 ± 11.1 cm2) and reduced global PALS (11.5 ± 7.5). Mean pulmonary capillary wedge pressure (PCWP) was raised (18.8 ± 7.5 mmHg) and mean pulmonary artery pressure (PAP) was 27.1 ± 9.9 mmHg, both slightly increased but not contraindicating heart transplantation. LV fibrosis was present in all specimens and 73% of the patients showed severe (i.e. >30%) LV fibrosis.
Global PALS was inversely correlated with PCWP (R -0.83; $p < 0.0001$) (figure) and with LV fibrosis (R -0.78; $p < 0.0001$), but did not correlate with LV EF (R 0.15; p= ns). Global PALS was correlated with LA diameter (R -0.35; $p = 0.05$), LA area (R -0.37; $p = 0.05$) and LA indexed volume (R -0.39; $p = 0.01$). Among the analyzed indexes, global PALS was the best index for predicting raised (<18 mmHg) PCWP (AUC 0.955).
Conclusions: In patients with end-stage HF undergoing heart transplant, abnormal LA function expressed as reduced global PALS is determined by the rise of LV filling pressure as well as by the degree of fibrosis but not by LV systolic function expressed as EF.

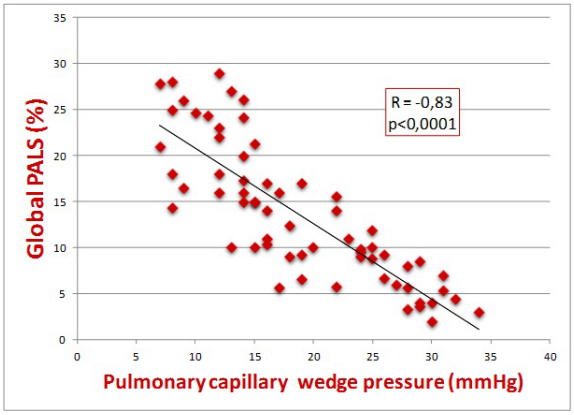

Fig 1

Chronic Heart Failure - Treatment

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Combined therapy with ACEI/ARB, beta-blocker, statin, antithrombotic drug and cardiovascular mortality in comorbide patients with heart failure, coronary artery disease, arterial hypertension

MM Loukianov[1]; SY Martsevich[1]; Y Mareev[1]; SS Yakushin[2]; AN Vorobyev[2]; AV Zagrebenyy[1]; RP Myasnikov[1]; AN Kozminsky[2]; EY Andreenko[1]; VG Klyashtorny[1]; EV Kudryashov[1]; KG Pereverzeva[2]; AD Deev[1]; OM Drapkina[1]; SA Boytsov[3]
[1]National Research Center for Preventive Medicine, Moscow, Russian Federation; *[2]Ryazan State Academician Medical University, Ryazan, Russian Federation*; *[3]National Research Center for Cardiology, Moscow, Russian Federation*

Aim: To evaluate prescription rate of ACE inhibitor (ACEi)/angiotensin receptor blocker (ARB), beta-blockers, statins, antithrombotic drugs (antiplatelet/anticoagulant) and cardiovascular (CV) mortality in patients with combination of heart failure (HF), coronary artery disease (CAD) and arterial hypertension, enrolled in outpatient registry RECVASA.
Methods: RECVASA registry included 3690 patients with CV diseases from 3 outpatient clinics in Ryazan region of Russia. For this analysis, we took patients with the combination of HF, CAD and arterial hypertension. CV mortality was estimated during 4-year of the follow-up period.
Results: 2303 patients were included (28.9% men, age 70.6 ± 10,7 years). 21.5% patients had atrial fibrillation (AF), 17.6% - history of myocardial infarction (MI), 11.9% - stroke in anamnesis. Accordingly, to clinical recommendations all patients have an indication for combined therapy with ACEI/ARB, beta-blockers, statins and antithrombotic (antiplatelet if the patient didn't have AF or anticoagulant in cases of AF). There were no patients with indications for double/triple antithrombotic therapy. Patients after MI had an additional indication for administration of ACEI and beta-blocker. Therapy with ACEI/ARB was administrated in 1676 (72.8%) cases, with beta-blocker - 1676 (72.8%), statins - 674 (29.3%), antithrombotic drugs in 1001 (43.5%).
Patients were divided according to the number of prescribed drugs. Therapy with all four components of drugs was administrated in 226 (9.8%) of patients, with 2-3 drugs in 1246 (54.1%) of patients and with 0-1 drugs in 831 (36%) of patients.
Mean follow-up was 3.7 ± 0.9 years. 430 (18.7%) patients died from all causes, including 297 (12.9%) from CV diseases. CV mortality was: 4.9% in patients with administration of the 4-component therapy; 12.7% and 15.4% with administration of 2-3 and 0-1 drugs, respectively. ($p = 0.0007$ and $p = 0.0001$ respectively for comparison between 4-component therapy and groups with administration of 2-3 and 0-1 drugs).
Risk ratio (RR) of CV death and 95% confidential interval (CI) were analyzed in multifactor Cox model (age, sex, administration of 0-1, 2-3 or 4 mentioned drugs, history of MI or stroke). Compared with reference group (0-1 drugs) risk of CV death was lower in patients, received 4-component therapy (RR = 0.30, 95% CI 0.16-0.55, $p = 0.0002$) and 2-3 drugs (RR = 0.70, 95% CI 0.62-0.91, $p = 0.003$).
Conclusion: Only one-tenth of patients with the combination of HF, CAD and arterial hypertension received 4-component therapy with ACEI/ARB, beta-blocker, statin, an antithrombotic drug in outpatient practice and 54.1% - 2-3 of these drugs. CV mortality and risk of CV death in patients with administration of this 4-component drug therapy were respectively 3.1 and 3.3 times less compared with cases of administration 0-1 of them.

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Heart failure over 19 years: are we on the right way?

N Nabil Kraiem[1]; I Fomin[1]; DS Polyakov[1]; FY Valiculova[1]
[1]Nizhny Novgorod State Medical Academy, Department of internal medicine, Nizhny Novgorod, Russian Federation

Introduction: heart failure (HF) must be treated as recommended in guidelines
Purpose: to find out how the treatment of heart failure has changed over 17 years
Methods: All medical data of the representative sample in the city of Nizhni Novgorod were analyzed to find out the prevalence of heart failure and the way this syndrome is treated. Data check and collection were started in 1998 to our days. HF therapy was analyzed depending on last HF guidelines 2017.
Results: within 17 years, 2056 people were checked for the presence of HF in 2000, 2007 and 2017. Over 17 years the prevalence of HF increased from 6.8% to 9.1% (? = 0.04), the prevalence of severe HF (NYHA III - IV classes) increased from 1.2% to 4.8% ($p < 0.001$).The averages of patients receiving drugs not considered to be disease modifying in 2000, 2007 and 2017 were 68.7%, 20.9% and 12.9% consecutively. Not depending of therapy type (mono or be or tri therapy) drug records of HF patients show that angiotensin-converting-enzyme inhibitors (ACEIs) were prescribed to 24.7% of patients in 2000 while no angiotensin II receptor blocker (ARB) was prescribed. After 7 years only 66.9% received ACEIs while ARBs prescribed only to 0.6% of patients. In 2017, 65.2% and 20.5% of patients received ACEIs and ARBs respectively. Beta Blockers (BB) prescription changed from 14.1% in 2000 to 34.3% in 2007 and 48.5% in 2017. Mineralocorticoid receptor antagonist (MRAs) were not prescribed in 2000, prescribed to 4.7% patients in 2007 and 10.6%. Considering therapy type, in 2000, 17.2% and 6.6% found to be treated in mono therapy by ACEIs and BB respectively. Important changes were identified after 7 years (40.1% and 9.9%) and in 2017 (28.0% and 3.8%). Bi therapy defined by combination of 2 recommended drugs was found in 7.6% of patients in 2000, 27.3% in 2007 and 39.5% in 2017. No patient was treated by tri therapy (ACEI or ARB, BB, MRA) in 2000, 0.6% in 2007 and 4.5% in 2017.
Conclusion: We found out a serious difference between actual guidelines on HF treatment and real therapy among ambulatory patients. We believe that inappropriate treatment choice is partially responsible for the 4 times increase of severe HF prevalence. More active work is needed to slow the development of HF.

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B-blockers and prognosis in cardiac amyloidosis

A Ntalianis[1]; A Koutsoukis[1]; E Tseliou[1]; E Repasos[1]; E Papadopoulou[1]; M Tselegiki[1]; D Ziogas[1]; E Kastritis[1]; K Tampakis[1]; I Stamoulopoulos[1]; A Koen[1]; S Toumanidis[1]; MA Dimopoulos[1]; I Paraskevaidis[1]
[1]*Alexandra University Hospital, Departmant of Therapeutics, Athens, Greece*

Background/Introduction: B-blockers (BB) administration in patients with light chain cardiac amyloidosis (LC-CA) might result in significant symptom deterioration. However, there are patients with LC-CA who tolerate even high BB doses without any important side effect. Theoretically, the anti-arrhythmic and cardioprotective effects of BB could improve prognosis in patients with LC-CA.
Purpose: To investigate the impact of BB treatment in patients with LC-CA
Methods: In the present retrospective study from 2002 to 2017, 85 patients with LC-CA were included. Mean age was 67 years. We investigated the impact of BB treatment, on survival rates of patients with LC-CA . All LC-CA patients received chemotherapy treatment according to previous and current guidelines
Results: Upon chemotherapy initiation, 30% of patients were under BB treatment and 7% under amiodarone or ivabradine. Fourty two percent of the patients were on furosemide (mean dose: 82 mg/d), while 4.6% was on renal replacement therapy (RRT) due to end stage renal failure. Mean survival was 24.5 ± 3 months. 5-year survival in the entire cohort was 45% and cardiovascular mortality was 70%. BB ($p = 0.033$) and lower doses of furosemide ($p = 0.011$) were associated with better survival rates.
Conclusions: The minority of patients with LC-CA either receive or tolerate BB. The prognosis of patients with LC-CA that receive BB treatment is better compared to those that do not receive BB.

P331

Safety and efficacy of valsartan-sacubitril in a cohort of patients with symptomatic heart failure receiving small doses of ACE

I Stamoulopoulos[1]; A Ntalianis[1]; E Papadopoulou[1]; E Tseliou[1]; S Sventzouri[1]; K Tampakis[1]; A Koutsoukis[1]; N Makris[1]; C Kontogiannis[1]; A Koen[1]; I Kanakakis[1]; K Stamatelopoulos[1]; I Paraskevaidis[1]
[1]*Alexandra University Hospital, Departmant of Therapeutics, Athens, Greece*

Background: Combined inhibition of the renin-angiotensin system and neprilysin (ARNI) significantly reduced mortality and morbidity in selected symptomatic patients with heart failure (HF) who could tolerate high doses of enalapril. The purpose of this study was to investigate the safety and efficacy of ARNI administration in patients with NYHA II and III receiving lower doses of ACE inhibitors (ACE-inh).
Methods: Patients with systolic HF (EF < = 35%), NYHA II-III, receiving a maximum tolerated but small dose of ACE-inh, beta-blocker and aldosterone inhibitor were prospectively included. An initial dose of ARNI 50mgX2 was administered for 1 week, up-titrated to 100mgX2 and 200mgX2 per week if tolerated. The safety and efficacy endpoints of the study at 12 months were: a) NYHA b) left ventricular ejection fraction and c) ARNI-related adverse events.
Results: A total of 27 patients were included (74% with ischemic HF, mean age: 60 ± 10 years). All patients before ARNI, they were receiving less than 50% of the maximum recommended ACE-inh dose. At 12 months, there was a statistically significant improvement in NYHA ($p = 0.01$) and a marginal statistically significant increase in EF (from 27.1 ± 3.9% to 33.6 ± 6.6%, $p = 0.08$). There was no statistically significant reduction in both SBP (from 112.3 ± 13.2 to 108.5 ± 11.8 mmHg, $p = 0.363$) and diastolic blood pressure (67.5 ± 10.4 at 62.3 ± 8 , 2mmHg, $p = 0.115$). In two cases, asymptomatic hypotension was observed with the maximum dose of ARNI for which transient discontinuation was required. No significant changes in eGFR (from 80.5 ± 23.7 to 74.9 ± 29.8 ml / min, $p = 0.507$) and K + (from 4.7 ± 0.4 to 4.6 ± 0.4 mmol / L, $p = 0.623$) were observed.
Conclusions: Administration of ARNI in patients with symptomatic systolic HF receiving low doses of ACE-inh is well tolerated and improves both symptoms and left ventricular function without significant adverse events.

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Barriers and motivations to physical activity in heart failure patients; is a specific approach needed for women?

E Emilie Cewers[1]; T Ben Gal[2]; A Joensson[1]; JM Weinstein[3]; T Jaarsma[1]
[1]*Linkoping University, Medical Faculty, Linkoping, Sweden*; [2]*Rabin Medical Center, Petah Tikva, Israel*; [3]*Soroka University Medical Center, Beer Sheva, Israel*

Introduction: Physical activity (PA) is an essential part of heart failure management but the adherence to exercise recommendations is low, especially in female patients. A similar sex discrepancy can be seen among healthy people, in whom research show differences in barriers and motivations. This study aimed to investigate sex differences in PA, barriers and motivations to PA and change in physical capacity. It also sought to evaluate the opinions of health care providers with regard to such differences and whether adaptations in care based on sex might be meaningful.
Methods: A mixed methodology study was conducted in two hospitals in Israel during February to May 2017. Concurrent triangulation design was used, in which interviews with health care providers were held in parallel to collection of quantitative data from heart failure patients on motivations, barriers, PA and physical capacity, measured through the Exercise Motivations Index, the Exercise Self Efficacy Scale and the 6 Minute Walk Test. Interviews were analysed through qualitative content analysis and quantitative data was studied via SPSS 24, particularly looking at differences between men and women. Quantitative and qualitative data were given equal priority and were integrated in the discussion.
Results: No sex differences in PA and capacity were found in the quantitative data, but some health care providers believed there were differences. Male patients reported higher motivations in 'I want a slower aging process and to feel younger' ($p = 0.04$) and 'Everyone else exercises, I want to do that too' ($p = 0.02$). Other items related to motivation or barriers showed no statistically significant sex differences. Qualitative data was ambivalent, and health care providers had divergent opinions regarding the existence of sex differences and the value of adapting care based on sex. 7 categories with associated subcategories were identified through qualitative content analysis. This method also revealed one pervading theme; 'Men and women; they are the same … But they are different.
Discussion: Contrasting to findings in earlier studies, no sex differences were found in PA or physical capacity although motivations were slightly different between genders. At the same time, health care providers had clear opinions about possible differences, possibly affecting their care. Given that the results pointed to potential sex differences in motivations and barriers, considering this when tailoring care might be of value.

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Barriers and challenges in self-care for heart failure patients with different cultural backgrounds

A Adam Joensson[1]; T Ben Gal[2]; E Cewers[1]; JM Weinstein[3]; T Jaarsma[1]
[1]*Linkoping University, Medical faculty, Linkoping, Sweden*; [2]*Rabin Medical Center, Petah Tikva, Israel*; [3]*Soroka University Medical Center, Beer Sheva, Israel*

Introduction: Heart failure (HF) is one of the most prevalent cardiovascular diseases and patients are advised to perform different self-care behaviours. Health care providers (HCPs) have an important role in providing self-care advise. The aim of this study is first, to examine if there are any specific barriers and challenges regarding the self-care of HF-patients with regard to their different cultural background and second, if the cultural background of their HCP play a part in the patients' adherence to self-care.
Methods: A qualitative study was performed with purposeful sampling method used. Data was collected through interviews focusing on cultural differences in self-care. Interviews were held with 12 HCPs of different cultural backgrounds from two different hospitals in Israel. Data was analysed with content analysis.
Results: Data on cultural issues could be summarized into 4 categories and 9 subcategories. Specific barriers in adhering to self-care depending on cultural background were identified such as cultural dietary traditions interfering with the recommended HF diet, willingness to do self-care and religious beliefs conflicting with medical treatment. It was also found that the cultural background of the HCP in some way could influence their patients' adherence to self-care. HCP also adapted their information and care, based on the cultural background of the patients. Shared backgrounds and awareness of differences were reported to positively influence self-care education while cultural differences could negatively affect this process.
During the analysis of material, information regarding other factors that indirectly might be associated with patient self-care was found.
Conclusions: Specific cultural and religious barriers in self-care for HF-patients were identified and the HCPs' cultural background also seems to influence their patients' self-care behaviour. Further research is necessary to confirm these suggested results and to assert the benefits of an adjusted care model based on cultural background.

P334

Paw prints on your heart: the influence of pets on heart failure readmission rate

L Barsky[1]; C Mcpherson[1]
[1]*Yale New Haven/Bridgeport Hospital, Cardiology, Bridgeport, United States of America*

Background/Introduction: Pet or domesticated animal ownership is an increasingly popular lifestyle trend that can have a complex impact upon the trajectory of a patient's heart failure. Indeed, while various studies support the health benefits of

having a pet, some suggest that associated stress and financial burden may promote adverse outcomes. Further, there has been no previous exploration of the specific impact of pets on heart failure readmission rate, an outcome affecting both patients and hospitals.
Purpose: This study sought to examine the effect of pet ownership on 60 day heart failure readmission rate. We hypothesized that owning a pet decreases the readmission frequency.
Methods: We queried the hospital's admission database to identify all patients admitted for a diagnosis of heart failure from January 2015 to March 2017. For those patients who consented to participate, we conducted a phone interview to inquire about pet ownership status, number and type of pets, ownership experience and outside hospital admission history. Medical chart review verified 60 day readmission status and diagnosis and provided further demographic and clinical data. Finally, we used a chi-square test to investigate correlations with readmission rates, demographic attributes and clinical attributes between the pet owner and non-pet owner populations.
Results: Of the 191 subjects in the study population, 44 owned at least one cat or dog, and 147 did not. Among pet owners, 15/44 (34%) were readmitted within 60 days, compared to 78/147 (53%) of non-pet owners (95% confidence interval, P = 0.027). There was no observed correlation between readmission rate and the variables of pet species or quantity owned, socioeconomic class, age, gender, alcohol and tobacco use, ejection fraction, coronary artery disease and clinical management. While pet owners tended to be younger, there was no significant difference in the other described attributes between the pet and non-pet owner groups. Both re-admitted and non-readmitted pet owners endorsed comparable levels of stress and happiness associated with their animals. They all identified their pets as companions.
Conclusions: Ownership of one or more cats or dogs appears to be associated with a lower 60 day heart failure readmission rate. Thus, physicians may suggest dog or cat adoption as a potentially beneficial lifestyle choice for their heart failure patients. As dog or cat ownership may require too much time or money for some individuals, further studies may explore the impact of smaller lower maintenance animals such as birds, rodents or fish on readmission rates.

P335
Comparing the effectiveness of cognitive behavioral interventions and motivational interviewing on improving self-care behaviors

H S J Han Shi Jocelyn Chew[1]; S Y Chair[1]; H Y Cheng[1]
[1]The Chinese University of Hong Kong, Nursing, Hong Kong, Hong Kong SAR People's Republic of China

Aim: To compare the effectiveness of cognitive behavioral interventions and motivational interviewing on improving self-care behaviors in patients with chronic heart failure.
Background: Chronic heart failure remains a major healthcare priority due to its high prevalence and disease burden. Although self-care has been advocated as the sustainable solution, it remains inadequate. Recent studies have shown the potential of integrating structured counseling elements into traditional educational programs to enhance self-care but the optimal counseling method remains unclear.
Design: A literature review.
Data Sources: Articles published between years of 2006 to 2016 were searched from CINAHL, MEDLINE, PubMed, ScienceDirect, PsychINFO, Cochrane Library, Scopus, ProQuest.
Review Methods: Using a systematic three-step search strategy, a literature review of self-care intervention studies that incorporated cognitive behavioural therapy and/or motivational interviewing was conducted. Quantitative and qualitative trial studies that met the inclusion criteria were appraised using the Joanna Brigg's Institute criteria.
Results: Both counselling methods produced higher yet limited significance in improving self-care, with motivational interviewing demonstrated higher potential. Sodium restriction and physical exercise seemed to be more responsive to counselling interventions, suggesting the need to develop behaviour specific strategies. Common elements included goal setting, action planning and problem solving. A striking limitation is the disproportionate number of patients who dropped-out, inconclusive results on the interventions' effectiveness and their unsustainable effects.
Conclusion: More research is needed to understand and address the motivational and operational needs of patients towards self-care instead of just applying counseling to change their outlook.

P336
Long-term tolerability of ivabradine in elderly patients with heart failure - data from oLder HF patients initiated on iVabradinE in the UK: quaLIty of liFE (LIVE:LIFE) study

S M Sarah Birkhoelzer[1]; D Stevens[2]; D Zachariah[1]; N Rowell[3]; J Taylor[4]; PR Kalra[1]
[1]Portsmouth Hospitals NHS Trust, Portsmouth, United Kingdom; *[2]Medical Affairs Department, Servier Laboratories, United Kingdom*; *[3]South Tees Hospitals NHS Foundation Trust, Middlesbrough, United Kingdom*; *[4]Glasgow Royal Infirmary, Glasgow, United Kingdom*

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Background: LIVE:LIFE study demonstrated significant improvements in health related quality of life (HRQoL) and functional status with ivabradine in patients with chronic heart failure (CHF) age = 70 yrs. Despite multiple comorbidities and polypharmacy, ivabradine was well tolerated.
Purpose: Assess long-term use and tolerability of ivabradine in older CHF patients.
Methods: LIVE:LIFE collected demographics, clinical & HRQoL (MLWHFQ, SF-12) data at baseline (V1), 2 (V2), 6 months (V3) from 240 patients across 44 UK primary & secondary care sites. Patients consented for the research team to check medical records at least 12-months after original consent (V4). Data were collected between June 2015 and April 2016 and included current medications, reasons for changes, hospitalisations and deaths. Tolerability of ivabradine was assessed where possible using a 5-point scale (very well, quite well, somewhat well, not well or not at all) by a healthcare professional.
Results: 184 patients had both V3 and V4 on the electronic case report form; 15 died prior to V4 and 6 had no data input at V4. Data were available on 163 patients at both V3 and V4 and form the current study group. Patients were elderly (mean age V4, 78 ± 6 yrs) and 61% were male. 60% had ischaemic aetiology. Co-morbidities were common: 58% hypertension, 33% diabetes and 44% asthma/COPD. The mean duration of follow-up since V1 was 456 ± 93 (± SD) days, mean interval between V3 (last direct study contact with the patient) and V4 was 267 ± 97 days. Patients were prescribed a mean of 9 daily medication at V3 and 11 at V4. At V3, the majority (143, 88%) were taking ivabradine (doses: 2.5 mg bd n = 46, 5 mg bd n = 82, 7.5 mg bd n = 15). Of 159 patients at V4 with data available regarding ivabradine use at that point 75% (119/159) remained on it (doses: 2.5 mg bd n = 29, 5 mg bd n = 76, 7.5 mg bd n = 14). Of the 40 patients who had stopped ivabradine before V4, in 18 cases recommended by the heart failure team, the remainder by primary care (n = 5), non-heart failure secondary care (n = 3), unknown (n = 14). At V4 healthcare professions felt able to comment on tolerability of ivabradine for 113 patients: "somewhat well or better" (n = 105). At V4, 58% were receiving a beta-blocker (61% at V3), 69% an angiotensin-converting-enzyme inhibitor/angiotensin receptor blocker (87% at V3), and 40% a mineralocorticoid receptor antagonist (39% at V3). Between V3 and V4 24% (39/163) patients had been hospitalized. Multiple admissions were noted for 12 patients.
Conclusion(s): In the majority of elderly patients with CHF ivabradine is well tolerated in the longer-term (around 15 months follow up), despite the presence of multiple co-morbidities and polypharmacy. These data reflect real-world practice in the UK - the final data (V4) were collected almost 9 months after the last study contact with the patient. Further evaluation is required to elucidate reasons for stopping ivabradine and neurohormonal antagonists.

P337
Effect of Carvedilol on Survival in Severe Chronic Heart Failure with reduced ejection fraction in sinus rhythm, atrial fibrillation or with a pacing device; a post-hoc analysis of COPERNICUS

Y Mareev[1]; N Ramparsad[1]; P Pellicori[1]; A Mcconnachie[1]; J JV Mcmurray[2]; M Packer[3]; JG Cleland[1]
[1]University of Glasgow, Robertson Centre for Biostatistics, Glasgow, United Kingdom; *[2]University of Glasgow, Glasgow, United Kingdom*; *[3]Baylor University Medical Center, Dallas, United States of America*

Background: An individual patient-data meta-analysis suggested that, compared to placebo, beta-blockers, reduced morbidity and mortality amongst patients with heart failure and a reduced left ventricular ejection (HFrEF) if they were in sinus rhythm but not for those in atrial fibrillation (AF). A subsequent analysis comparing carvedilol with metoprolol tartrate in COMET suggested that carvedilol reduced mortality both for patients in sinus rhythm and AF but not for patients with right ventricular pacing devices (RVPD). The reasons for the disparate trial results for AF are uncertain but could reflect longer duration of follow-up in COMET, differences in classifying patients with RVPD or deleterious effects of metoprolol tartrate (unlikely). Accordingly, we analysed data from COPERNICUS, a trial comparing carvedilol to placebo that was stopped early for overwhelming benefit but has not yet provided a definitive report on outcome by heart rhythm.

Methods & Results: Patients were classified at baseline according to the presence or absence of RVPD that could prevent heart rate reduction. Patients without RVPD were classified as sinus rhythm or AF. Access to anonymized data was provided by GSK.
Of 2,287 patients whose rhythm could be classified (<99%), 1,630 were in sinus rhythm, 414 in AF and 243 with RVPD. Of these, 1202, 268 and 184 respectively completed the titration phase. Compared to placebo, heart rates were lower at the end of titration for those assigned to carvedilol in sinus rhythm (68bpm [IQR: 62-76] vs 80bpm [72-88] or AF (68bpm [60-80] vs 80bpm [72-87]) but were similar for those with RVPD (72bpm [66-78] vs 72bpm [68-80])
In a model adjusted for sex and age, all-cause mortality was lower for patients assigned to carvedilol in sinus rhythm (HR: 0.52 [0.39-0.69], $p < 0.001$), but not in AF (HR: 0.77 [0.45-1.32], $p = 0.34$) or with RVPD (HR: 1.49 [0.87-2.56], $p = 0.114$) (interaction between treatment and rhythm: $p < 0.001$). For patients in AF, further analysis suggested a higher mortality during the titration phase for those assigned to carvedilol (HR 2.25 [0.91 - 5.57]; $p = 0.08$) but a lower mortality during the maintenance phase (HR 0.37 [0.17-0.79]; $p = 0.011$; test for time-interaction $p = 0.003$). For those in sinus rhythm, carvedilol reduced mortality during both titration (HR 0.40 [0.25-0.63]; $p < 0.01$) and maintenance phases (HR 0.60 [0.42-0.86]; $p = 0.005$). For patients with RVPD assigned to carvedilol, mortality was not reduced in either phase (HR 1.40 [0.60- 3.31] and 1.58 [0.80-3.13]).
Conclusions: This post-hoc analysis suggests that beta-blockers may not be effective and could be harmful for patients with HFrEF and RVPD. In the longer-term, carvedilol appears similarly effective for patients in sinus rhythm and AF but there may be an early excess risk for those with AF.

P338
Tolerability and safety of Sacubitril/Valsartan in real-life practice

JN Joana Neiva[1]; IGO Gomez-Otero[2]; AVR Varela-Roman[2]; MMG Moure Gonzalez[2]; ASB Seoane Blanco[2]
[1]Hospital de Vila Franca de Xira, Cardiology, Vila Franca de Xira, Portugal; *[2]University Hospital of Santiago de Compostela, Centro de Investigación Biomédica en Red de Enfermedades Cardiovasculares (CIBERCV), Santiago de Compostela, Spain*

Introduction: After PARADIGM-HF, current ESC guidelines recommend sacubitril/valsartan (SV) for patients (P) with ongoing symptomatic chronic heart failure with reduced ejection fraction (HFrEF), despite first line medical therapy. Experience regarding tolerability and safety in real world populations is less well described.
Purpose: To assess tolerability and success in achieving maximum SV dose, as well as detailing the side effect profile, in a real world population.
Methods: Retrospective and descriptive study extended to all P initiated on SV in a specialized HF unit in a single center since October 2016. Data collected included demographics, initial dose, titration, discontinuation and adverse events. Clinical parameters were documented at each evaluation. Up-titration occurred every 2-4 weeks as per clinical judgment. Descriptive statistics were used for analysis.
Results: Within a population of 106P (79% male; 68,2+10,7years; 45,3% ischemic etiology; mean EF 29,5%; NYHA II-III 99,1%) 61,3% initiated on low doses (24/26mg) and the remaining on 49/51mg. At initiation visit 4P had systolic blood pressure (SBP) < 100mmHg, 1P serum creatinine (Cr) >2,5mg/dL and 6,6% potassium (K) >5,4mmol/L. 13P (12,3%) were still in process of up-titration. After up-titration phase (44+19days) 51,6% achieved maximum dose of 97/103mmHg; 28% were on medium dose and 11,8% remained on 24/26mg without tolerating a dose increase. The main reasons to not achieve highest dose were dizziness/hypotension (47,2%; 4P with SBP < 90mmHg) and hyperkalemia (44,4%; maximum 5,7mmol/L). After a mean follow-up time of 194 days (4-421), 45,3% remained on maximum dose; 5,9% were down titrated to a tolerable dose and 8.2% progressed in titration. The download dose occurred in all cases due to symptomatic hypotension. 11P (10,4%) discontinued SV (vs 17,8% in PARADIGM-HF), 8 of them in titration phase. The commonest reason was a composite of hypotension/dizziness (n = 5; 3P with SBP < 90mmHg); other reasons included acute renal failure (n = 1; decreasing 36% of eGFR), economic reasons (n = 2), gastrointestinal disturbance (n = 1), left ventricular assist device implantation (n = 1) and inappropriate initiation (n = 1). No episodes of angioedema.
Regarding tolerance, SBP decreased 4mmHg (122+17 vs 118+17), Cr increased 0,05mg/dL (1,11+0,34 vs 1,16+0,41) and K decreased 0,03mmol/L (4,84+0,39 vs 4,81+0,42). Of those who had worsening of renal function, 3,8% (4P) had a decrease in eGFR>35% (maximum decrease of 42,6%).
Conclusion: Our data suggests that SV is well tolerated and has good safety in real-life. True hypotension was the dominant cause for discontinuation. Caution should be taken to consider reducing or rationalize other medications with anti-hypertensive side effects to avoid it. The overall adverse reactions were lower when compared to PARADIGM-HF, however our mean follow-up period was significantly shorter.

P339
Changes in pharmacological treatment during first year of follow-up of patients included in a heart failure unit

D Iglesias Del Valle[1]; V Martinez Dosantos[1]; E Garcia Ramirez[1]; JS De Juan Baguda[2]; Z Blazquez Bermejo[3]; E De La Cruz Berlanga[1]; C Casanova Rodriguez[1]; R Cano Carrizal[1]; E Prieto Moriche[1]; A Martin Penato Molina[1]; R Cadenas Chamorro[1]; B Paredes Gonzalez[1]; A Garcia Garcia[1]; I Plaza Perez[1]
[1]University Hospital Infanta Sofia, Madrid, Spain; *[2]University Hospital 12 de Octubre, Madrid, Spain*; *[3]Hospital del Mar, Barcelona, Spain*

Introduction: Several drugs have shown prognostic benefit in heart failure with reduced ejection fraction (HFrEF). However, they cannot always be administered to all patients in whom they are recommended. In addition, in many cases the target doses of these drugs are not reached.
Purpose: To analyze how many patients are given these recommended drugs and what doses are reached during the first year of follow-up in a heart failure unit (HFU).
Methods: We collected all patients with HFrEF included in our unit from July 2014 to December 2016. We collected prospectively data of baseline characteristics as well as data related to pharmacological treatment, type of drugs and doses administered, at baseline, at 6 months and at 1 year follow-up. We calculated the percentage of patients with each type of treatment and the percentage of dose respect to target dose.
Results: We included 95 patients with a mean age of 64.5 years (±13.2), 70.5% males. 66.3% of patients had hypertension and 35.8% had diabetes. Most frequent etiologies of HFrEF were ischemic 32.6%, idiopathic 27.4%, enolic 14.7% and hypertensive 10.5%. NYHA functional class at baseline was I 6.3%, II 41.1%, III 47.4% and IV 5.3%. Mean LVEF at baseline was 25.2% (±7.6) and mean NT-proBNP levels were 5544.5 μg/L (±5511.8). Mortality rate at 1 year follow-up was 5.6%. Table shows the percentage of patients with each pharmacological type and the average percentage of dose respect to target dose at baseline, at 6 months and at 1 year of inclusion in our HFU.
Conclusions: During the first year of follow-up, the percentage of patients with ACEI decreased in favor of a higher percentage with ARB or ARNI. The percentage with beta-blocker and that of ivabradine increased and that of MRA remained stable. Regarding the percentage of dose respect to target dose, it increased in all drugs except for ivabradine.

	Baseline	6 months	1 year			
%patients	%dose	%patients	%dose	%patients	%dose	
ACEI	70.5	38.6	61.5	46.1	58.8	53.2
ARB	16.8	46.6	20.8	54.3	21.4	58.6
Beta-blocker	91.6	52.9	94.5	57.6	94.2	62.0
MRA	81.1	64.7	81.3	64.9	80.2	70.3
ARNI	0	-	5.5	55.0	10.5	52.8
Ivabradine	20.0	75.4	27.5	72.0	27.9	72.2

ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; MRA = mineralocorticoid receptor antagonist; ARNI = angiotensin receptor neprylisin inhibitor.

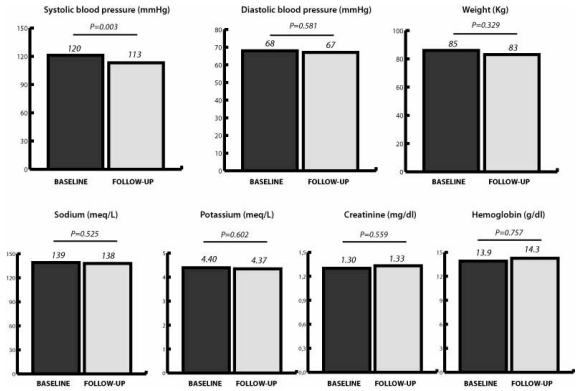
P340
The impact of baseline characteristics differences in patients treated in clinical practice with sacubitril/valsartan versus PARADIGM-HF.

P Pieter Martens[1]; H Belien[1]; M Dupont[1]; W Mullens[1]
[1]Hospital Oost-Limburg (ZOL), Cardiology, Genk, Belgium

Background: Sacubitril/valsartan significantly reduced heart failure hospitalization and mortality in PARADIGM-HF. However, real world data from sacubitril/valsartan use are lacking, which might be useful to overcome hurdles in clinical practice towards its implementation.
Methods: We retrospectively assessed all baseline and follow-up data of consecutive heart failure patients receiving therapy with sacubitril/valsartan according to the Belgian reimbursement criteria, between December 2016 and July 2017 in a single center. Baseline characteristics, follow-up data and dose titration of sacubitril/valsartan were compared between patients in clinical practice and in PARADIGM-HF.

Results: A total of 120 patients (81% male) received therapy with sacubitril/valsartan. In comparison to the patients receiving sacubitril/valsartan in PARADIGM-HF, patients in clinical practice were older, had a higher serum creatinine, higher New York Heart Association (NYHA-class), lower systolic blood pressure (SBP) and a lower left ventricular ejection fraction (LVEF) (p-value all <0.05). Baseline characteristics more closely resembled the patients dropping out during the run-in faze than patients undergoing actual randomization. Even in comparison to patient experiencing dropout during the run-in phase, real world patients had a lower SBP ($p = 0.008$), lower LVEF ($p < 0.001$) and higher creatinine ($p = 0.034$). Patients were at high absolute baseline risk for adverse outcome as illustrated by the EMPHASIS-HF risk score of 6(IQR 3), in comparison to 5(IQR4) in PARADIGM-HF. After initiation of sacubitril/valsartan, NYHA-class significantly improved ($p < 0.001$). SBP dropped more than reported in PARADIGM-HF (7.1 ± 8.0mmhg vs. 3.2 ± 0.4mmHg;$p < 0.001$). Other clinical and biochemical factors did not change significantly (see figure). A total of 20.1% of patients tolerated dose uptitration during follow-up. Symptomatic hypotension (50%) and kidney insufficiency (30%) were the most common reasons for absence of uptitration. Patients received similar RAAS-inhibition before and after initiation of sacubitril/valsartan (57 ± 29 vs 55 ± 27% of target dose; p= 0.672), indicating optimal switch and uptitration of sacubitril/valsartan. However in comparison to patients enrolled in PARADIGM-HF, patients in clinical practice received a significant lower dose of sacubitril/valsartan (219 ± 122mg vs. 375 ± 75mg;$p < 0.001$).

Conclusion: Patients in clinical practice exhibit baseline characteristics that were associated with dropout during the run-in faze of PARADIGM-HF, which might lead to prescription of lower doses of sacubitril/valsartan in clinical practice. Nevertheless, patients in clinical practice are at high risk of adverse outcome, as illustrated by the EMPHASIS-HF risk score. As the relative risk reducing capacity of sacubitril/valsartan does not decreases in higher risk patients, the absolute risk reduction effect of sacubitril/valsartan might be more pronounced in patients encountered in clinical practice.



P341

Use of mineralocorticoid receptor antagonists in real-world patients with nonischemic heart failure and reduced ejection fraction: an analysis of HIJ-HF II study

Y Yuko Matsui[1]; A Suzuki[1]; K Nagara[1]; S Haruki[1]; T Kogure[1]; N Kikuchi[1]; H Hattori[1]; E Kawada[1]; T Suzuki[1]; T Shiga[1]; N Hagiwara[1]
[1]Tokyo Women's Medical University, Cardiology, Tokyo, Japan

Introduction: Mineralocorticoid receptor antagonists (MRAs) improve outcomes in heart failure with reduced ejection fraction (HFrEF), but may be under-utilized in contemporary clinical practice. The aim of this study was to assess predictors of MRAs non-use in HFrEF patients with nonischemic heart disease.

	OR	95% CI	p
Age ≥75	1.540	0.603-3.934	0.367
Men	1.415	0.600-3.335	0.428
without ICD	**6.572**	**1.138-37.959**	**0.035**
NYHA functional class III or IV	0.454	0.164-1.259	0.129
Hb <12g/dl	1.216	0.457-3.237	0.695
Albumin ≤3.0mg/dl	1.889	0.586-6.091	0.287
eGFR <60ml/min/1.73cm^2	1.599	0.654-3.907	0.304
serum potassium per 0.1mEq/ml increase	1.030	0.939-1.129	0.536
BNP <500pg/dl	**3.029**	**1.308-7.012**	**0.010**
LVEF per 1% increase	1.030	0.970-1.094	0.330
without ACE-I or ARB	2.514	0.942-6.713	0.066
without Beta-blocker	1.533	0.559-4.206	0.406
without Oral inotropic	5.291	0.597-46.935	0.135
without Thiazide diuretic	2.932	0.709-12.118	0.137
without Digoxin	0.884	0.304-2.568	0.821
without Statin	0.585	0.232-1.478	0.257
without Nitrate	4.085	0.416-40.117	0.227

Risk factors associated with MRA non-use

Methods: We studied 214 HFrEF patients with nonischemic heart disease from a multicenter hospital-based cohort consisted of hospitalized HF patients between 2013 and 2014 (HIJ-HF II study). HIJ-HF II study was a retrospective observational study using the Japanese Diagnosis Procedure Combination (DPC) Database. Reduced left ventricular ejection fraction (LVEF) was defined less than 40%.

Results: HFrEF patients' average age was 66 +/- 17 and 138 (64%) patients were male. 145 (68%) patients were receiving MRAs. By the multivariate logistic regression analysis, there was a significant higher rates of MRAs non-use in patients without implantable cardioverter defibrillator (ICD) receiving (OR 6.572, 95% CI 1.138 to 37.959, $p < 0.05$), BNP less than 500 pg/ml (OR 3.029, 95% CI 1.308 to 7.012, $p < 0.05$). There was a trend toward higher rates of MRAs non-use in patients without angiotensin-converting-enzyme inhibitor (ACE-I) or angiotensin II receptor blocker (ARB) (OR 2.514, 95% CI 0.942 to 6.713, $p < 0.09$) (Figure).

Conclusion: MRAs remain underused in nonischemic HFrEF patients. We should understand the indications and benefits of MRAs in appropriate HFrEF patients suggested in guideline, especially with lower BNP and without ICD receiving.

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Changes in myocardial iron content following administration of intravenous iron (Myocardial-IRON)

I Ingrid Cardells Beltran[1]; G Minana[1]; P Palau[2]; P Llacer[3]; L Facila[4]; L Almenar[5]; M Lopez Lereu[1]; JV Monmeneu[1]; A Serrano[2]; V Montagud[4]; V Bodi[1]; R De La Espriella Juan[1]; J Sanchis[1]; A Bayes Genis[6]; J Nunez[1]
[1]University Hospital Clinic of Valencia, Valencia, Spain; *[2]Hospital General de Castellón, Castellon, Spain*; *[3]Hospital de Manises, Valencia, Spain*; *[4]University General Hospital of Valencia, Valencia, Spain*; *[5]Hospital Universitario y Politécnico La Fe, Valencia, Spain*; *[6]University Hospital Trias i Pujol, Barcelona, Spain*

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Introduction: Treatment with intravenous ferric carboxymaltose (FCM) has shown to improve symptoms, functional capacity, and quality of life in patients with heart failure (HF) and iron deficiency (ID). However, the underlying mechanisms explaining these beneficial effects remains not fully understood. We hypothesize that myocardial iron changes, evaluated by cardiac magnetic resonance (CMR) after FCM would correlate with simultaneous changes in parameters of severity in HF.

Purpose: The aim of this study was to quantify CMR changes in myocardial iron content after administration of intravenous FCM in patients with HF and ID.

Methods: This is a multicentre, double-blind, randomized study. Fifty patients with stable symptomatic HF with left ventricular ejection fraction < 50% and ID will be randomly assigned 1:1 to receive CMF or placebo. Intramyocardial iron will be evaluated by T2* and T1 mapping CMR sequences before, 7 and 30 days after FCM. After 30 days, patients assigned to placebo will receive intravenous FCM in case of persistent ID. The main endpoint will be changes in myocardial iron content at 7 and 30 days. Secondary endpoints will include the correlation of these changes with the evolution of surrogate markers of disease severity: a) left ventricle ejection fraction, b) functional capacity, c) quality of life, and d) biomarkers.

Conclusions: The results of this study will add important knowledge about the effects of FCM on myocardial tissue and function.

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Comparative efficacy of renin-angiotensin system modulators on prognosis, right and left heart functional parameters in chronic heart failure in relation to mid-ranged or preserved ejection fraction

LR Liana Tumasyan[1]; KG Adamyan[1]
[1]*Institute of Cardiology, Yerevan, Armenia*

The aim of study was to compare efficacy of long-term therapy with ramipril (R, up to 10 mg), candesartan (C, up to 32 mg) alone and their combination with spironolacton (S, up to 50 mg) and their interaction on prognosis, left (LV) and right ventricular (RV), left (LA) and right atrial (RA) functional parameters by Doppler and tissue echocardiography, NT-pro-BNP (pg/ml) and hsCRP (ng/ml) levels in pts with III NYHA FC heart failure in relation to mid-ranged (HFmEF) or preserved (HFpEF) ejection fraction (EF).
Methods: 133 pts (age 60.1) with HFmEF (0.4 = EF <0.5) and 130 pts (age 63.2) with HFpEF (EF = 0.5) were randomly assigned to groups A and A‘ (n = 28 and 27, receiving R), B and B‘ (n = 27 and 26, receiving C), C and C‘ (n = 27 and 26, receiving R+S), D and D‘ (n = 25 and 26, receiving C+R) and E and E‘ (n = 26 and 25, receiving C+S) in addition to diuretics and beta-blockers.
Results: 1-, 2- and 3-year mortality (%) were 35.7 and 33.3, 42.9 and 40.7 and 50 and 48.1 in A and A‘; 33.3 and 30.8, 40.7 and 38.5 and 48.1 and 46.2 in B and B‘; 33.3 and 30.9; 40.7 and 38.4; 48.1 and 46.2 in C and C‘; 28 and 26.9; 32 and 30.8; 40 and 38.5 in D and D‘; and 26.9 and 24; 30.8 and 28; 38.5 and 36 in E and E‘ groups. 1-year hospitalization rates were 57.1 and 55.5 in A and A‘; 51.8 and 50 in B and B‘; 40.7 and 38.5 in C and C‘; 40 and 38.5 in D and D‘; and 34.6 and 32 in E and E‘, respectively. Survival analysis revealed relative risk (RR) reduction of 1-, 2- and 3-year mortality at 24.6 and 27.9; 28.2 and 31.2; 23 and 25.2 (p <0.05) in C+S groups with HFmEF and HFpEF, respectively, compared to group A and A‘. Significant reduction of hospitalization at 28.7 and 35.3 and 29.9 and 30.6 was depicted in groups receiving R+S and C+R (p <0.05) and at 39.4 and 42.3 in C+S group (p <0.01), in pts with HFmEF and HFpEF, respectively.1-year C+S treatment significantly (%, p <0.01 for all) decreased levels of NT-pro-BNP at 40.1.9, e‘ at 40.2, Ar-A at 74.1, increased PV SC at 62.1, RAFI at 52.9 and LAFI at 44.9 in HFmEF, and hsCRP at 44.6, TAPSE at 52.2, s‘ at 36.2, PA ET at 19.8 in HFpEF. 1-year R+S and R+C treatment, respectively, significantly (%, p <0.05 for all) improved levels of NT-pro-BNP at 35.1 and 36.6, TAPSE at 39.6 and 40.5, s‘ at 29.1 and 32.2, PA ET at 15.1 and 16.2. in HFmEF, NT-pro-BNP at 30.6 and 32.2, e‘ at 35.6 and 36.2, Ar-A at 52.2 and 54.1, RAFI at 42..8 and 43.3 in HFFpEF.
Conclusions: 1) Combined use of C+S associated with significant reduction of morbidity and mortality, while R+S and R+C treatment has resulted to significant improvement of hospitalization in pts with both HFmEF and HFpEF. 2) Changes of Ar-A = 50%, RAFI and LAFI, s‘, e‘ = 50%, NT-pro-BNP, hsCRP = 40%; PAET = 25% identified pts with cardiovascular risk reduction. 3) Prognostic improvement in pts treated by C+S was related to improvement of NT-pro-BNP level, LV diastolic functional, LA and RA functional parameters in HFmEF and to hsCRP and RV functional parameters changes in HFpEF.

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Prevalence of appropriate ICD shocks after primary prevention ICD implantation in chronic heart failure with reduced ejection fraction

D Denes Vagany[1]; ZS Majoros[1]; B Muk[1]; B Szabo[2]; P Bogyi[1]; M Szabo[1]; K Kosa[1]; ZS Bari[1]; B Polgar[1]; T Borsanyi[1]; M Dekany[1]; GZ Duray[1]; RG Kiss[1]; N Nyolczas[1]
[1]*Medical Centre, Hungarian Defence Forces, Cardiology, Budapest, Hungary*;
[2]*Orebro University, Cardiology, Orebro, Sweden*

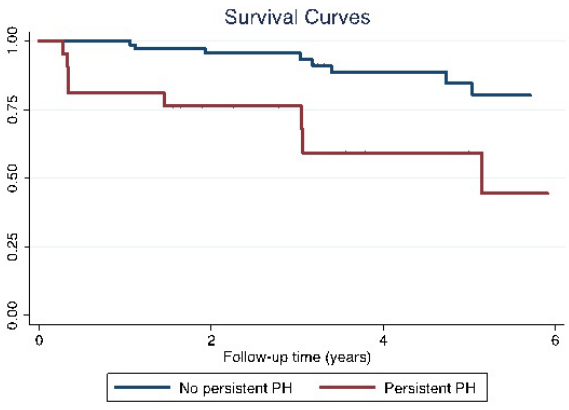
Background: According to the current ESC guidelines for the diagnosis and treatment of acute and chronic heart failure (HF) an implantable cardioverter–defibrillator (ICD) is recommended for primary prevention (PP) of sudden cardiac death (SCD) - regardless of aetiology - in patients with symptomatic HF (NYHA Class II–III), and a left ventricular ejection fraction = 35% despite = 3 months of optimal medical treatment (OMT) who are expected to survive longer than one year with good functional status. The PP ICD absolute benefit is greater in patients (pts) with ischaemic HF. The recently published DANISH study showed that ICD in non-ischemic HF does not reduce all-cause mortality. The survival benefit in association with an ICD implantation was observed only in patients below 70 years of age in that trial.
Aim: The aim of our study was to investigate the prevalence of appropriate ICD shocks in a real-life HFrEF patient cohort, who received device therapy according to the current ESC guidelines.
Methods: We analysed the data of 235 HFrEF pts referred for PP ICD implantation to our institute between 2013 and 2014 (male: 76.6%, ischemic etiology: 48.1%, mean age: 63.4 ± 10.6 years, NYHA: 2.8 ± 0.8, LVEF: 26.1 ± 6.5%, CRT-D: 57.8%), who received their devices according to the current ESC guidelines. Every pt was on OMT at least 3 months before device implantation.
Results: 113 out of the 235 pts had ischemic and 122 had non-ischemic etiology. During the 31.5 ± 12.7 months follow-up we detected 14 appropriate ICD shocks in the subgroup of pts with ischemic HF (12.4%) and 9 appropriate ICD shocks in non-ischemic pts (7.4%). In the ischemic subgroup 11 appropriate shocks (15.5%) were observed among pts < 70 years (71 pts) and 3 appropriate shocks (7.1%) in pts = 70 years of age (42 pts). In the non-ischemic patient group 9 appropriate shocks (9.1%) occurred in pts who were < 70 years old (99 pts). There was no appropriate ICD shock in patients = 70 years of age.
Conclusion: Our observation, in line with the results of the DANISH study, may indicate that elderly patients (= 70 years) with HFrEF and non-ischemic etiology benefit less from PP ICD implantation than those with ischemic etiology or those younger than 70 years.

P345

Persistent pulmonary hypertension after cardiac resynchronization therapy independently predicts death

M Maria Trepa[1]; M Santos[1]; B Braganca[2]; RB Santos[1]; M Oliveira[1]; R Costa[1]; C Roque[1]; VA Dias[1]; H Reis[1]; S Torres[1]
[1]*Hospital Center of Porto, Cardiology, Porto, Portugal*; [2]*University of Porto, Porto, Portugal*

Introduction and **Purpose:** Pulmonary hypertension (PH) is a prognostic factor in patients with heart failure with reduced ejection fraction undergoing cardiac resynchronization therapy (CRT). Whether the change in pulmonary artery systolic pressure (PASP) after CRT has prognostic meaning is less established. We aimed to study the clinical correlates of persistent PH after CRT and its prognostic significance.
Methods: We retrospectively reviewed clinical and echocardiographic data of patients undergoing CRT at our center since 2012. We included those who had available echocardiographic data before and 6-12 months after CRT. Persistent PH was defined as PASP over 40mmHg before and after CRT implantation. All-cause mortality was assessed by chart review.
Results: Of the 207 patients included, 90 (43%) had available Doppler measurements on tricuspid regurgitation before and after CRT. The mean age was 69+- 10 yo with 59% of male patients and 54% of non-ischemic etiology. Most patients (79%) were in NYHA class III previous to CRT. The mean baseline PASP was 39 +- 15 mmHg with 33 patients (37%) having a baseline PASP > 40 mmHg. There were no statistically significant differences in age, sex, etiology, classic cardiovascular risk factors and current treatment strategies between patients with and without PH.
There were 21 (23%) patients who had persistent PH after CRT. These were more likely to have atrial fibrillation (44% vs 76%, p = 0.008) and non-LBBB EKG pattern (15% vs 33%, p= 0.09), lower hemoglobin level (13.2g/dL vs 12.4 g/dL, p = 0.06)) and higher NT-proBNP levels (mean: 1578pg/mL vs 4545pg/mL, p= 0.022). The cardiac phenotype of patients with persistent PH had significantly larger atrial and ventricular cavities.
Interestingly, the change in PASP did not correlate with LVEF change after device implantation (r=-0.06 ; p = 0.64).
Over a mean follow-up of 3.6 ± 1.8 years, there were 17 deaths. Persistent PH patients had a 4-fold increased risk of dying (HR 4.31; 95%CI: 1.61-11.51). It independently predicted death after adjusting for age and gender (HR 4.80; 95%CI: 1.71-13.48), the change in LVEF (HR 5.43; 95%CI: 1.19-24.69), or baseline NT-proBNP (HR 4.54; 95%CI: 1.50-13.75).
Conclusions: Persistent PH after CRT implantation is associated with a more severe clinical and echocardiographic profile. It marks patients with significantly increased risk of dying either because of the baseline severity of the disease, or the lack of response to CRT. In both cases, persistent PH after CRT powerfully signals HF patients with worse prognosis.



P346

The problem of response to cardiac resynchronization therapy: who are non-responders?

AM Soldatova[1]; VA Kuznetsov[1]; SM Dyachkov[1]; TN Enina[1]; DV Krinochkin[1]
[1]*Tyumen Cardiology Research center, Tyumen, Russian Federation*

Background: In patients with congestive heart failure (CHF) treated with cardiac resynchronization therapy (CRT) a reduction of = 15% in left ventricular end-systolic volume (LVESV) is a commonly used criterion of the response. Some patients have significant clinical improvement, decrease in NYHA functional class, good long-term survival, however, they demonstrate suboptimal improvement of cardiac remodeling after CRT and they are identified as nonresponders.
Purpose: To evaluate clinical, morphological, functional features and mortality in patients with suboptimal CRT response.
Methods: The study enrolled 109 patients (mean age 54.6 ± 9.9 years, 83.5% men) with NYHA functional class II-IV. Clinical, electrocardiographic and echocardiographic parameters were evaluated at baseline, 1, 3 months and each 6 months after implantation. According to the best decrease of LVESV (mean follow-up period 34.8 ± 16.7 months) patients were classified as non-progressors (n = 18; decrease in LVESV 0-14%), responders (n = 45; decrease in LVESV 15-29%) and super-responders (SR) (n = 46; reduction in LVESV = 30%).
Results: At baseline groups were matched for main clinical characteristics, the proportion of patients with atrial fibrillation, width of the QRS complex, and the presence of left bundle-branch block (LBBB). Echocardiographic parameters didn't differ between the groups.
All groups demonstrated significant reverse remodeling, increase in left ventricular ejection fraction (LVEF), increase in 6-minute walking distance. SR demonstrated the best improvement of clinical and functional parameters after CRT. However, improvement in LVEF, LVESV, NYHA functional class between responders and non-progressors were found similar as well as in dynamics mean values of these parameters were comparable.
The survival rates were 100% in SR, 80% in responders and 88.9% in non-progressors (Log-rank test p = 0.004). Survival rates in responders and non-progressors didn't differ significantly (Log-Rank test p = 0.213) between the groups.
Conclusion: Patients with reduction in LVESV 0-14% demonstrate improvement in clinical status and LVEF and survival rates compared to subjects with reduction in LVESV 15-30%. Non-progressors demonstrate similar survival as responders in long-term period.
Taking into account the natural course of CHF we consider that functional stabilisation and absence of CHF progression in patients with LVESV reduction 0-14% is a variant of good response and these patients should not be identified as non-responders. Thus, the only use of percentage change in LVESV to define CRT response is not always correct.

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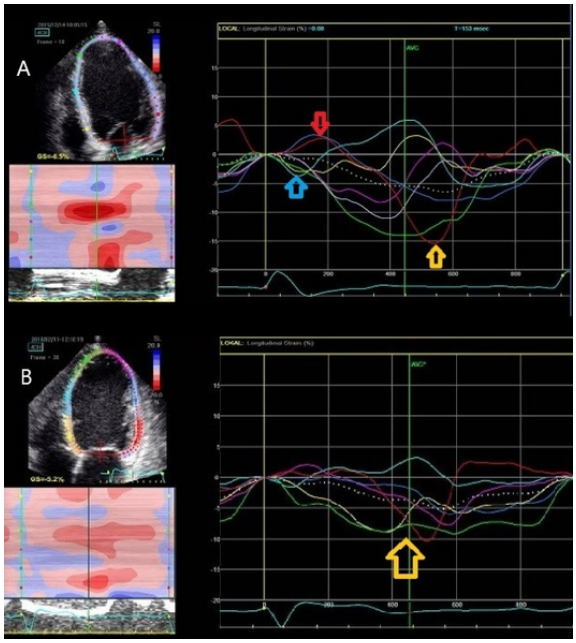
Role of the definition of electrocardiographic and echocardiographic variants of left bundle branch block in predicting response to cardiac resynchronization therapy.

S Svetlana Kashtanova[1]; M Utsumueva[1]; E Gupalo[1]; V Shitov[1]; G Tarasovsky[1]; V Kiktev[1]; M Saidova[1]; N Mironova[1]; S Golitsyn[1]
[1]*National medical research center of cardiology, Moscow, Russian Federation*

Introduction: Cardiac resynchronization therapy (CRT) improves prognosis in patients with heart failure (HF) and left bundle branch block (LBBB). However, a large number of patients does not benefit from CRT. The search of the reproduced markers of response on this therapy is an important problem.



Different echo contraction patterns

Purpose: To assess the value of the complex analysis of electrocardiographic (ECG) and echocardiographic (echo) variants of LBBB in predicting the success of CRT.
Methods. Our study included 17 patients (age 58,76 ± 8,16 years (mean ± SD), 65% men) with HF due to ischemic (12%) or non-ischemic (88%) cardiomyopathy, who had the left ventricular (LV) ejection fraction (LVEF) < 35% despite optimal pharmacological therapy, QRS duration = 130ms, LBBB and sinus rhythm. All patients underwent successful CRT implantation. Depending on the presence /absence of ECG-criteria, proposed by Strauss D.G. et. al, patients were divided into 2 groups: 1-strict LBBB (QRS duration = 140ms in men or = 130 ms in women, QS/rS in lead V1 and mid-QRS complex slurring/notching in >2 of leads V1,V2,V5,V6,I,aVL) and 2-other LBBB morphology. In addition to standard echocardiography, global longitudinal 2-dimensional strain (GLS) and LBBB contraction pattern were analysed. Also, patients were divided into 2 groups based on the presence of one of the echo patterns of LV dyssynchrony: "classical/typical LBBB" and "heterogeneous/atypical". (Figure. Different contraction patterns by 2-dimensional strain echocardiography. A. Classical LBBB contraction pattern, including early terminated shortening of at least 1 basal or midventricular segment in the septal wall (blue arrow), early stretching of at least 1 basal or midventricular segment in the lateral wall (red arrow), late lateral peak contraction after aortic valve closure (yellow arrow).
B. Atypical LBBB contraction pattern: segments show asynchronous peak shortening timed at aortic valve closure (yellow arrow)). Response to CRT was defined as a reduction in LV end-systolic volume (LVESV) of >15% at 6 months follow up.
Results: Within the group consisting of 17 patients, 14 patients (82%) responded to CRT. Among these 14 patients, 12 (86%) had strict LBBB criteria by ECG and "classical" LBBB contraction pattern. From the remaining 3, who did not respond to CRT, 2 patients did not have true LBBB-criteria by echo and ECG. The mean GLS was significantly worse in responders than in non-responders (364 ms ± 81ms vs 241 ms ± 50ms, $p < 0.05$).
Conclusions. Complex analysis of strict LBBB ECG criteria and echo contraction pattern in combination with GLS are promising potential parameters to predict benefit from CRT in patients with HF.

P348

Differences in VWF activity in patients with von Willebrand disease type 2A versus LVAD patients with the acquired von Willebrand syndrome.

S Deconinck[1]; L Delrue[2]; C Tersteeg[1]; E Bailleul[2]; N Vandeputte[1]; I Pareyn[1]; H Deckmijn[1]; M Goethals[2]; S Verstreken[2]; R Dierckx[2]; S De Meyer[1]; N Itzhar-Baikian[1]; K Vanhoorelbeke[1]; M Marc Vanderheyden[2]
[1]*KU Leuven, KULAK, Laboratory for Thrombosis Research, IRF Life Sciences,, Kortrijk, Belgium*; [2]*OLV Hospital Aalst, Cardiovascular Center, Aalst, Belgium*

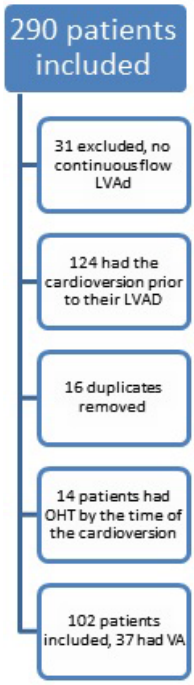
Background: Patients suffering from von Willebrand disease (VWD) type 2A are diagnosed by an increased bleeding diathesis due to an impaired von Willebrand

factor(VWF) function with severe loss in high molecular weight (HMW) VWF multimers. Patients with implanted left ventricular assist devices (LVAD) show a moderate decrease in HMW VWF multimers and are therefore nowadays diagnosed with the acquired von Willebrand syndrome (aVWS). However, only a small portion of LVAD patients suffers from bleeding complications.
Aim: Side by side comparison of VWF function in patients with VWD type 2A and LVAD-induced aVWS to demonstrate the difference in VWF activity, and hence their different effect on bleeding, in both groups of patients.
Methods: Plasma samples from 9 known VWD type 2A and from 9 LVAD patients were analyzed for VWF:Ag, VWF:CB and VWF:RCo using ELISA and for VWF multimers using sodium dodecyl sulphate (SDS) agarose gel electrophoresis and compared to plasma of healthy donors.
Results As expected, VWF function was impaired in all VWD type 2A patients with a severe reduction in HMW VWF multimers compared to healthy individuals (0.0% (0.0-12.3) versus 34.2% (31.7-38.9) respectively, $p < 0.0001$) ensuing in decreased (< 0.7) VWF:CB/VWF:Ag and VWF:RCo/VWF:Ag ratios. In contrast, VWF function was less affected in LVAD patients where only a moderate reduction in HMW VWF multimers was noted (20.3% (15.8-21.7)) with six out of 9 LVAD patients having a VWF:CB/VWF:Ag or VWF:RCo/VWF:Ag ratio within normal range (= 0.7).
Conclusions: Whereas the decrease in HMW VWF multimers together with the depressed VWF function are responsible for the severe bleeding disorder observed in VWD type 2A pts, HMW VWF multimers and hence VWF function are only moderately impaired in LVAD-induced aVWS patients,. Accordingly, these small defects in VWF function can not alone be responsible for the bleeding diathesis in LVAD pts which might explain why only a small portion of them suffer from bleeding complications.

P349
Outcomes following electrical cardioversion for ventricular arrhythmias in patients with Left Ventricular Assist Devices (LVADs)

F Farah Al-Saffar[1]; A Naeem[2]; S Dunlay[3]; D Yip[4]; B Boilson[3]; E Steidley[1]; SK Mulpuru[1]
[1]Mayo Clinic, Cardiology, Scottsdale, United States of America; *[2]Maricopa Integrated Health System, Internal Medicine, Phoenix, United States of America*; *[3]Mayo Clinic, Cardiology, Rochester, United States of America*; *[4]Mayo Clinic, Jacksonville, United States of America*

Background: Ventricular arrhythmias (VA) are common in patients with left ventricular assist device (LVAD) either due to the underlying worsening heart failure; scar formation, LVAD suck down events, or by alteration of ion-channel dynamics.
Purpose: The characteristics of VA in LVAD patients undergoing electrical cardioversion have not been previously described. We sought to examine the success rates and outcomes following electrical cardioversion in this population.
Methods: Adult patients with LVADs obtaining health care at the Mayo Clinic enterprise practice (Minnesota, Arizona, and Florida) from January 2008 to December 2017 were included (figure). The target population was patients who have continuous-flow LVADs and had VA requiring cardioversion. We examined patient demographics were examined, type of cardiomyopathy, LVAD indication, and cardioversion success rates and subsequent outcomes. Shock strength, and the decision to shock externally or via implantable cardioverter defibrillator (ICD) was at the discretion of the supervising clinician. Therapy failure was defines as failure of the first shock to restore sinus rhythm, or recurrence of VA briefly after cardioversion.
Results: A total of 37 patients (mean age 56.55 ± 14.8 years, 25 [67.5%] were men) undergoing electrical cardioversion for VA were included (figure). 14 patients had non-ischemic cardiomyopathy and 22 had ischemic cardiomyopathy. In 18 cases the LVAD was a bridge to transplant (BTT) while in 19 cases it was a destination therapy (DT). Eleven cases (29.7%) had ventricular fibrillation. Thirteen patients in the BTT group were on amiodarone vs. 14 in the DT group. In 14 cases (38.89%) there was a failure of the first therapy or recurrence of VA. VA also tended not to respond as well to submaximal energy cardioversion. There was a higher rate of failure to convert to sinus rhythm in BTT LVAD compared to DT (47.06% vs 31.58% respectively), although not statistically significant. Patients on amiodarone had higher therapy failure (OR 2.78, [CI 0.99 - 7.76], p value 0.05).
Conclusions: Low energy shocks in LVAD patients may be associated with lower success rates. There was also a higher success rate of cardioversion in patients with DT LVAD. Patients on amiodarone were more prone to therapy failure, which could be a precursor of them having a previously-identified arrhythmogenic substrate. This suggests the need for more vigilant management when facing VA in these patients.



Figure

P350
Novel inflammatory biomarkers after long-term ventricular assist device implantation

M Holek[1]; J Kettner[1]; A Jabor[2]; J Franekova[2]
[1]Institute for Clinical and Experimental Medicine (IKEM), Department of Cardiology, Prague, Czech Republic; *[2]Institute for Clinical and Experimental Medicine (IKEM), Department of Laboratory Methods, Prague, Czech Republic*

Introduction: Long-term left ventricular assist device (LVAD) implantation is proved treatment option for patients with end-stage heart failure. Infectious complications (IC) are one of the main causes worsening prognosis after LVAD implantation. Procalcitonin (PCT) is nowadays widely used and presepsin (PSEP) is also one of promising novel biomarkers for diagnosis of a bacterial infection. However, data about PCT and PSEP dynamics in LVAD patients are lacking.
Methods: A total of 50 consecutive patients indicated to LVAD implantation were included. PCT and PSEP levels were prospectively assessed before surgery and during 30 day follow-up - 1st, 2nd, 14th and 30th post-operative day (POD). Values were compared according to the presence of IC and are presented as median with interquartile range in μg/l (PCT) or ng/l (PSEP).
Results: In all patients PCT levels were low before surgery (0,16, 0,10-0,34). They raised significantly within 1st (5,49, 2,52-18,42; $p < 0,001$) and 2nd POD (5,65, 2,47-19,53; $p < 0,001$). Till 14th and 30th POD we observed decrease of PCT back to baseline values (0,21 /0,11-0,68/ and 0,09, /0,07-0,19/ respectively). PSEP levels were mildly elevated before LVAD implantation (543 /340-882/), raised significantly within 1st (892 /557-1362/, $p = 0,002$) and 2nd (1015 /659-1494/, $p < 0,001$) POD and decreased in 14th (838 /505-1620/) and 30th POD (566 /420-867/).
IC occurred after LVAD implantation in 11 patients (22%). Interestingly, there was no significant difference in PCT or PSEP levels between patients with or without IC during whole follow-up.
20 subjects (40%) had acute renal failure (ARF) and 17 of them needed renal replacement therapy (RRT) initiated between 1st and 7th POD. Patients with ARF had significantly higher PCT levels 2 days after surgery and further (day 2 - 24,15 /4,28-76,7/ vs. 3,3 /2,21-9,03/, $p = 0,045$, day 14 - 0,68 /0,24-2,25/ vs. 0,13 /0,09-0,28/, $p < 0,001$, day 30 - 0,21 /0,12-0,34/ vs. 0,08 /0,04-0,12/, $p = 0,005$). ARF increased PSEP levels significantly only 14 days after LVAD implantation (1926 /838-5936/ vs. 688 /430-1181/, $p = 0,005$).
Right ventricular assist device (RVAD) had to be implanted in 7 patients (14%). Also subjects with RVAD had higher PCT and PSEP values. This difference reached the significance only for PCT 14 days after surgery (8,02 /0,37-31,95/ vs. 0,17 /0,11-0,37/, $p = 0,018$).

Conclusion: Our data show that ability of PCT or PSEP to detect infectious complications in patients after LVAD implantation is limited and their concentrations more likely correlate with post-operative complications in general. Although specific mechanism is not known, explanation could possibly be activation of systemic inflammatory response syndrome (SIRS) caused by critical perioperative state including organ dysfunction, cardiopulmonary bypass during surgery and contact with non-physiological surface in LVAD/RVAD or RRT.

P351

Short-term mechanical bridge to heart transplantation

N S Piatrovich[1]; L G Shestakova[1]; Y P Ostrovsky[1]; R G Yarosh[1]
[1]Republican Scientific and Practical Centre of Cardiology, Department of extracorporeal blood circulation, Minsk, Belarus

Background: Heart transplantation (HT) is a golden standart for treating the end-stage chronic heart failure (CHF). Mono- or biventicular assist devices,extracorporeal membrane oxygenation or a total artificial heart are used in potential recipients with unstable hemodynamics, refractory to the maximum doses of cardiotonic agents during 24-48 hours and multi-organ dysfunction.Mechanical circulatory support (MCS) salvages time to complete a transplant evaluation.
Purpose: To analyze and estimate the effectiveness of pre-transplant application of temporary MCS in patients with CHF used as a bridge for heart transplantation or for putting on a waiting list.
Methods: The study conducted a retrospective analysis of 13 patients with decompensation of CHF, requiring temporary MCS. In 38,5% (n = 5) the ventricular support system Centrimag Levitronix was used (3 left- and 2 biventricular assist devices), in 61,5%(n = 8)- peripheral extracorporeal membrane oxygenation in combination with invasive methods of LV unloading: percutaneous atrioseptostomy (n = 6), drainage of LV (n = 2) and intraaortic balloon pumping (n = 1).Selective antegrade perfusion was performed in 4 cases to prevent lower limbs ischemia. 53,8% (n = 7) required renal replacement therapy, 7,7%(n = 1)- hepatic replacement therapy (albumin sorption) .
Results: In Belarus during the period 2009-2017 273 heart transplants were performed. 11,4%(n = 31) were preceded by MCS(10 short-term and 21 long-term). The main ethiology in 61,5% was dilated cardiomyopathy, in 30,8%- ischemic, in 7,7%- acute myocardial infarction. Indication for MCS was decompensation of CHF: AP 88 ± 19,5 mm Hg on the background of initropic support(100%), CI 2,13 ± 0,51 l/min/m^2, PAP 50,91 ± 11,48 mmHg, PAWP 22,5 ± 6,6 mmHg, WI 4,87 ± 1,75, LVEF 16,83 ± 5,59%, RVEF 30,55 ± 6,78%, SV 48,67 ± 22,98 ml,proBNP 9365 pg/ml, pH 7,3 ± 0,1, BE -6,23 ± 6,5 mmol/l, lactate 6,48 ± 3,1 mmol/L, AST 530U/L, ALT 771,17U/L, LDH 822,9 U/l, bilirubin 75,86 mmol/l.Mean duration of MCS was 14,8 ± 7,4 days. In 100% there was a significant positive dynamic of biochemical indices and decrease in lactate by 5,4 times. Echocardiography examination revealed reduction volume of left ventricle and increase of LVEF by 14,68%, RVEF by 23,18%, CI by 43,19%. Ten patients underwent heart transplantation. One ECMO case was converted to a long-term heart assist device. Three patients(23,1%) died due to complications(perioperative myocardial infarction, massive bleeding, irreversible multiorgan dysfunction, DIC, sepsis). Hospital survival was 76,9%.
Conclusions: Short-term MCS effectively provides maintenance of vital functions, resolution of organ disorders, normalization of biochemical indices and greatly improves survival for patients with severe refractory hemodynamic instability awaiting HT.

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Treatment of hypercholesterolaemia with PCSK-9 inhibitors in patients after cardiac transplantation

M Michael Kuehl[1]; J Jozwiak[2]; C Binner[3]; J Fischer[3]; J Hahn[3]; A Meyer[3]; A Addas[3]; K Jawad[3]; J Garbade[3]; M Borger[3]
[1]Heart Center of Leipzig, Rhythmology, Caridac Surgery, Leipzig, Germany; *[2]Heart Center of Leipzig, Cardiology, Leipzig, Germany*; *[3]Heart Center of Leipzig, Cardiothoracic Surgery, Leipzig, Germany*

Background: Hypercholesterolaemia is common in patients after cardiac transplantation affecting over 90% of patients 5 years post transplantation. Statin therapy after transplantation has received a class I indication irrespective of cholesterol levels. It has been shown to improve survival and has been implicated in reducing fatal rejections, decreasing terminal cancer risk and reducing the risk of cardiac allograft vasculopathy (CAV). However, some patients cannot tolerate statins because of their side effects or demonstrate residual hypercholesterolaemia. Monoclonal antibodies that inhibit proprotein convertase subtilisin-kexin type 9 (PCSK9) have been shown to reduce low-density lipoprotein (LDL) cholesterol levels and the risk of cardiovascular events in patients with dyslipidaemia. There are no published data on the effect of this medication class on cholesterol levels in patients after cardiac transplantation.
Purpose: To examine the effects of treatment with PCSK9 inhibitors on cholesterol, LDL and HDL levels, acute rejection episodes and ejection fraction in patients after cardiac transplantation.
Methods: In this retrospective study we investigated patients who were treated with Evolocumab or Alirocumab either because of intolerance of statins or residual hypercholesterolaemia with evidence of CAV. We compared the data of patients prior to the start with these medications with their most recent dataset.
Results: We identified ten patients (nine men; mean age 58 ± 6 years) who underwent cardiac transplantation 8.3 ± 4.5 (range 3-15) years ago. CAV of varying severity was present in seven patients. The reason for PCSK9 inhibitor therapy (Evolocumab: 140mg every two weeks n = 8; Alirocumab: 75mg every two weeks n = 2) was statin intolerance (n = 6) or residual hypercholesterolaemia despite statin therapy (n = 4). The treatment duration was on average 296 ± 124 days and lead to a reduction of total Cholesterol (281 ± 52 mg/dl to 197 ± 36 mg/dl; p <0.001) and LDL Cholesterol (170 ± 22 mg/dl to 100 ± 39 mg/dl; p <0.001). No significant effects on HDL Cholesterol, BNP, Creatine Kinase or hepatic enzymes were noticed. There were no unplanned hospitalisations, episodes of rejections, change of ejection fraction or opportunistic infections (CMV, aspergillosis, candidiasis). Both patients on Alirocumab developed liver pathologies: One patient died of hepatocellular carcinoma and the other developed hepatitis E.
Conclusion: Our study demonstrates that PCSK9 inhibitors lead to a significant reduction of total and LDL Cholesterol in heart transplantation recipients with hypercholesteraemia and therapeutic failure of statin regimens or statin intolerance. No effect on cardiac function or episodes of rejections were noticed. Larger and long-term studies are needed to establish the safety and efficacy of Evolocumab and Alirocumab after cardiac transplantation with a special focus on the development or progression of CAV as well as liver pathologies.

P353

Risk factors to develop new-onset diabetes mellitus after heart transplantation

A Abril Molina[1]; A Grande-Trillo[1]; D Rangel-Sousa[1]; JM Sobrino-Marquez[1]; E Lage-Galle[1]; C Gonzalez-Portilla-Concha[1]; J Rodriguez-Ortuno[1]
[1]University Hospital of Virgen del Rocio, Heart Failure and Heart Transplantation Unit, Seville, Spain

Introduction:
New-onset diabetes mellitus (DM) after heart transplantation (HT) is associated, as well as established previous DM, with worse prognosis. Our aim is to identify risk factors related to the development of DM during the first year after HT in patients with prediabetes before HT.
Methods: Retrospective analysis of HT recipients from 2007 to 2016 in our center with prediabetes status (HbA1c = 5.7%) before HT. We analyzed immunosuppressive therapy at hospital discharge and during the first year, body mass index (BMI), pre-transplant HbA1c level and the development of new-onset diabetes during first year after HT.
Results: We analyzed 106 patients (50 ± 12 years old; 73,8% male). 27,4% (n = 29) developed DM during first year after HT. Univariate and multivariate analysis are shown in the Table 1.
Conclusions: Rate of new-onset DM in the first year after HT in patients with prediabetes is high. Higher levels of tacrolimus and pre-transplant HbA1c are independent risk factors for the development of DM. To pay attention of these levels

Table 1

Univariate analysis

	No develop DM	New-onset DM	p-value
Gender (male)	75.32%	72.4%	0.47
Age (years)	50±12	50±14	0.8
BMI (kg/m^2)	24.92	26.62	0.09
HbA1c pre-transplant (%)	5.68	6.29	0.004
Prednisone at discharge (mg)	10.54	10.61	0.41
Tacrolimus levels (ng/ml)†	10.16	11.63	0.009
Everolimus treatment (%)‡	7.8%	24.1%	0.03

Multivariate analysis

	Odds Ratio	CI 95%	p-value
BMI (kg/m^2)	1.05	(0.95-1.16)	0.835
HbA1c pre-transplant (%)	5.11	(1.79-14.56)	0.002
Tacrolimus levels (ng/ml)†	1.31	(1.05-1.63)	0.016
Everolimus treatment	3.8	(0.85-17.24)	0.08

†Mean tacrolimus levels during first year after heart transplantation. ‡ Patients treated with everolimus (%) during first year after heart transplantation. Abbreviations: BMI: Body mass index; DM: diabetes mellitus

and establish healthy lifestyle in these patients could reduce the incidence of DM after HT.

P354

Is age of 60 reasonable refusal of heart transplantation?

V Krachak[1]; V Podpalov[2]; L Shestakova[1]; Y Ostrovsky[3]

[1]Republican Scientific and Practical Centre of Cardiology, Extracorporeal circulation, Minsk, Belarus; *[2]Republican Scientific and Practical Centre of Cardiology, Cardiac surgery #3, Minsk, Belarus*; *[3]Republican Scientific and Practical Centre of Cardiology, Minsk, Belarus*

Introduction: Now heart transplantation (HT) in elderly people is becoming a burning task. The age of 60 is considered to be a cutoff point after which the outcomes of HT are controversial and HT is seemed to be not always reasonable.
Purpose: To estimate outcomes after HT in people aged 60 years and older.
Methods: 260 HT operations have been conducted in our Centre during HT program developing since 2009. Among all operated patients 2 groups were selected: the 1st group - the main group with 34 patients aged 60 years and older; the 2nd group - the control group with 67 patients aged 50-59 years. The average age in the main group was 54,76 ± 2,93 years and in the control group - 63,91 ± 3,1 years (??0,0001). There were no significant differences in proportions of women and men: 2,9%(n = 1) and 97,1%(n = 33) respectively in the 1st group versus 13,4%(n = 9) and 86,6%(n = 58) in the 2nd group (p>0,05). The most wide spread etiology leading to HT was dilated cardiomyopathy which was in 50% (n = 17) in the 1st group and 53,7% (n = 36) in the 2nd group of patients; then ischemic cardiomyopathy came 35,3% (n = 12) versus and 41,8% (n = 28) respectively; other cases occupied 14,7% (n = 5) and 4,5% (n = 3) respectively. The groups of patients were similar by the following parameters: body mass index was 22 ± 9,69 in the 1st group versus 23,3 ± 10,67 in the 2nd group (p = 0,2); systolic pulmonary artery pressure - 49,82 ± 10,4 versus 50,59 ± 11,69 mm Hg respectively (p = 0,96), donor age - 35,09 ± 8,4 versus 35,93 ± 8,73 years respectively (p = 0,062), cold ischemic time - 192,83 ± 43,79 versus 203,05 ± 57,75 min respectively (p = 0,34). 30-day and 1-year survival rates were estimated as outcomes after HT.
Results: Patients from the main group treated in ICU after HT for 10,5 ± 8,36 days, the time was similar with the patients from the control group - 7,97 ± 4,61 days (p = 0,62).There were no significant differences in outcome in 2 groups: 30-day survival was 79,4% in the main group and 86,6% in the control group (p>0,05); 1-year survival was 67,6% in the 1st group and 77,6% in the 2nd group (p>0,05).
Conclusion: According to gained data age of 60 years and older doesn't seem to be a contraindication for heart transplantation.

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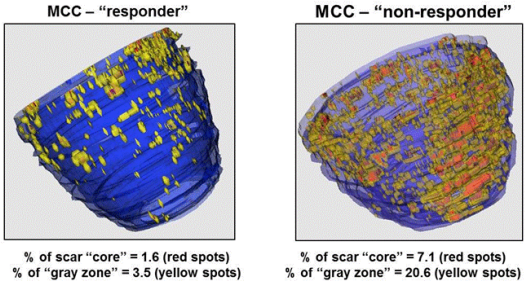
Structural changes of the left ventricular myocardium according to magnetic resonance imaging and response to cardiac contractility modulation therapy

E M Elena Gupalo[1]; NA Mironova[1]; OP Aparina[1]; OV Stukalova[1]; MD Utsumueva[1]; SP Golitsyn[1]

[1]Russian Cardiology Research Center, Moscow, Russian Federation

The novel therapeutic option in patients (pts) with chronic heart failure (CHF), low left ventricular ejection fraction (LVEF) and narrow QRS complex is cardiac contractility modulation (CCM). Pts with non-ischemic etiology of HF, LVEF of = 25% have the greater response to CCM than others. Cardiac MRI provides a noninvasive phenotyping tool for accurate and easy detection and quantification of myocardial fibrosis by probing the retention of gadolinium-contrast agent in myocardial tissue reflection the grade of myocardium structural changes. The value of LV structural changes for the response to CCM therapy is not yet known.
The aim of the study was to evaluate the value of left ventricular myocardial fibrosis according to MRI data for the response of CCM therapy.
Materials and methods: The study included 12 pts (10 male, mean age 46 ± 14 years) with chronic heart failure (CHF) NYHA functional class II-III, normal duration of the QRS complexes (96 ± 16 ms) and significantly reduced LVEF (28 ± 4% at the time of inclusion in the study) despite optimal medical. The etiology of CHF was ischemic cardiomyopathy in 2 pts and non-ischemic in 10 pts. Cardiac MRI was performed in all pts with high resolution late gadolinium enhancement (LGE) before devices' implantation. Left ventricular fibrosis quantification was performed with the original software LGE Heart Analyzer. In all pts the device for MCC (Optimizer IV or Optimizer SMART) was implanted. At 6 months follow-up the echo parameters, Nt-proBNP, a 6-minute walking test (SMWT) were assessed.
Results: According to the cardiac MRI, the volume of fibrosis was 1.6 [1.1, 5.5]% of the total volume of the myocardium. In 5 (41.6%) pts, this index exceeded 5%. In these 5 pts, the improvement of LVEF was not detected. In contrast, the rest 7 (58.3%) pts with 1.35 [0.73, 1.6]% fibrosis volume demonstrated an increase in LVEF by an average of 11 ± 5.6 after 6 months of CCM therapy. The increase in LVEF was accompanied by a decrease in the of Nt-proBNP level by an average of 479 [340, 1000] pg/ml and an increase in walking distance in SMWT at 192 ± 36 m.
Conclusions: Cardiac MRI with quantitative evaluation of scar tissue carries key information that allows to predict the increase of LVEF during CCM therapy in patients with CHF.

Three-dimensional reconstruction of MRI LGE left ventricular images obtained with the originally developed software LGE Heart Analyzer



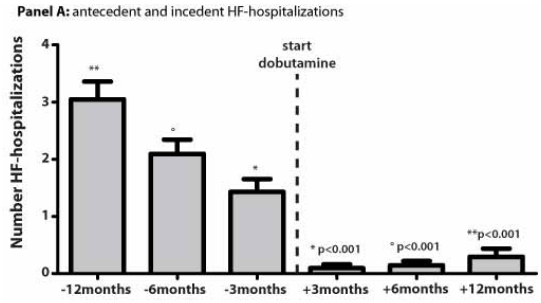
P356

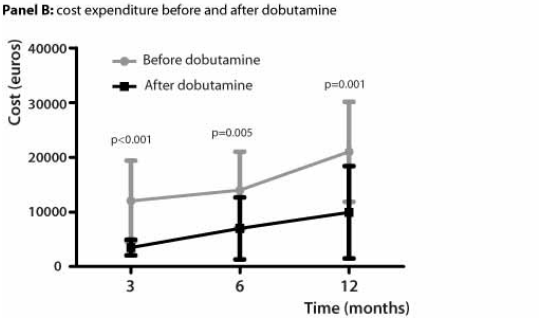
Effects of intravenous home Dobutamine in palliative end-stage heart failure on quality of life, heart failure hospitalization and cost-expenditure.

P Pieter Martens[1]; J Vercamme[1]; W Ceyssens[1]; L Jacobs[1]; M Dupont[1]; W Mullens[1]

[1]Hospital Oost-Limburg (ZOL), Cardiology, Genk, Belgium

Background: In patients with palliative end-stage heart failure, interventions that could provide symptomatic relief and prevent hospital admissions are important. Intravenous inotropes have been advocated by guidelines for such a **Purpose:** We sought to determine the effect of an easy to employ continuous intravenous home dobutamine regimen on symptomatic status, hospital-stay, mortality and cost-expenditure.
Methods: All consecutive end-stage heart failure patients not eligible for advanced therapies and discharged with intravenous continuous home dobutamine from a single-tertiary center between April 2011 and January 2017, were retrospectively analyzed. Dobutamine was infused through a single-lumen central venous catheter with a small pump which was refilled by a nurse once on a daily basis. All patients received a similar dose of 2 vials (250mg/20ml) of dobutamine with 10 cc of glucose 5% in a single 50ml syringe. This 50ml volume was administered at 1.9ml/hour, which equates to approximately 4 mcg/kg/min for an 80kg patient. Symptomatic status was longitudinally assessed as the change in New York Heart association (NYHA) class and patient global assessment (PGA)-scale. Antecedent and incident heart failure hospitalizations were determined in a paired fashion and the impact cost-expenditure was assessed.





Results: A total of 21 patients (age 77 ± 9 years) were followed for 869 ± 647 days. At first follow-up (6 ± 1 weeks) after the initiation of dobutamine, patients had a significant improvement in NYHA-class (-1.29 ± 0.64; p <0.001), PGA-scale (<0.001) and NT-proBNP (6247 pg/ml vs 2543 pgml; p = 0.033). Incident heart failure hospitalizations assessed at 3, 6 and 12 months were significantly reduced (p <0.001 for all) in comparison to antecedent heart failure hospitalizations over the same time period (see figure, panel A). Cost expenditure was significantly lower after the initiation of dobutamine in comparison to the cost related to heart failure hospitalization the before initiation of dobutamine over the same timeframe. Nursing costs and medication cost formed the highest part of expenditure following initiation of IV dobutamine. Mortality rate at 1-year was 48% with 9/12 (75%) patients dying at home, most often from progressive pump failure.
Conclusion: Continuous intravenous home dobutamine in patients with palliative end-stage heart failure is feasible, and significantly improves symptomatic status, reduces heart failure hospitalizations and health-care related costs

P357

Bone marrow cell therapy in patients with chronic ischemic heart disease: a meta-analysis of randomized controlled trials

A Anweshan Samanta[1]; MR Afzal[2]; L Derbas[1]; SD Roy[1]; SS Taduru[1]; V Jeevanantham[3]; B Dawn[4]
[1]University of Missouri - Kansas City, Internal Medicine, Kansas City, United States of America; *[2]The Ohio State University, Division of Cardiovascular Medicine, Columbus, United States of America*; *[3]St. Anthony Hospital, Ohlahoma City, United States of America*; *[4]University of Kansas Medical Center, Division of Cardiovascular Diseases, Kansas City, United States of America*

Background: Although several randomized controlled trials (RCTs) have documented benefits of bone marrow cell (BMC) therapy in patients with chronic ischemic heart disease, the efficacy of this therapy still remains controversial.
Purpose: We hypothesized that BMC therapy would improve left ventricular (LV) parameters in patients with CIHD.

Table: Mean change in LV functional and structural parameters in BMC-treated CIHD patients compared with standard therapy.

Cardiac Parameter	Weighted Mean Difference	95% Confidence Interval	*P* Value
LVEF (%)	3.99	2.63 to 5.35	<0.00001
LVESV (ml)	-9.33	-16.59 to -2.06	0.01
LVEDV (ml)	1.46	-4.68 to 7.60	0.64
Infarct Size (%)	-4.92	-6.98 to -2.86	<0.00001

Methods: We performed a systemic review and meta-analysis of data from published RCTs that evaluated the efficacy of BMCs in patients with CIHD. Database searches through May 31, 2017 identified 23 studies enrolling 1026 patients. The effects of BMC therapy on LV ejection fraction (LVEF), LV end-systolic volume (LVESV), LV end-diastolic volume (LVEDV) and infarct size were analyzed. Changes in outcomes of interest were analyzed with random-effects meta-analysis.
Results: Compared with standard therapy, BMC therapy improved LVEF (3.99%; 95% confidence interval [CI]: 2.63 to 5.35; P < 0.00001) and reduced LVESV (-9.33 ml; 95% CI: -16.59 to -2.06; P = 0.01). BMC therapy reduced infarct size (-4.92%; 95% CI: -6.98 to -2.86; P < 0.00001) when compared with standard therapy in these patients with CIHD. Cell therapy did not have any significant impact on LVEDV. A separate analysis of RCTs using cardiac MRI confirmed the benefit of BMC therapy on LVEF in these patients (1.55%, 95% CI: 0.13 to 2.97; P = 0.03).
Conclusions: Results of meta-analysis of pooled data from RCTs of BMC therapy in patients with CIHD indicate a modest yet significant beneficial effect on cardiac function. The improvement in LVEF was confirmed in a separate analysis of trials using cardiac MRI.

P358

Worsening renal function and hyperkalaemia in a real-life cohort treated with sacubitril/valsartan: findings from a prospective registry

L Rodriguez Sotelo[1]; AM Iniesta[1]; A Esteban-Fernandez[2]; M Gomez-Bueno[3]; J De-Juan[4]; P Diez-Villanueva[5]; A Ayesta[6]; D Iglesias[7]; M Garcia-Aguado[8]; JA Perea-Egido[9]; L Vicent[10]; L Pena Conde[1]; SO Rosillo[1]; JL Lopez-Sendon[1]; M Martinez-Selles[10]
[1]University Hospital La Paz, Cardiology department, Madrid, Spain; *[2]Hospital Clinic San Carlos, Madrid, Spain*; *[3]University Hospital Puerta de Hierro Majadahonda, Madrid, Spain*; *[4]University Hospital 12 de Octubre, Madrid, Spain*; *[5]University Hospital De La Princesa, Madrid, Spain*; *[6]Hospital del Sureste, Arganda del Rey, Madrid, Spain*; *[7]University Hospital Infanta Sofia, Madrid, Spain*; *[8]Hospital de Mostoles, Madrid, Spain*; *[9]Hospital de Getafe, Madrid, Spain*; *[10]University Hospital Gregorio Maranon, Madrid, Spain*

Background: Since PARADIGM-HF trial various international heart failure (HF) consensus and guidelines have included the use of sacubitril/valsartan (SV) for the management of symptomatic HF with reduced ejection fraction as a class I recommendation, due to its proven benefit compared to enalapril. Despite the fact that worsening renal function (WRF) and hyperkalaemia (HK) were less frequent in the SV group, these are two undesirable adverse effects that could limit the widespread use.
Purpose: The aim of this study was to analyse the incidence of WRF and HK after introduction of SV in daily clinical practice, and to determine whether there were associated factors.
Methods: Prospective registry of outpatients from 10 hospitals receiving SV as part of their HF treatment, with at least 6-months follow-up. WRF was defined as a decrease of 50% or more in glomerular filtration rate (GFR). HK was defined as potassium level > 5.5 mmol/L.
Results: We included 427 patients (median age 68,34 ± 11,76 years; female 29,7%), 29 (6.8%) developed WRF and 21 (4.9%) HK. Table 1 shows the baseline characteristics according to WRF. Patients with WRF had prior to the beginning of therapy lower GFR (46.1 ± 16.9 vs 64.5 ± 21.2 p < 0.001), higher levels of NT-proBNP (1916, IQR 936-3917 ng/L vs 3773, IQR 2126-6454 ng/L, p = 0.024), as well as a worse functional class (NYHA III-IV: 51.7% vs 28.7% p = 0.009). The only factor related to HK during follow-up was WRF (28.6% vs 5.7%, p < 0.001). Patients with WRF received a lower SV dose at the end of follow-up (67.2 ± 55.5 vs 111.6 ± 70.6 mg b.i.d. p = 0.001), had a higher rate of SV discontinuation (24.1% vs 10.6% p = 0.027), and a higher mortality (10.3% vs 2.3% p = 0.011), readmission rate (37.9% vs 14.3%, p = 0.001), and visits to the emergency department (34.5% vs 17.1%, p = 0.019) than patients without WRF.
Conclusions: WRF and HK in the real-life scenario were less frequent than expected. When present, WRF is associated with unfavourable outcomes. Patients with a poor baseline renal function, advanced functional class, and high levels of NT-proBNP are at higher risk for WRF.

Table 1.

Variable	WRF n = 29	No WRF n = 395	p
Female sex, n (%)	10 (34.5)	116 (29.4)	0.54
Age (years) (mean ± SD)	70.5 ± 9.7	68.2 ± 11.9	0.32
Hypertension, n (%)	20 (69)	297 (74.6)	0.50
Diabetes mellitus, n (%)	16 (55.2)	154 (38.7)	0.08
Left ventricular ejection fraction (%), mean ± SD	31.27 ± 6.3	28.7 ± 6.9	0.06
Ischemic heart disease, n (%)	15 (51.7)	210 (52.9)	0.90

P359

Cardiac resynchronisation therapy in heart failure patients with ischaemic vs non-ischaemic aetiology: results from 11088 patients in the ESC CRT Survey II

C Camilla Normand[1]; C Linde[2]; A Auricchio[3]; N Bogale[1]; J Cleland[4]; A Gitt[5]; C Stellbrink[6]; S Anker[7]; G Filippatos[8]; M Gasparini[9]; G Hindricks[10]; C Blomstrom Lundqvist[11]; P Ponikowski[12]; F Ruschitzka[13]; K Dickstein[1]
[1]Stavanger University Hospital, Cardiology, Stavanger, Norway; *[2]Karolinska University Hospital, Stockholm, Sweden*; *[3]Cardiocentro Ticino, Lugano, Switzerland*; *[4]Imperial College London, London, United Kingdom*; *[5]Stiftung Institut für Herzinfarktforschung, Ludwigshafen, Germany*; *[6]Bielefeld Hospital, Bielefeld, Germany*; *[7]Charité - Universitätsmedizin Berlin, Berlin, Germany*; *[8]Athens Medical School, Athens, Greece*; *[9]Clinical Institute Humanitas IRCCS, Rozzano, Italy*; *[10]Heart Center of Leipzig, Leipzig, Germany*; *[11]Uppsala University, Uppsala, Sweden*; *[12]Wroclaw Medical University, Wroclaw, Poland*; *[13]University Hospital Zurich, Zurich, Switzerland*

On behalf of: CRT Survey II

Funding Acknowledgements: The work was supported by EHRA, HFA, Biotronik, Boston Scientific, Medtronic, Sorin, St. Jude, Abbott, Bayer, Bristol-Myers Squibb and Servier.

Background: Cardiac Resynchronization Therapy (CRT) reduces morbidity and mortality in selected patients with heart failure (HF) and electrical dyssynchrony.
Purpose/Methods: In 2016 HFA and EHRA conducted a survey of CRT implantations in 11,088 patients in 42 ESC member states. We have analysed the results, comparing patients with ischaemic vs non-ischaemic HF aetiology.
Results: Hospitalization for HF during the past year was common in both groups and use of HF medication was similar. Patients with ischaemic HF were older, more frequently men, with significantly less LBBB. They more often had a history of hypertension and non-cardiovascular co-morbidities including diabetes, anaemia and chronic kidney disease.
Conclusions: Patients in CRT Survey II with ischaemic HF aetiology were significantly older, more often male with more co-morbidity than those with non-ischaemic HF. However, they were similar in regard to clinical status.

Ischaemic vs Non-Ischaemic HF Aetiology

	Ischaemic HF (47%) n = 4875	Non-Ischaemic HF (53%) n = 5453
Age (year, median, IQR)	71 (65-77)	68 (60-75)
Men (%)	86	67
Past Medical History: (%)		
HF hospitalization during past year	49	46
Hypertension	72	58
Atrial fibrillation	41	40
Diabetes Mellitus	39	26
Anaemia	19	11
Chronic kidney disease	36	27
Pre-implant evaluation		
NYHA Class III & IV (%)	61	57
LVEF (%,median, IQR)	28 (23-33)	29 (23-33)
LBBB (%)	71	80
QRS (ms, median, IQR)	160 (140-172)	160(144-176)
Medication on discharge (%)		
Loop diuretics	84	80
ACE inhibitors/ARBs	86	88
MRAs	64	64
Beta blockers	90	89

IQR –interquartile range, HF-heart failure. All differences are statistically significant with $p < 0.05$.

P360

Clinical impact of implantable cardioverter defibrillators in pre- and post- left ventricular assist device ventricular arrhythmias

VJL Goh[1]; CP Lim[2]; KL Kerk[2]; Y Chia[1]; TE Tan[2]; C Sivathasan[2]; JL Soon[2]; V Chao[2]; DKL Sim[2]; LLY Teo[2]
[1]Singapore General Hospital, Singapore, Singapore; *[2]National Heart Centre Singapore, Singapore, Singapore*

Background/Introduction: The significance of ventricular arrhythmias (VA) and implantable cardioverter defibrillator (ICD) therapy in patients on continuous flow LVAD (CF-LVAD) support remains controversial. Patients with pre-LVAD VA have been shown to have higher incidence of post-LVAD VA, but the utility of ICD therapy in these patients remains under studied.
Purpose: We aimed to evaluate the impact of pre-LVAD VA, post-LVAD VA, and ICD therapy on outcomes in patients with ongoing CF-LVAD support.
Methods: We performed a retrospective analysis of 87 patients receiving LVADs between May 2009 and July 2017 in a tertiary hospital in Singapore. Outcomes assessed included all-cause mortality, hospitalisation, and time to death or transplant. Pre-LVAD VA was defined as any VA occuring before LVAD implantation, and post-LVAD VA was defined as VA occurring = 30 days post-LVAD implantation. Hazard ratios were adjusted for age, sex, etiology of heart failure and INTERMACS status.
Results: Patients with pre-LVAD VA (n = 29) were younger (45 vs 53 years, $p < 0.01$), less likely to have ischemic cardiomyopathy (28% vs 59%, $p < 0.01$) and more likely to have ICDs implanted pre-LVAD (69% vs 43%, $p < 0.05$), compared to those without pre-LVAD VA. There were no differences in gender (79% vs 84% male, n = 0.5), patients with INTERMACS 1 and 2 at implantation (55% vs 43%, n = 0.4), or years on LVAD support (1.7 [1.3, 3.9] vs 2.0 [1.0, 3.6] years) between patients with and without pre-LVAD VA respectively. As expected, patients with pre-LVAD VA had higher incidence of post-LVAD VA (12.1 vs 2.3 events per patient year (EPPY), $p = 0.04$). There was no difference in mortality between patients with or without: pre-LVAD VA (24% vs 28%, $p = 0.8$), post-LVAD VA (31% vs 24%, $P = 0.6$, n= 29), or ICDs (31% vs 21%, $p = 0.3$, n = 45). Similarly, there was no difference in all-cause hospitalisations in patients with or without pre-LVAD VA (median 1.63 vs 1.22 EPPY, $p = 0.7$), post-LVAD VA (median 1.68 vs 1.22 EPPY, $p = 0.8$) or ICDs (median 1.79 vs 1.07 EPPY, $p = 0.08$). Time to death/transplant was not significantly different between patients with or without pre-LVAD VA, post-LVAD VA, and ICDs (Figure 1). In a subgroup analysis of patients with pre-LVAD VA, there was no mortality benefit for patients with concurrent ICDs (No ICDs, n = 42: 11% vs ICDs, n = 45: 30%, $P = 0.38$). Patients with ICDs experienced a mean of 6.1, 5.1 and 0.2 EPPY of ICD shocks, anti-tachycardia pacing, and ICD-related hospitalisations respectively.
Conclusions: The presence of pre-LVAD VA, post-LVAD VA, and ICDs had no significant impact on mortality or hospitalisations in our cohort, and pre-LVAD implantation of ICDs in patients with pre-LVAD VA did not improve mortality. The high rate of ICD therapy and ICD-related hospitalisations may represent unnecessary burden in patients with concurrent CF-LVAD and ICD therapy.

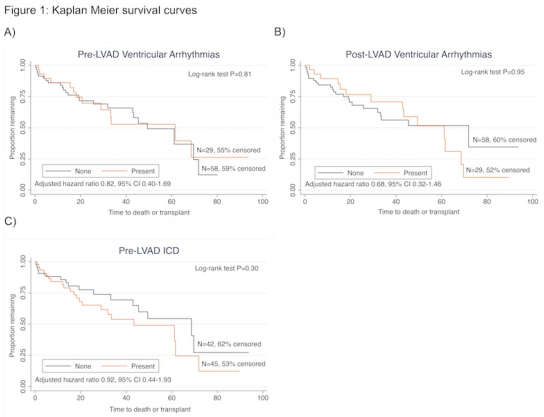


Figure 1: Kaplan Meier Survival Curves

P361

The efficiency of stem cord cells transplantation in patients with heart failure and ischemic cardiomyopathy: the emphasis on biomarkers levels

D Dina Shorikova[1]; E Shorikov[1]; A Gabrielan[2]
[1]Bucovinian State Medical University, Chernivtsy, Ukraine; *[2]National Institute of Surgery and Transplantology n. a. O. O. Shalimov, Kyiv, Ukraine*

The use of the stem cord cells may be considered as one of the perspective methods of the treatment of heart failure (HF), but we must learn the cardiac biomarkers response after this intervention.
We have learnt 86 patients with chronic HF which was developed on the basis of ischemic cardiopathy (IC) and systolic dysfunction (ejection fraction < 40,0%), which were included in the waitlist of heart transplantation. The patients treated by conservative therapy, the bypass interventions were used and transplantation of cord blood stem cell was administered to all. We have set the levels of NTproBNP,

human vascular endothelial growth factor (VEGF) ?? soluble platelet endothelial adhesion molecule-1 (sPECAM-1) in patients.

Risk factors in "good responders" and "b

Factors	"good responders"	"bad responders"	Results
Arterial hypertension	24,0%	58,0%	OR = 0,23[0,09-0,59]
Diabetes mellitus	35,0%	13,0%	OR = 3,51[1,21-10,1]
Total cholesterol	5,13±1,11	5,86±1,04	p = 0,0026
LDL-cholesterol	2,76±0,51	3,01±0,55	p = 0,036
Body mass index	29,3±2,76	29,6±3,11	p = 0,64

Results: The median of proBNP concentration in group HF before the stem cells transplantation was 499,0 (178,2 - 1404,0) p?g/ml. Six month after transplantation was set the decrease of the of proBNP: the median was 241,5 (193,0 - 892,0) pcg/ml (? < 0,05). Inverse dependence was set for the changes of biomarkers as sPECAM-1 ?? VEGF-165. The gain of sPECAM-1 after transplantation was unreliable (p>0,05) and equal to 18,8% - from 71,86 ng/ml (44,36 - 105,06) to 85,96 ng/ml (49,08 - 123,44). The VEGF increment was similar to sPECAM-1 and matched to 19,9%: from the 46,2 ng/ml (8,7-67,1) to 55,4 ng/ml (25,3-72,2) (p>0,05). However, the results of biomarkers' levels changes showed widespread sample range; using K-mean clustering we specified two groups of patients': "good responders" and "bad responders". Analysis of the influence of the occurrence of cardiovascular risk factors in both groups proved that the presence of arterial hypertension, higher levels of total cholesterol and LDL-cholesterol was associated with group of "good responders", but the group of "bad responders" has the greater rate of diabetes mellitus of type 2 (table).
Conclusion: The stem cells transplantation in six months resulted of reliable decrease of proBNP level and unreliable increase of VEGF and sPECAM-1 in HF and IC patients. The response of biomarkers' changes in patients after stem cells transplantation reliably associated with the concomitant arterial hypertension, diabetes mellitus and dyslipidemia.

P362

Influence of the type of circulatory/ventricular assistance in the primary graft failure and heart transplantation mortality

R Raquel Lopez Vilella[1]; I Sanchez Lazaro[1]; MP Fuset Cabanes[2]; A Pajares Moncho[3]; L Donate Bertolin[4]; R Gimeno Costa[2]; I Moreno Puigdollers[3]; I Zarragoikoetxea Jauregui[3]; L Martinez Dolz[1]; A Castellanos Ortega[2]; R Vicente Guillen[3]; S Torregrosa Puerta[4]; L Almenar Bonet[1]
[1]Hospital Universitario y Politécnico La Fe, Heart Failure and Transplant Unit. Cardiology Department, Valencia, Spain; *[2]Hospital Universitario y Politécnico La Fe, Intensive care unit, Valencia, Spain*; *[3]Hospital Universitario y Politécnico La Fe, Anesthesiology Department, Valencia, Spain*; *[4]Hospital Universitario y Politécnico La Fe, Cardiovascular Surgery Department, Valencia, Spain*

Background and Objective: In recent years, the percentage of heart transplantation (HT) with short / medium-term assistance devices has increased. This study aims at analyzing primary graft failure and hospital mortality according to the type and duration of care.
Methods: From January 2013 to December 2017 all patients undergoing urgent HT with circulatory / ventricular assistance were retrospectively and consecutively recruited. Combined transplants, retransplantations and pediatric transplants were excluded. The sample was divided in 10 groups (table 1).
Results: A total of 53 patients were recruited, 79% men, average age 49 ± 13 years. 26 patients (51%) had mechanical ventilation at the time of the HT. Primary graft failure occurred in 20 patients (38.5%), whilst it was more frequent in patients assisted with ECMO (8 patients in group 1 (45%) and 7 in group 2 (54%), p 0.5). 14 deads (27%) were registered, whereas a higher mortality was observed in the group assisted with ECMO (6 patients in group 1 (34%) and 4 in group 2 (31%), p 0.6). Mortality was 12.5% in the group of non-urgent Levitronix.
Conclusions: Despite not showing statistical significance due to the low number of patients in some subgroups, hospital mortality was high in HT patients with circulatory assistance. A trend towards a higher incidence of primary graft failure and mortality in patients assisted with ECMO was observed. The direct implantation of a centrifugal pump as a bridge to urgent transplantation could identify a subgroup with a better prognosis.

Group	n (%)	Description	PGF (%)	HM (%)
Group 1	18 (34%)	ECMO with mechanical ventilation	45 %	34%
Group 2	14 (26.2%)	ECMO without mechanical ventilation	54%	31%
Group 3	1 (1.9%)	ECMO and, afterwards, Levitronix HT with both	0	0
Group 4	2 (3.8%)	ECMO and, afterwards, Levitronix HT with Levitronix	0	0
Group 5	7 (13.2%)	Non-urgent left Levitronix	33%	17%
Group 6	1 (1.9%)	Non-urgent right Levitronix	0	0
Group 7	1 (1.9%)	Non-urgent biventricular Levitronix	0	0
Group 8	1 (1.9%)	ECMO y Levitronix, HT with both	100%	100%
Group 9	3 (5.7%)	ECMO y Levitronix, HT with Levitronix	0	0
Group 10	5 (9.4%)	Urgent Levitronix	35%	20%

ECMO: Extracorporeal membrane oxygenation; HM: Hospital mortality; HT: Heart transplantation; PGF: Primary graft failure

P363

The influence of the level of anxiety and depression and type a personality on adherence in outpatients with chronic heart failure

SU Volkova[1]; EV Panteeva[1]
[1]Tyumen State Medical University, Tyumen, Russian Federation

Aim: to identify the level of anxiety and depression, the prevalence of personality type D (distressing) in ambulatory patients with chronic heart failure (CHF)., as well as their impact on patient adherence to prescribed therapy
Material and Methods: The study included 98 people, observed on the basis of MMAU "city polyclinic ?4" with CVD and concomitant CHF, of which 24.6% men and 75.4% women , mean age 71 ± 2.1 years. All patients initial screening, including hospital scale of anxiety and depression (HADS), the test Moriscos green to determine adherence to treatment, a test for detecting psycho (DS-14) questionnaire for measuring quality of life (SF-36). Statistical processing of research results, preparation of registers for long-term dynamic observation was carried out using the software package Microsoft Office Excel 2007.
Results: Basically, the group was represented by patients with 1-stage CHF - 78%, CHF 2A stage in 22% of subjects. The main reason for the development of CHF was a combination of CHD and hypertension - 71%, only hypertension was found in 29%. According to the questionnaire HADS subclinical anxiety was diagnosed in 25% of the observed, clinical anxiety is diagnosed in 16.5% and mainly among women (82,4% of the subgroup). Subclinical depression was diagnosed in 23.5% of patients; the clinical depression was 14.1%, also mainly women (75% of the subgroup). Psycho D was found in 17 patients (22,07%), of which 76.5% of women. Assessing adherence to therapy may be noted that in our patients is mainly observed with high - 88,2% and the average at 11.7%. Moreover, among patients with identified psycho D - high commitment to treatment and medical appointments indicated 70% of patients, 30%- medium. Among patients with an average adherence to treatment 60% had abnormalities in the HADS test, while among patients with high adherence to therapy was 55%, while the level of anxiety and depression in these groups differed.
Conclusions: Based on the results obtained, it is advisable to study the influence of the level of anxiety and depression, as well as behavioral type of the individual (psycho) on the course of CHF, and to determine the individual approach to the treatment and correction of psychological features to enhance compliance in patients with CHF, depending on individual psychological characteristics

P364

Changing of some markers of inflammation and remodeling in post-infarction patients with chronic heart failure after ubidecarenone treatment

I A Leonova[1]; S Boldueva[1]; G Kuharchik[2]; L Sichinava[1]; L Gaykovaya[1]
[1]North-Western Sate Medical University named I.I. Mechnikov, St-Petersburg, Russian Federation; *[2]Almazov National Medical Research Centre, Saint-Petersburg, Russian Federation*

Objective: to evaluate the effect of ubidecharenone on the processes of inflammation in the myocardium and remodeling of the left ventricle (LV) in patients with chronic heart failure (CHF) after a previous myocardial infarction (MI).
Materials and Methods: 108 post-infarction patients with II-III functional class CHF were included in the study. Patients were randomized into 2 groups: 1 group - patients who received standard therapy and ubdecarenone 30 mg/TID within 3 months; 2 group - received only standard therapy. All patients were initially and after 3 months determined the level of bio-markers: NT-proBNP, hs-CRP, galectin-3, ST-2.

Results: the level of NT-proBNP after 3 months significantly decreased in both groups: in the 1st group from 490.70 (250.50, 752.90) pg/ml to 134.55 (80.82, 202.10) pg/ml ($p < 0.05$) and in the 2 group from 701.25 (271.40, 1385.50) pg/ml to 230.80 (178.90, 443.40) pg/ml ($p < 0$, 05). In spite of the initial values of NT-proBNP concentrations in groups 1 and 2 did not differ, after 3 months it were significantly lower in group 1 than in group 2 (p?0.05). After 3 months both groups showed a decrease in the content of hs-CRP compared to the baseline: in patients from group 1, 3.4 (1.8, 6.7) mg/l to 1.5 (0.8, 3.0 ($p < 0.05$) and in patients of the 2nd group from 3.85 (2.15, 8.70) mg/l to 1.35 (0.725, 3.4) mg/l ($p < 0$, 05). It should be noted that in some patients the values of hs-CRP were kept above 3 mg /l, which indicates that they still have a high risk of cardiovascular accidents (in group 1 -23.5% and in group 2 -28.3%). The content of galectin-3 in both groups was not initially different, it was 19.22 (10.88, 43.50) ng/ml in the 1st group and 23.31 (14.77, 31.56) ng/ml in the 2nd group (p?0.05). The results of a pairwise comparison of the content of galectin-3 in each of the groups showed that only in group 1 there was a decrease in the content of galectin-3 after 3 months compared to the baseline data (16.76 (9.92,34.50) ng/ml vs 19 , 22 (10.88, 43.50) ng/ml). After 3 months the level of galectin-3 exceeded 17.8 ng/ml in 1 group in 49% of patients (6% more than initially), and in the 2 group - in 60.4% of patients (11% more than initially). After 3 months of treatment, the content of ST-2 in patients of group 1 decreased from 75.11 (63.36, 100.43) ng/ml to 54.02 (48.84, 86.79) ng/ml ($p < 0$, 05), and in the 2 group the ST-2 content remained unchanged, reaching initially 71.42 (49.29, 98.90) ng/ml and after 3 months - 75.24 (51.74, 105.73) ng/ml (p?0.05).

Conclusion: The administration of ubedecarenone in addition to the standard treatment of post-infarction patients with chronic heart failure leads to a decrease in the activity of the inflammatory process and fibrosis in the myocardium.

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What do patients think about their chronic heart failure pharmacotherapy?

R Radek Pelouch[1]
[1]*University Hospital Hradec Kralove, Department of Cardiovascular Medicine I, Hradec Kralove, Czech Republic*

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Introduction: Although pharmacotherapy of chronic heart failure (CHF) is well established on the basis of Evidence based medicine, heart failure decompensation (HFD) rate still remains high. In accordance with literature we have proved in our previous study that adherence to CHF therapy is a real problem and significant cause of HFD. Unfortunately reasons of patient's noncompliance are mostly unclear.

Purpose: The aim of the study is to analyze CHF patient's opinions on their pharmacotherapy and to study factors influencing drug adherence

Methods: 81 stable CHF patients (mean age 64 ± 12.0 years, 67% of male, median NYHA II) were prospectively enrolled to the study examining their compliance to pharmacotherapy. Serum levels of prescribed drugs were used as an indicator of medication adherence (median of assessed drugs 4). As a part of study protocol patients filled in a questionnaire related to their drugs use habits and their opinions and feelings regarding to pharmacotherapy.

Results: Average number of used medication has been 8 drugs. 56.8% of patients knew correct number of used drugs. 46.9% were able to name complete medication, 19.8% didn't know any drug name. 92.6% were confident about flawless medication use. Questioned about skipping dose per week, 80.3% of patients denied omission of any daily dose any time, 12.3% estimated one dose skip per week, 7.4% two doses skip. More frequently they forgot midday or evening doses, comparing the morning dose (8.6% and 8.6 % to 2.5%).

Regarding side effects (SE) of the medication, 46.9% of patients denied any of them and only 1.2% had frequent SE. 27.2% suffered from occasional and 1.2% from significant lack of appetite. Only 3.7% declared influence of SE to their drug taking. On the contrary, 87.7% denied any influence of drug's size and shape.

Personality of phycian prescribing the drug was important for 75.3% of patients.

76.5% were satisfied with quality of their life. Using scale 0-100% they evaluated their health status on the average value 62.5 ± 18.64%. 19.8% of patients expected better quality of life without taking any medication. On the contrary, 98.8% considered using drugs as very important for them.

As described above, 92.6% of patients said they had used medication completely well and 80.3% of them denied omission of any daily dose any time. Actually, this is in contradiction with results of their serum drug levels - all of evaluated drugs were detected in the sera of 75.4%, one of them was missing in the sera of 12.3% and more than one in 11.1%. Finally, none of evaluated drugs was found in the sera of 1.2%.

Conclusions: Almost everybody consider regular use of medication as very important. Nevertheless, using an objective method, we demonstrated lower drug adherence than patients supposed. Neither side effects nor tablets size/shape affect significantly regular drugs use. Most of our stable chronic heart failure patients are satisfied with quality of their life.

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Effect of catheter denervation of renal arteries on intracardiac hemodynamics and quality of life in patients with chronic heart failure

A Kurlianskaya[1]; T Tatyana Troyanova-Shchutskaia[1]; D Goncharik[1]; T Asmalouskaya[1]; T Denisevich[1]
[1]*Republican Scientific and Practical Centre of Cardiology, Minsk, Belarus*

Background: Catheter denervation of renal arteries (CDRA) is an innovative method of treatment in patients with chronic heart failure (CHF), which allows controlling the effects of the sympathetic nervous system by the use of high-frequency current destroying sympathetic nerves in the adventitia of the renal arteries.

Parametr	At baseline	In 6 months after CDRA	In 12 months after CDRA	p 0-6	p 0-12
End diastolic dimension (EDD), mm	70 (64; 74)	68 (65; 77)	69 (66; 72)	0.925	0.289
End systolic dimension (ESD), mm	58 (52; 62)	55 (51; 67)	56 (51; 62)	0.547	0.535
End diastolic volume (EDV), ml	238 (205; 318)	249 (185; 292)	209 (162; 272)	0.050	0.035
End systolic volume (ESV), mm	160 (137; 224)	155 (117; 210)	126 (97; 193)	0.085	0.149
Left ventricular ejection fraction (LVEF)	31 (28; 34)	35 (29; 40)	39 (33; 41)	0.206	0.056
Mitral regurgitation (MR)	2 (2;3)	2 (2;2;)	2 (2;2)	0.753	0.638

Purpose: to investigate the effect of CDRA on intracardiac dynamics and quality of life (QOL) in patients with CHF for 12 months of follow-up.

Methods. The study included 25 patients with CHF III functional class (FC) NYHA, ejection fraction < 35%, QRS < 130ms. All patients underwent transthoracic echocardiography before and in 6 and 12 months after CDRA. The quality of life (QOL) was assessed using the Minnesota Living With Heart Failure Questionnaire.

Results: Changes in the parameters of intracardiac hemodynamics in patients before, 6 and 12 months after CDRA are demonstrated in table.

An improvement of echocardiographic parameters after the CDRA was accompanied by an improvement in the clinical status of patients: a decrease in dyspnea, an increase in exercise tolerance, an increase in the level of QOL. Initially median values of QOL were 57 (44; 61) points, in 6 months after CDRA - 47 (32; 55) points, in 12 months - 42 (24, 44).

Conclusions: The obtained data allows to provide the evidence of the positive effect of CDRA on the parameters of intracardiac hemodynamics. LVEF significantly increased, EDV significantly decreased in 12 months after CDRA. The tendency of decrease in ESV was also noted. FC of CHF decreased in 75% of patients, that was accompanied by improvement of QOL patients.

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Salt consumption and long term prognosis of coronary patients with heart failure; is it equally aggravating for all? Results from Hellenic Heart Failure study.

C Christina Chrysohoou[1]; M Kouvari[2]; P Aggelopoulos[2]; G Metallinos[1]; E Tsiamis[1]; C Pitsavos[1]; D Tousoulis[1]
[1]*University of Athens, Athens, Greece*; [2]*Harokopio University, Nutrition Science - Dietetics, Athens, Greece*

Background/Introduction: Dietary salt restriction is a unanimously propagated recommendation in the prevention and management of heart failure. Nonetheless, considering salt as a flavor enhancer triggering appetite, its strict restriction in the context of anorexia- and cachexia- associated disease, raises many doubts.

Purpose: the role of discretionary and hidden salt intake on 10 year prognosis of Acute Coronary Syndrome (ACS) patients was investigated.

Methods: from May 2006 to March 2009, 1,000 consecutive patients who were hospitalized at a Cardiologic Clinic in Athens with ACS diagnosis were enrolled in the study. In 2016, 10y follow-up (2006-2016) was performed in 745 participants. A validated food frequency questionnaire was used, to assess, among other dietary habits, discretionary salt intake (i.e. addition in cooking or in table) as well as consumption of major hidden-salt food sources (i.e. processed / fried meat products, canned food, feta cheese, yellow-cheese, salted nuts, bread and other bakery products).
Results: 10y fatal/non fatal ACS events were 60% in heart failure patients who reported use of salt shaker in table and 47% in patients who avoided this habit (p = 0.03). Multivariate logistic regression analysis highlighted that patients who reported use of salt shaker in table were twice as likely to develop a new cardiac episode within the decade (OR = 2.19 95% CI (1.12, 4.3), p = 0.02). Salt addition during cooking did not reach significance. Principal component analysis was performed for major hidden-salt-sources. Two out of four patterns identified, reached significance in a multivariate analysis; a pattern characterized by processed/fried meat products, fast food and salty yellow cheese was associated with unfavorable ACS prognosis (OR = 1.4 95%CI (0.97, 2.04)) whilst a pattern with healthier food choices (i.e. nuts, canned fish/vegetables, olives and feta cheese) was inversely associated with 10 year recurrent events (OR = 0.55 95%CI (0.37, 0.82)). A significant interaction was observed between age and addition of salt in table as well as the aforementioned hidden salt patterns (all ps for interaction>0.05). Stratified analysis revealed that use of salt shaker retained its significance only in younger patients (OR = 2.80 95% CI (1.18, 5.3), p = 0.02). Additionally, the potential protective effect of healthy, yet rich in salt, food choices reached significance in patients >65 years old (OR = 0.27 95% CI (0.10, 0.71), p = 0.008). Conclusion: for a more efficient treatment approach priorities should be set as regards salt restriction. Recommendations regarding salt consumption should combine the downsides attributed to excessive salt intake with the beneficial role of this flavor enhancer in appetite; with the focus oriented towards patients in advanced age threatened by a high catabolic state, which determines their prognosis.

P368

Ambulatory intravenous inotropic support and or levosimendan in failing pediatric and congenital heart disease: safety, survival, improvement or transplantation

S C Apostolopoulou[1]; GA Vagenakis[1]; A Tsoutsinos[1]; F Kakava[1]; S Rammos[1]
[1]*Onassis Cardiac Surgery Center, Athens, Greece*

Background/Introduction: End-stage heart failure (HF) frequently needs continuous inotropic support in hospital and has high morbidity and mortality. It is often treated with mechanical circulatory support or transplantation, both options associated with significant adverse events and not readily available in many countries.
Purpose: To review our experience using continuous ambulatory inotropes (AI) and/or periodic levosimendan (LS) infusions in pediatric end-stage HF patients in a tertiary care center
Methods: This is a retrospective analysis of our end-stage HF population treated with AI and LS focusing on outcome, efficacy, safety and follow up including deaths, stabilization and recovery.
Results: The study included 27 patients aged 9.3 ± 7.4 (0.1-26.1) years with severe HF (6 myocarditis, 13 dilated cardiomyopathy, 2 restrictive cardiomyopathy, 6 repaired congenital heart disease) needing continuous inotropic support. Overall, 21 patients received dobutamine and milrinone AI through a permanent central catheter for 1.1 ± 0.9 (0.3-3.7) years. Additionally, 14 AI patients and the remaining 6 study patients received periodic LS infusions for 1.4 ± 1.0 (0.1-4.2) years. Inotropes were used for 1.4-0.4 years as bridge to recovery in 6 improved myocarditis patients, who remained stable after discontinuation on follow-up. AI and or LS infusions were used as bridge to transplantation in 6 patients with only 3 survivors, in 2 of which inotropes preoperatively reversed severe combined pre and postcapillary pulmonary hypertension allowing successful heart only transplantation. Finally, inotropes were used as mainstay therapy in 15 patients for 0.3-4.2 years, mostly with good quality of life and family dynamics. Four patients died of worsening HF after 0.8-2.1 years of therapy. During 3.6 ± 5.3 (0.3-21.3) years of follow-up, we observed 4 central line infections treated with antibiotics and 4 catheter reinsertions due to dislodgement. Parenteral inotropes were also discontinued in 1 cardiomyopathy patient who received a left ventricular assist device and is still waiting for transplant 2.5 years later.
Conclusions: AI and/or LS infusions in HF is safe and beneficial for long periods even in small infants and children, allowing stabilization, discharge from hospital and cost reduction, good quality of life. It may provide precious time for heart transplantation or myocardial remodeling, improvement and possible discontinuation even after long periods of support.

P369

The use of extracorporeal photopheresis in the treatment of acute cardiac allograft rejection

T Timea Teszak[1]; A Assabiny[1]; A Kiraly[1]; Z Tarjanyi[1]; N Parazs[1]; ZS Szakal-Toth[1]; I Hartyanszky[1]; Z Szabolcs[1]; Z Farkas[2]; M Reti[2]; B Sax[1]; B Merkely[1]
[1]*Semmelweis University Heart and Vascular Center, Budapest, Hungary*; [2]*Szent Laszlo Hospital, Budapest, Hungary*

Background: Despite novel immunosuppressive agents, cardiac allograft rejection is still a major etiological factor in premature mortality after heart transplantation. Furthermore, these medications increase infectious disease mortality, too. Extracorporeal photopheresis (ECP) is an immunomodulatory therapy which was first used in the treatment of cutaneous T-cell lymphoma. Its use has now expanded to include also the treatment of cardiac allograft rejection; however, there is still no clear evidence on its exact indication.
Purpose: We aimed to evaluate the effect and efficacy of ECP in adult Hungarian heart transplant recipients.
Methods: From September 2013 to September 2017 we studied 9 patients treated with ECP who underwent heart transplantation for end-stage heart failure in our University. We characterized the duration and the side effects of ECP, the grade of rejection in transvenous endomyocardial biopsies (EMB) and the left ventricular ejection fraction (LVEF) measured by transthoracic echocardiography both before and after ECP treatment period. Data values were characterized by either mean ± standard deviation or median(min-max).
Results: The 9 patients underwent 24(2-38) ECP treatments beside standard immunosuppressive therapy. ECP treatment was initiated 186(15-3523) days after cardiac transplantation. Whereas before the ECP treatment the majority of patients (89%) were diagnosed with grade 2 acute cellular rejection in EMB according to the classification published by the International Society for Heart and Lung Transplantation, there was no rejection exceeding grade 1 acute cellular rejection post-ECP treatment. Furthermore, the average grade of rejection improved with approximately one class (grade 1.22 ± 0.67 vs. grade 0.43 ± 0.53; p = 0.038) after the ECP treatment period. LVEF discreetly increased from a baseline LVEF of 54 ± 8% to 61 ± 6% (p = 0.181) at follow-up after ECP, although it should be noted that in 6 out of 9 patients ECP treatment was initiated before any decrease in LVEF. There were no major side effects during the 208 ECP treatments. Two deaths occurred during the ECP treatment period which resulted from progression of cardiac allograft rejection; however, one of the patients refused the continuation of ECP after the second treatment.
Conclusion: We observed that ECP in cardiac transplantation is efficient: it appears to be a significant advance in reducing the severity of rejection episodes. Furthermore, it is safe and well tolerated without important side effects. Despite its promising favourable effects, further studies which focus on both the exact mechanisms of action and the standard treatment protocol are required for the maximization of its therapeutic benefit.

P370

Comprehensive heart failure self-management programme: evaluation of a pilot group intervention

I Caramlau[1]; J Gallagher[1]; B Hannon[2]; L O'connor[3]; T Mannion[3]; E Kennedy[4]; L Masterson[4]; L O'neill[5]; L Peotta[1]; S Clarke[1]; N Pender[1]; B Mcadam[6]
[1]*Beaumont Hospital, Psychology, Dublin, Ireland*; [2]*Beaumont Hospital, Cardiac Rehabilitation, Dublin, Ireland*; [3]*Beaumont Hospital, Supportive Heart Unit, Dublin, Ireland*; [4]*Beaumont Hospital, Nutrition and Dietetics, Dublin, Ireland*; [5]*Beaumont Hospital, Pharmacy, Dublin, Ireland*; [6]*Beaumont Hospital, Cardiology, Dublin, Ireland*

Background: Heart failure (HF) is a chronic, life-limiting condition affecting approximately 2% of people in Ireland, and is associated with frequent hospital admissions and significantly reduced quality of life. To self-manage their condition effectively, patients with HF need to engage in multiple self-care behaviours (e.g. poly-pharmacy, monitoring and responding to symptoms, maintaining a low salt diet and managing fluid intake), as well as managing the emotional impact of living with a chronic condition. Despite its importance, poor self-management remains a challenge in the treatment of HF.
Purpose: This study examined the feasibility of a comprehensive HF self-management group intervention underpinned by cognitive behavioural principles. The core components of the programme included modules on understanding HF, symptom monitoring, medication adherence, healthy eating, physical exercise, managing fatigue, managing breathlessness, managing difficult emotions, and strategies to compensate for HF-associated cognitive difficulties.
Methods: Participants were predominantly in NYHA class III, diagnosed with ischaemic cardiomyopathy and HF-preserved, had = 2 co-morbidities, and were attending a specialist HF service for >3 months. Patients were invited to participate

in a 6-week outpatient HF self-management group programme. In addition to a consultant cardiologist, this multi-disciplinary programme comprised of input from psychologists, a pharmacist, a dietician, and two Clinical Nurse Specialists (HF & Cardiac Rehabilitation). Using a pre-post design, the impact of this HF self-management intervention on patient reported outcomes was evaluated using the following measures: the Self-Care of Heart Failure Index (SCHIFI), the Medication Adherence Report Scale (MARS), and the HeartQoL.
Results: 50 eligible patients with HF were invited to participate in a screening assessment, resulting in 28 patients being referred to the HF self-management programme. Ultimately, 26 patients [88% male; mean age= 68.8 years [SD = 7.5)] attended the programme, with an overall attendance rate of 96%. Comparing Time 1 and Time 2, paired-sample T-tests showed a significant improvement in all 3 subscales of HF self-care behaviours: self-care maintenance t(25)=-3.4, p<.05, self-care management, t(25)=-2.6, p<.05, and self-care confidence, t(25)=-5.9, p<.05. An increase in medication adherence was also observed, reflected by a decrease in MARS scores [t(25) = 1.9, p<.05]. Health-related Quality of life (HeartQoL) was not significantly improved [t(25)=-2.2, p=.65]. High levels of patient satisfaction with the self-management programme were also reported.
Conclusions: A comprehensive group-based HF self-management intervention was both feasible and acceptable to patients, and improved both HF self management and medication adherence. A robust and adequately powered randomized controlled trial is warranted to evaluate the effectiveness of this intervention.

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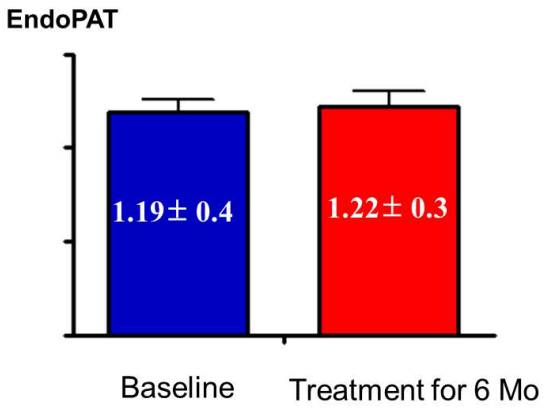
Effect of vitamin D on endothelial function in Patients with chronic heart failure

S J Ha[1]; YY Choi[2]; YM Woo[1]; JY Jang[3]; JS Woo[2]
[1]GangNeung Asan Hospital, Cardiology, GangNeung, Korea Republic of; *[2]Kyunghee Medical Center, Seoul, Korea Republic of*; *[3]Gyeongsang National University Changwon Hospital, cardiology, Changwon, Korea Republic of*

Background: In patients with heart failure (HF), low levels of 25-hydroxyvitamin D (25OHD) are common and are associated with increased mortality risk.
OBJECTIVES: The VIVID-HF (Ventricular and Vascular function of Vitamin D in Patient with Heart Failure) study was an investigator-initiated, multicenter, prospective, randomized, placebo-controlled trial to establish safety and efficacy of oral vitamin D3 (cholecalciferol) supplementation in stable HF patients.
METHODS: Seventy three HF patients with 25OHD level < 75 nmol/L (30 ng/mL) were randomized to receive 4000 IU vitamin D daily or matching placebo for 6 months. The primary endpoint was the change of endothelial function assessed by EndoPAT between baseline and 6 months. Secondary endpoints included the change in echocardiographic parameters and differences of quality of life (6 minute walk test and New York Heart Association functional status: NYHA status) at 6 month.
RESULTS: During study periods, there was no adverse event in both groups. Vitamin D supplementation did not improve endothelial dysfunction (EndoPAT: baseline, 1.19 ± 0.4 vs 6 month later, 1.22 ± 0.3, p = 0.65). In addition, 6-minute walking distance (baseline, 292.9 ± 120.35 vs 6 month later, 283.7 ± 116.84 m, p= 0.125), and NYHA status also did not improve. In this period, there was no significant change in echocardiographic parameters.



Endo PAT comparison

Conclusions: A daily vitamin D dose of 4000 IU would be safe but did not improve endothelial function, echocardiographic parameters, 6-minute walking distance, and NYHA status.

P372
New onset diabetes mellitus after transplant (NODAT) in heart transplant recipients-incidence, predictors and outcomes

L Lavanya Saiva[1]; N Boyle[1]; S Murphy[1]; C Halley[1]; N Mahon[1]; J O'neill[1]
[1]Mater Misericordiae University Hospital, Heart and Lung Transplant Unit, Dublin, Ireland

Background: The success of solid organ transplantation has been increasing with advances in surgical and pharmacological techniques. With improvements in patients survival increasing attention is focussed on complications that contribute to long term morbidity and mortality post-transplant. NODAT is a common complication of solid organ transplantation. There are limited number of studies in post heart transplant patients. We sought to assess the Incidence, Predictors and Outcomes in patients with NODAT.
Methods and Results: we retrospectively analysed 100 patients transplanted from 2007 to 2017. Patients with Pre-transplant diabetes were excluded from the study. Out of 100 patients, 10% (n = 10) developed NODAT. Median time to develop NODAT was 4.3 ± 2.1 months and majority of patients (90%) developed within 6 months. More than four episodes of rejection requiring treatment were noted in 30 % (n = 3) of patients and 50% (n = 5) had at least one episode of rejection. Graft function was found to be normal in all of our patients and 30% (n = 3) of our patients had mild to moderate coronary allograft vasculopathy. The Infection rate was noted to be higher, affecting 70% (n = 7) of our patients. The Results are summarized in the pic attached.
Conclusion: NODAT is common affecting 10% of our heart transplant population. Careful screening for NODAT is important and also the frequency of screening needs to be increased during the first year of transplant as the incidence of NODAT seems to be higher during the first year after transplantation.

Total number (n=10)	Mean	S.D	Range	Percent	No. of Patients
Sex					
Female	NA	NA	NA	20%	2
Male	NA	NA	NA	80%	8
Age	53.6yrs	15.78yrs	16-69	NA	NA
Age at NODAT	49.3yrs	14.78yrs	15-62	NA	NA
Time to develop NODAT	4.3months	7.14months	1-24months	NA	NA
Indication for transplant					
Ischemic aetiology	NA	NA	NA	30%	3
Dilated Cardiomyopathy	NA	NA	NA	50%	5
Valvular Heart Disease	NA	NA	NA	10%	1
Congenital Heart Disease	NA	NA	NA	10%	1
Type Of NODAT					
IDDM	NA	NA	NA	90%	9
NIDDM	NA	NA	NA	10%	1
Hba1c	50.25mmol	9.6mmol	36-92.5mmol	NA	NA
Creatinine	132.5umol	44.4Bumol	47.5-195umol	NA	NA
BMI	25.8	3.28	21.5-30	NA	NA
Immunosuppression					
Tacrolimus	NA	NA	NA	80%	8
Cyclosporine	NA	NA	NA	20%	2
Prednisolone	NA	NA	NA	100%	10
MMF	NA	NA	NA	100%	10
Infections					
Respiratory	NA	NA	NA	50%	5
Urinary Tract	NA	NA	NA	10%	1
Cytomegalovirus	NA	NA	NA	10%	1

(IDDM-Insulin dependent diabetes mellitus, NIDDM-Non insulin dependent diabetes mellitus, BMI-Body mass index, HBA1C-Haemoglobin A1C, MMF-Mycophenolate Mofetil)

P373
Endothelial function and skin temperature during psychological stress in heart and respiratory failure patients

E Elisa Perez Cabanas[1]; V Pelaez-Hernandez[1]; SC Torres-Montiel[1]; FA Figueroa-Herrera[1]; M Rivera-Rodriguez[1]; A Orea-Tejeda[1]; D Gonzalez-Islas[1]; CL Olivo-Villalobos[1]; CA Chavez- Mendez[1]; GV Davila-Said[1]
[1]National Institute of Repiratory Diseases, Heart Failure and Respiratory Distress Clinic, Ciudad de Mexico, Mexico

On behalf of: Heart Failure and Respiratory Distress Clinic

Background: Patients with cardiac and respiratory pathologies usually present endothelial dysfunction, which is responsible of the alterations in skin temperature, during physical and psychological stressors. The changes in thermoregulation response can show the endothelial function state and the emotional state of the patients when they are exposed to psychological stress.
Purpose: To describe the bilateral skin temperature response during the presentation of psychological stressor, between mild and severe endothelial dysfunction in heart and respiratory failure patients.
Method: A cross-sectional study was carried out in 40 patients with heart failure and chronic respiratory disease diagnostic (COPD, pulmonary embolism or Obstructive Sleep Apnea Syndrome). We evaluated the endothelial function with the Maximum Amplitude Time/ Total Time of the pulse wave (MAT/TT index) in five different times (baseline, at 30, 60, 90, 120 minutes after an ischemia period) by a photoplethysmography test. The patients were divided into two groups based on endothelial

dysfunction: Mild group (MG), patients who reduced the MAT/TT index in any of the five moments after ischemia; severe group (SG), patients who not reduced the MAT/TT index in any of the five moments after ischemia. Skin temperature recording was made with a temperature sensor placed on the third phalanx of the little finger of Left (LH) and Right Hand (RH), during a psychophysiological stress profile with three phases of five minutes each (baseline, arithmetic stressor, recovery). For this profile was used a biofeedback equipment. Differences between groups were determined with a Mann-Whitney U test in the SPSS 21 program for windows.

Results: Despite the fact that patients with severe endothelial dysfunction (n = 25; M. age = 69.72 ± 12.61; 52% women) show low skin temperature compared to patients with mild dysfunction (n = 15; M. age = 67.53 ± 15.54; 60% women), during the three phases of psychophysiological stress profile; baseline (LH: SG-M = 31.17 ± 3.64 |MG-M = 32.05 ± 2.87, RH: SG-M = 31.81 ± 3.77 |MG-M = 32.61 ± 2.53); stressor (LH: SG-M = 31.30 ± 3.60 |MG-M = 32.16 ± 2.76, RH: SG-M = 32.17 ± 3.76 |MG-M = 32.95 ± 2.29) and recovery (LH: SG-M = 31.68 ± 3.60 |MG-M = 32.52 ± 2.47, RH: SG-M = 32.60 ± 3.76 |MG-M = 33.41 ± 1.86). Differences in sex (p=.62); M. age (p=.76); LH temperature (p=.57); RH temperature (p=.79) during baseline; LH temperature (p=.50); RH temperature (p=.66) during stressor; LH temperature (p=.44); RH temperature (p=.62) during recovery, were not statistically significant.

Conclusion: The results indicate that the endothelial dysfunction impacts on thermoregulation. However, the endothelial dysfunction severity was not completely reflected in the skin temperature response during psychological stress in heart and respiratory failure patients. So, we suggest continuing this research line and increase the sample size.

P374

Sacubitril-valsartan: does the functional class improve objectively estimated by cardiopulmonary exercise testing?

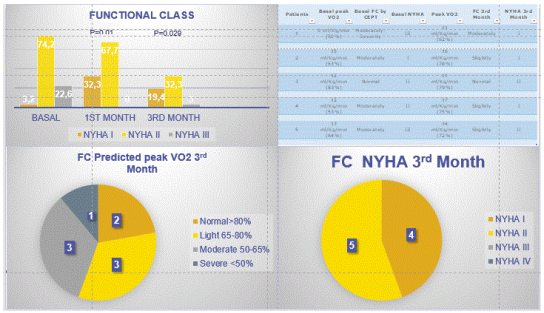
C Cristina Beltran Herrera[1]; V Suberviola[1]; S Briongos[1]; M Sarrion[1]; A Sanchez[1]; C Cortina[1]; ML Giganto[1]; E Gomez[1]; R Munoz[1]
[1]*University Hospital Infanta Leonor, Madrid, Spain*

Introduction: The new drug Sacubitril-Valsartan (ARNI) has demonstrated to improve the functional class (FC) measured by NYHA in patients (pts) with heart failure (HF) and ventricular dysfunction. The most objective method of assessing FC in HF is the peak oxygen uptake (Vo2) in a cardiopulmonary exercise testing (CPET). Our objective is to assess whether the use of ARNI in pts with HF also improves the FC measured by peakVo2.

Methods: We analyzed 31 pts with HF and left ventricular dysfunction from October 2016 to March 2017 which had been treated with Sacubitril-Valsartan evaluated in a cardiology day clinic. The FC was evaluated by NYHA before treatment, on the first and third month. CEPT was performed on the third month in 9 pts, and then compared with a baseline test before ARNI available in 5 pts. According to the % peak of Vo2 reached predicted by Wasseman values it was estimated that, the FC was: normal FC> 80% predicted, FC slightly reduced 60-79%, FC moderately reduced 59-50% and FC severely reduced < 50%.

Results: 80% males, 71 ± 10 years, LVEF 27 ± 5%, NTproBNP 3123 ± 2811, 49% ischemic C., 39% idiopathic C. 96.8% pts take beta-blockers, 58.1% MRA. The NYHA FC pretreatment, first and third month after treatment is shown in the graph, there was a significant improvement with the drug. The absolute value of peak vO2 as well as its values predicted at baseline and in the third month are shown in the table and graphs. Except in 1 patient, there was absolute improvement in the peak Vo2 measured in the third month, and in the FC estimated by CEPT. The pte that didn't show improvement maintained a normal capacity before and after treatment. If the FC is compared at third month as estimated by NYHA and Vo2, there are discrepancies, 100% in FC I-II by NYHA and 55% in FC I-II by peak vO2 (graph)

Conclusions: In our real life series, ARNI significantly improves the FC determined by NYHA. If the FC is estimated by peak Vo2, more objective, pts tend to present worse functional class than measured by NYHA. Even so, the absolute values of peak Vo2 and the FC estimated by this parameter improve after 3 months of ARNI. These are preliminary data and further studies are required in this regard but we point out that sacubitril-valsartan is an effective drug in the functional improvement of these pts.



Functional class.VO2 Pre-post Sacubitril

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Efficiency and safety of physical rehabilitation in patients with chronic heart failure III-IV class NYHA candidates for heart transplantation

MA Bortsova[1]; MU Sitnikova[1]; EA Demchenko[2]; TA Lelyavina[1]; OA Babich[2]; VL Galenko[1]; PA Fedotov[1]
[1]*Federal Almazov North-West Medical Research Centre, Heart Failure, Saint-Petersburg, Russian Federation*; [2]*Federal Almazov North-West Medical Research Centre, Saint-Petersburg, Russian Federation*

Purpose: To asses the efficiency of physical rehabilitation in patients with chronic heart failure (CHF) III-IV class NYHA candidates for heart transplantation (HT).

Methods: In pilot study were included 51 men, candidates for heart transplantation, aged 20-65 years old, LVEF = 30% Simpson, ischemic etiology or dilated cardiomyopathy, stabilizated in NYHA class III-IV CHF during = 2 weeks, BP = 90/60 mm Hg, HR = 100 beats per minute, treated with standart therapy of CHF. Patients with sustained ventricular tachycardia, myocardial infarction (MI) and pulmonary embolism (PE) during the previous 3 months, unstable angina pectoris during 1 month and stroke for 6 months were not included. Safety of physical rehabilitation program (PRP) was monitored with continuous cardiomonitoring during training in the presence of a cardiologist and a physiotherapist. Patients were randomized into 2 groups: 1-st - participating in PRP (n = 26), 2-nd (control) - standard therapy of CHF (n = 25). The duration of follow-up was 6 months.

Results: Both groups were comparable in age, background cardiac and concomitant pathology. In both groups, patients received standard CHF therapy: in 1-st group and in 2-nd group: ACEI/ARA - 24 and 23 patients, ß-blockers - 23 and 21 patients, aldosterone antagonists - 24 and 16 patients, loop diuretics - 26 and 25 patients , thiazides - 8 and 4 patients, amiodarone - 14 and 10 patients, respectively. In both groups, a comparable number of patients finish the study: In 1-st group - 18 patients, early completion of 8 patients: 2 deaths, 6 - HT. In 2-nd group - 16 patients, early completion of 7 patients: 3 deaths, 4 - HT. In both groups, there were no statistically significant differences in the number of deaths. In both groups up to 6-th month, there was a comparable number of patients who switched to II NYHA class : 6 in group 1 and 5 in group 2.

In the 1-st group there were not observed life-threatening ventricular arrhythmia during exercising and within 3 hours after. After 6 months in 1-st group PE was not established while in 2-nd group were observed 4 cases, without statistical significance. In group 1, there was a statistically significant decrease in the number of the lower respiratory tract infections (LRTI): bronchitis + pneumonia compared to the 2-nd group: 5 and 18 patients, respectively (p = 0.001).

Conclusions: 1. Participation in an individually designed PRP does not increase mortality and the number of life-threatening ventricular arrhythmias in patients with stabilization of CHF in III-IV NYHA class. 2. Participation in an individually designed PRP does not cause progression of CHF in patients with stabilization of CHF in III-IV NYHA class. 3. Patients participating in an individually PRP have a lower number of LRTI compared with the control group.

P376

Prolonged use of Levitronix - right ventricular assist device (RVAD) in patients with long term left ventricular assist device (LVAD)

A Adnan Yousaf[1]; S Mihiyaddin[1]; M Aldweik[1]; S Ashraf[1]
[1]*Regional Cardiac Centre Morriston Hospital, Swansea, United Kingdom*

Aim : Severe right ventricular failure after implantation of long-term LVAD (LTLVAD) is common and occasionally requires the need for right heart support. The choices for RVAD support are limited mainly by short term devices.
Material and methods: 7 published papers were looked up reviewing data including one with multicentre trial of patients who had LTLVAD and required Centrimag RVAD implantation. There were 423 patients, 73 had Heartmate I, 20 Thoratec PVAD, 43 Jarvik 2000, 12 HeartWare and 275 HeartMate II. Mean age was 38.6 (range13-59) years. 73.9% were male, 21.7% had ICM and 78,3% DCM. 64 had preoperative mechanical ventilation, 83 had IABP and 37% had multiple inotropic support. 36.5% patients underwent early right VAD insertion (<24 hours) 26.1% delayed (>24hours) while 17.24% were moribound patients salvaged with BiVAD Centrimag as a bridge to decision and later on upgraded for a LTLVAD and required continuous support of RVAD Centrimag.
Results: Postoperative mean ventilation time 4.7 days, ICU stay of 12.3 days and hospital stay was 22.8 days. Mean duration of LTLVAD and RVAD support was 212 (range 4-619 days) and 44 (range 6 to 207) days, respectively. Operative mortality was 17.4%., 78.3% patients had their RVAD explanted, 26.1% were bridged to transplant, 8.7% had full myocardial recovery and had LTLVAD explanted. 74 patients are ongoing. There was no incidence of pump failure or thrombosis. The vast majority of patients were mobilised and exercised out of bed while on BIVAD support.
Conclusion: Prolonged use of RVAD Centrimag appears to be safe and effective for recovery or bridge to transplantation in patients with severe right ventricular failure and LTLVAD. Retrospectively it appears BiVAD devices could be used for long term in patients waiting for a transplant beyond 6 months from analysing these papers.

P377

Heart failure with mid-range ejection fraction:the effects of short-term physical training

D Dragan Marinkovic[1]; M Deljanin-Ilic[1]; V Stoickov[1]; B Ilic[1]; I Krstic[1]; S Stojanovic[1]; D Petrovic[1]
[1]*University of Nis, Medical Faculty, Institute of Cardiology Niska Banja, Nis, Serbia*

Heart failure with mid-range ejection fraction (HFmrEF), the "midlle child", as a new entity, in heart failure familly, has limited data regarding exercise tolerance and training, functional capacity and quality of life (QOL). Available data suggest that it constitutes a sizeable proportion(10-20%) of the HF population, has a unique clinical, echocardiographic, haemodynamic, and biomarker profile compared with HFrEF and HFpEF, and carries a poor prognosis.
Aim: To evaluate the effects of short-term physical training on physical exercise, tolerance and level of markers of inflammation, neuro-humoral activation and endothelial function, in patients wit HFmrEF.
Methods: The study involved 33 HF patients (21 males); mean age 60.3 ± 5.7 years, with established ischemic heart disease, mean EF 44,58 ± 5,23%, which fulfill criteria for HFmrEF. All patients were included in three-weeks rehabilitation program in the residential center, based on strictly controlled and individually prescribed physical training. Before and after rehabilitation, all patients were underwent exercise stress test, and from the veins blood samples, biochemical markers of inflammation, atrial natriuretic peptide (ANP), brain natriuretic peptide (BNP) an endothelin (ET) were determined.
Results: At the end of the study the hs-CRP and fibrinogen level were showed a decreasing trend (p = 0.42; p = 0.68 n.s). After cardiovascular rehabilitation a significant reduction in white blood cells count was recorded (p = 0.022). Erythrocyte sedimentation rate after rehabilitation was higher, but not significant. In all pts, the concentration of ANP and BNP was lower after 3 weeks compared to baseline values (p = 0.023; p = 0.019). In contrast, the value of endothelin after rehabilitation was higher than baseline value (p = 0.112), but not significant. At end of this study, significantly higher serum HDL-cholesterol in CHF patients was found (p = 0.001). Exercise tolerance after rehabilitation was improved (55.35 ± 5,23 W vs 74.69 ± 6.13 W; p = 0.047), as well as quality of life assessed by Minnesota Living With Heart Failure Questionnaire (58,69 ± 3,69 vs 38,39 ± 2,24 p = 0.035)
Conclusion: The results of our study showed that, in patients with the midrange LVEF residential short-term training has favourable impact expressed throught decreasing of the level of inflammatory status and neuropeptids. Those positive effects are associated with significant increases of exercise tolerance and improvement of quality of life.

P378

Efficacy and safety of Urapidil and Nitroglycerin injection in acute coronary syndrome patients with acute heart failure and hypertension

J Jing Gao[1]; Q Hua[1]; JY He[1]; YL Wang[1]; J Tan[1]; ZX Fan[1]
[1]*Xuan Wu Hospital, Capital Medical University, department of cardiology, Beijing, China People's Republic of*

Background: Acute heart failure is a complex clinical syndrome responsible for high morbidity and mortality and frequently complicated by concomitant hypertension and acute coronary syndrome. Despite advances in the management of heart failure, the prognosis of these patients remains poor and there is a critical need for new treatment strategies improving the clinical outcomes.
Objective: To compare the efficacy and safety of Urapidil and nitroglycerin in acute coronary syndrome (ACS) patients with acute heart failure(AHF) and hypertension.
Methods: Thirty ACS patients with AHF and hypertension were randomly divided into Urapidil treatment group(n = 14) and nitroglycerin treatment group(n = 16).Patients in Urapidil treatment group were treated with Urapidil (50-300μg/min) and those in Nitroglycerin treatment group were treated with Nitroglycerin (5-20μg/min) for 48-140h according to their blood pressure(SBP 159.44 ± 30.95mmHg vs 146.70 ± 31.63mmHg; DBP 86.64 ± 21.00mmHg vs 82.57 ± 17.09mmHg)and cardiac function.All patients were monitored for blood pressure, heart rate, cardiac function test by echocardiography, NT-proBNP and blood biochemical index including glucose,blood lipid level, liver function, renal function, situation at the time of before treatment, 24h, 48h, 72h, 7d after treatment.
Results: The diameter of left atrium, left ventricular diastolic diameter, EDV and ESV of left ventricle were significantly lower in Urapidil treatment group than in Nitroglycerin treatment group after 48h. (37.3 ± 2.12mm vs 42.8 ± 4.87mm, p = 0.06; 51.11 ± 4.57mm vs 57.90 ± 7.44mm, p = 0.30; 124.22 ± 24.2ml vs 178.56 ± 52.98ml, p = 0.013; 52.67 ± 20.88ml vs 87.67 ± 38.13ml, p = 0.028). No significant differences between two groups in all the other parameters (P>0.05). And no significant difference between two groups in major adverse cardiovascular events on days 7 and 30(P>0.05).
Conclusion: Urapidil is a safe and effective vasculardilator for ACS patients with AHF and hypertension.

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6 minute walk tests performed at home are accurate and reliable

AE Burch[1]; D Scherr[2]; A Rieth[3]; JJ Griffin[4]; N Bianco[5]; T Odeneg[2]; SF Sears[1]
[1]*East Carolina Heart Institute, Psychology , Greenville, United States of America*; [2]*Medical University of Graz, Department of Medicine, Graz, Austria*; [3]*Kerckhoff Heart Center, Department of Cardiology, Bad Nauheim, Germany*; [4]*Cardiovascular Associates, Virginia Beach, United States of America*; [5]*ZOLL Medical, Pittsburgh, United States of America*

Background: Walking is fundamental to independence and cardiovascular well-being, with a 6-minute walk test (6MWT) being one of the common tools to track patients objectively. The purpose of this study was to evaluate the accuracy and reliability of the wearable cardioverter defibrillator (WCD) guided 6MWT performed at home by heart failure patients in comparison to a conventional in clinic test.
Methods: Patients (n = 198) with heart failure and a low ejection fraction prescribed a WCD were randomized to two groups. Group 1 completed a standard 6MWT while wearing the WCD. This 6MWT was performed in clinic under medical direction and the results were recorded by the clinician. Group 2 completed the WCD-guided 6MWT. This 6MWT was also performed in the clinic but without medical direction and results were recorded by the WCD accelerometer (results were also recorded by a clinician who did not interact with the patient). Over 8 weeks, both groups performed up to 8 unsupervised WCD-guided 6MWTs at home with results recorded by the WCD. Differences between group 1 and group 2, in clinic WCD-guided 6MWT and first at home WCD-guided 6MWT, and repeated at home 6MWTs were analyzed.
Results: For the initial in-clinic 6MWT there was no significant group difference in mean distance walked (group 1 = 306.3 meters, group 2 = 295.1 meters, p = 0.46). Of those who completed = one 6MWT at home, there was a 6 step difference between the in clinic WCD-guided 6MWT (group 2) and the first at home 6MWT performed (Wilcoxon signed-rank test; medians: 553 steps and 547 steps respectively, p = 0.004). For a subset of patients (n = 70) with 8 at home 6MWTs there was no significant difference over eight weeks in the number of steps walked (F(7,552) = 0.34, p = 0.93).
Conclusion: Results of the in clinic 6MWT are similar between clinician-guided and WCD-guided patients. Distances walked with a WCD-guided walk test were consistent whether conducted in the office or at home. The 6 step difference between the in clinic WCD-guided 6MWT and the first at home test is unlikely to have clinical significance. In addition, the at home WCD-guided 6MWT demonstrates good repeatability over time.

The WCD-guided 6MWT performed at home is a reliable alternative to administering the test in the clinic.

P380

Comparative effectiveness of enalapril, lisinopril and ramipril in the treatment of patients with chronic heart failure. A propensity score matched cohort study

T Tobias Taeger[1]; F Henning[1]; H Froehlich[1]; D Schellberg[1]; M Grundtvig[2]; K Goode[3]; S Kazmi[3]; T Hole[4]; HA Katus[1]; D Atar[5]; JGF Cleland[6]; S Agewall[5]; A Clark[3]; L Frankenstein[1]
[1]University Hospital of Heidelberg, Department of Cardiology, Heidelberg, Germany; *[2]Innlandet Hospital, Medical Department, Lillehammer, Norway*; *[3]Castle Hill Hospital, Hull, United Kingdom*; *[4]Norwegian University of Science and Technology, Medical Faculty, Trondheim, Norway*; *[5]Oslo University Hospital, Department of Cardiology, Oslo, Norway*; *[6]Imperial College London, London, United Kingdom*

Background: Angiotensin converting enzyme inhibitors (ACEIs) are recommended as first-line therapy in patients with heart failure with reduced ejection fraction (HFrEF). The comparative effectiveness of different ACEIs is not known.
Methods and **Results:** 4,723 out-patients with stable HFrEF prescribed either enalapril, lisinopril, or ramipril were identified from three registries in Norway, England, and Germany. In three separate matching procedures, patients were individually matched with respect to both dose equivalents and their respective propensity scores for ACEI treatment.
During a follow-up of 21,939 patient-years, 360 (49.5%), 337 (52.4%), and 1,119 (33.4%) patients died amongst those precsribed enalapril, lisinopril, and ramipril, respectively. In univariable analysis of the general sample, enalapril and lisinopril were both associated with higher mortality as compared with ramipril treatment (HR 1.46, 95% CI 1.30-1.65, $p < 0.001$, and HR 1.38, CI 1.22-1.56, $p < 0.001$, respectively). Patients prescribed enalapril or lisinopril had similar mortality (HR 1.06, 95% CI 0.92-1.24, $p = 0.41$). However, there was no significant association between ACEI choice and all-cause mortality in any of the matched samples (HR 1.07, 95% CI 0.91-1.25, $p = 0.40$; HR 1.12, 95% CI 0.96-1.32, $p = 0.16$; and HR 1.08, HR 1.10, 95% CI 0.93-1.31, $p = 0.25$ for enalapril vs. ramipril, lisinopril vs. ramipril, and enalapril vs. lisinopril, respectively). Results were confirmed in subgroup analyses with respect to age, sex, left ventricular ejection fraction, NYHA functional class, cause of HFrEF, rhythm, and systolic blood pressure.
Conclusion: Our results suggest that enalapril, lisinopril and ramipril are equally effective in the treatment of patients with HFrEF when given at equivalent doses.

P381

The clinical implication of donor-recipient mismatch in heart transplant recipients; data from the Korean Organ Transplantation Registry

J Jaewon Oh[1]; JO Choi[2]; HJ Cho[3]; HY Lee[3]; SH Jung[4]; JJ Kim[4]; ES Jeon[2]; SM Kang[1]
[1]Yonsei University College of Medicine, Cardiology Division, Seoul, Korea Republic of; *[2]Samsung Medical Center, Cardiology, Seoul, Korea Republic of*; *[3]Seoul National University College of Medicine, Cardiology, Seoul, Korea Republic of*; *[4]Asan Medical Center, Cardiovascular Surgery, Seoul, Korea Republic of*

Introduction: The International Society for Heart and Lung Transplantation (ISHLT) guidelines recommend donor-recipient matching against inappropriate weight match (IWM) for heart transplant. Few studies have explored this size matching recommendation, especially with regard to body weight and gender matching in Asian heart transplant recipients. We aimed to determine whether any difference could be observed between donor-recipient mismatching with regard to clinical outcomes in Korean heart transplant recipients.
Methods: Data from adult heart transplants (recipients = 18 years of age) between 2014 and 2017 were obtained from the Korean Organ Transplantation Registry (KOTRY). We defined IWM, defined as donor weight < 70% of recipient's weight. The clinical end-points were all-cause 30-day mortality and cumulative mortality during follow-up period.
Results: IWM was associated with increased 30-day mortality as well as cumulative mortality in Korean heart transplant recipients. Male recipients of female allografts as well as female recipients of male allografts had increased cumulative mortality compared with gender-matched transplants.
Conclusion: Our results indicate that donor weight < 70% of recipient weight increases 30 day and cumulative mortality in Korean heart transplant recipients. Gender mismatch increases mortality independently of weight match.

P382

Dynamics and prognostic value of B-type natriuretic peptide in left ventricular assist device recipients

M Papathanasiou[1]; R Sofianos[1]; L Tsourelis[2]; M Kamler[2]; N Pizanis[2]; T Rassaf[1]; P Luedike[1]
[1]University Hospital Essen, Department of Cardiology and Angiology, West German Heart and Vascular Center, Essen, Germany; *[2]University Hospital Essen, Department of Thoracic and Cardiovascular Surgery, West German Heart and Vascular Center, Essen, Germany*

Background: The prognostic utility of B-type natriuretic peptide (BNP) in heart failure is well recognized. Previous studies demonstrated that BNP levels decrease after left ventricular assist device (LVAD) implantation.
Purpose: We sought to investigate the predictive value of baseline and changes in BNP levels in LVAD recipients.
Methods: BNP was measured in baseline and follow-up plasma samples from consecutive patients receiving a continuous-flow LVAD from 2010 through 2016. Absolute values and changes from baseline were related to 180-day all-cause death or the combined end-point of all-cause death or hospitalization.
Results: Our study included 103 consecutive adult patients with a mean age of 59 years. Median BNP at baseline was 885 (Interquartile range, IQR: 450 to1624) pg/ml, significantly decreasing to 289 (IQR: 154-534) pg/ml 90 days after LVAD implantation ($p < 0.001$). Overall 63 (61%) patients survived to 90-day follow-up. In all subjects, BNP remained above the cut-off of 35 pg/ml for chronic heart failure and in 91% above 100 pg/ml. Cox proportional hazards regression analysis revealed that higher baseline and follow-up BNP levels were not associated with increased risk of death at 180 days ($p = 0.12$ and $p = 0.43$, respectively). In the univariate analysis 90-day BNP, but not baseline BNP, was significantly associated with the combined death/hospitalization outcome (HR 1.03, 95% CI 1.01-1.06; $p = 0.006$). This significance was not preserved after adjusting for multiple covariates (HR 1.01, 95% CI 0.98-1.04; $p = 0.62$). At 90 days, there was no BNP lowering in 20.6% of subjects. This was not associated with higher risk for death or the composite of death/hospitalization at 180 days ($p = 0.11$ and $p = 0.06$ respectively).
Conclusions: BNP levels significantly decrease but remain highly abnormal in the vast majority of patients following LVAD implantation. BNP absolute levels and changes from baseline are not independently associated with clinical outcome. These findings suggest an impaired prognostic performance of BNP after LVAD implantation.

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Remote model in the system of outpatient cardioreabilitation in subjects with chronic heart failure

N Lyamina[1]; E Kotelnikova[1]; V Senchikhin[1]; T Lipchanskaya[1]
[1]Research Institute of Cardiology Saratov State Medical University named after V.I. Razumovskiy, Saratov, Russian Federation

Background : The remote management of treatment and rehabilitation process including self-management, telemedical healthcare and remote monitoring (RM) can be executed for outpatient cardiac rehabilitation (CR) in subjects with chronic heart failure (CHF).
Purpose: Remote observational model evaluation in outpatient CR in subjects with I-III NYHA CHF after myocardial infarction (MI).
Methods: The study included 24 subjects: 22/91.7% of men, 55.3 ± 8.3 y.o.; NYHA 2.04 ± 0.25; 75% after PCI due to MI; mean GRACE scale score 92 ± 12. Home CR programs included controlled walking 5 times/week. Remote rehabilitation monitoring (3 months) included ECG autotransmitting, physical activity and physiological indicators control, asynchronous telemedicine and office counseling. ECG telemonitoring was performed by the principle of autotransmitting with mobile devices and the ECG Dongle Internet application. Physical activity (PA) was measured by Beurer AS80 digital pedometer with transmitting data to the smartphone and the mobile application Easyfit (GmbH, Germany). PA tolerance was estimated in Borg scale points. Type of attitude towards the disease was assessed by the LOBI questionnaire. Remote correction of rehabilitation assignment was carried out in the mode of asynchronous telemedicine counseling; correction of drug therapy was performed during office counseling. CR effectiveness was assessed by the results of 6-min walk distance test (WDT) and the dynamics of NYHA functional class, as well as the patients' activity indices in the RM system and dynamics of the personal response to the disease.
Results: Patients with I-III NYHA CHF were included in the RM program on 31 ± 5 days of MI. Initially disadaptive behavioral reactions prevailed (87.0%). No signs of personal disadaptation had 12.5% subjects. According to the RM parameters data transmission was stopped by 3 patients (12.5% of participants) after 4 ± 1.2 weeks of follow up. After 3 months of CR with a walking time of 37 ± 5 min/day, average number of 3223.6 ± 27.7 steps/day, total distance traveled 9.9 ± 2.7 km/week and a stable subjective reaction (0.6 ± 0.3 and 0.7 ± 0.2 Borg scale points) the dynamics

of WDT (443 ± 32 m vs. 352 ± 27, p <0.05) and NYHA CHF (1.71 vs. 2.04, p <0.05) were observed. Asymptomatic episodes of myocardial ischemia were recorded in 2 subjects (9.5%); rhythm disturbances - in 8 (38.1%). The number of patients with minimal manifestations of maladjustment increased (12.5% vs 33.3%, p <0.001). The proportion of subjects with intrapsychic orientation disorders was slightly decreased (from 66.7% to 61.9%).
Conclusions: : The RM system based on mobile communication is successful as a model of rehabilitation care for outpatient management in CHF patients. The complex predisposing factor of RM application is to increase the motivation of patients by involving them in the self-management process improving the quality of communication between the doctor and the patient and increasing patients' physical activity.

P384
Impact of introduction of a formal heart failure programme in a developing nation- a single centre study

CY Chun Yuan Khoo[1]; CT Ng[1]; TL Tran[2]; TT Pham[2]; M Le[2]; TL Le[2]; TAN Nghiem[2]; DC Truong[2]; CP Lim[1]; LY Teo[1]; LH Chan[1]; DAVID Sim[1]
[1]National Heart Centre Singapore, Singapore, Singapore; *[2]175 Military Hospital, Ho Chi Minh, Vietnam*

Background/Purpose: Formal heart failure (HF) programmes are lacking in developing countries. Prescription rates of evidence based HF medications remains suboptimal. Heart failure self-care among patients in these countries is poor. Comprehensive HF programme has been shown to result in clinical benefits in developed countries. We seek to study if similar benefits may be accrued among HF patients in a developing country in South East Asia.
Methods: This is a prospective observational study. We enrolled patients with left ventricular systolic function (LVEF) = 40% with at least 1 HF admission in the previous 12 months into a new HF programme in the 175 Military Hospital in Vietnam. The patients would have to be willing to pay medical costs at an unsubsidized fee. The HF programme was helmed by 3 local cardiologists and 3 specialist nurses trained in HF. Besides routine physical examinations, the patients were educated on their condition and medications. Advice was given for exercise and dietary restrictions. The clinical status, laboratory results and medications of the patients were reviewed 3 months later and compared to their baseline **Results: Results:** Out of the 50 patients enrolled, 34 were male (68%). Mean age was 63.9 ± 10.8 years. Mean LVEF was 35.1 ± 6.4%. At baseline, majority of the patients (62%; N = 31) were in New York Heart Association (NYHA) functional class III, while the remainder were in NYHA II.
After a duration of 3 months, mean systolic blood pressure was reduced from 122mmHg to 111mmHg (P = 0.004). Mean heart rate was reduced from 78/min to 68/min (P < 0.001). There was also a reduction in mean NT-proBNP levels from 7133pg/ml to 4563pg/ml (P = 0.007). Hospitalisation rates were reduced from 70% to 22% (P < 0.001). There was an increase in beta-blocker prescription rates (32% to 68%). Adherence to HF therapy improved from 54% to 94% (P < 0.001) at 3 months followup. Functional status of the patients also improved, with more patients in NYHA II (38% to 88%; P < 0.001).
Conclusion: The implementation of a formal HF programme improves clinical outcomes among HF patients in this single-centre study in a developing nation. Larger studies over a longer duration of time would be beneficial in studying potential cost savings translated from the health benefits.

P385
Drug utilization in the outpatient heart failure clinic at the University hospital of Iceland- adherence to guidelines

IE Gisladottir[1]; PS Gunnarsson[1]; I Gunnthorsdottir[1]; I S Inga Sigurros Thrainsdottir[1]; A Ketilsdottir[1]; G Gudlaugsdottir[1]; K Andersen[1]
[1]University of Iceland, Cardiology, Reykjavik, Iceland

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Background: Heart failure is a common and severe type of cardiovascular disease. Four major drug classes are used in the treatment of heart failure, ACE and ARB inhibitors, beta blockers and mineralcorticoid receptor antagonists (MRAs). The objective of this study was to evaluate the drug utilization of patients in the outpatient heart failure clinic at the University hospital of Iceland and to estimate the adherence to the 2016 ESC guidelines for acute and chronic heart failure.
Methods: A retrospective and descriptive study was preformed using data collected from the electronic medical records system of the University Hospital for patients, 18 years or older, based on their last visit to the outpatient heart failure clinic in 2016. Target doses were obtained from the 2016 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure.
Results: In total, 253 patients had at least one visit to the outpatient clinic for patients with heart failure in 2016. The average age of patients was 69 years and the majority of patients were men (75.5%). A total of 219 (87%) patients were treated with ACE or ARB inhibitors, 227 (90%) patients were treated with beta-blockers and 130 (51%) patients were treated with MRAs. The target dose was reached in 14% of patients receiving ACE or ARB inhibitors, 12% of patients receiving beta blockers and 16% of patients receiving MRAs. The main reasons for dose adjustments and drug selection were renal failure and hypotension. 25,4% of patients had serum creatinine higher than 150 μmol/L. 11% of patients younger than 80 years old had systolic pressure lower than 100 mmHg and 15% of patients 80 years or older had systolic pressure lower than 120 mmHg. In addition 14% of patients had other side effects as reason for lowering of dosage or discontinuation of treatment.
Conclusions: The main findings of the study are that low proportion of patients with heart failure are treated according to the ESC guidelines for acute and chronic heart failure. The main reasons that patients did not reach target dose were worsening of renal function, hypotension or patients were still in up titration phase. These results are consistent with similar studies that have been conducted in Europe.

P386
Eplerenone titration in real-world heart failure patients: a multicenter survey

A Karavidas[1]; D Farmakis[2]; V Bistola[2]; A Kitsiou[3]; C Chatzieleftheriou[4]; C Papadopoulos[5]; J Zarifis[6]; I Styliadis[7]; S Adamopoulos[8]; J Parissis[2]
[1]General Hospital of Athens G. Gennimatas, Athens, Greece; *[2]Attikon University Hospital, Heart Failure Unit, Cardiology Department, Athens, Greece*; *[3]Sismanoglion Hospital, Athens, Greece*; *[4]Drama General Hospital, Department of Cardiology, Drama, Greece*; *[5]Hellenic Red Cross Hospital, Athens, Greece*; *[6]General Hospital G. Papanikolaou, Thessaloniki, Greece*; *[7]Hospital Papageorgiou, Thessaloniki, Greece*; *[8]Onassis Cardiac Surgery Center, Athens, Greece*

Background: Mineralocorticoid receptor antagonists (MRA) constitute a cornerstone of current therapy for heart failure with reduced ejection fraction (HFrEF). However, concerns about MRA-associated renal function worsening and hyperkalemia have been raised. In addition, prescription and particularly titration of life-saving therapies vary considerably in different HF populations.
Purpose: We sought to investigate titration rates of eplerenone in real-world HFrEF patients followed regularly in HF clinics and its effects on clinical parameters, renal function and serum potassium levels.
Methods: We enrolled a total of 413 consecutive patients on eplerenone, 79% male, 92% in NYHA class II or III, with mean left ventricular ejection fraction 30 ± 8%, from different HF clinics throughout Greece. Eplerenone dosing along with clinical parameters, renal function, serum potassium and quality of life were evaluated at baseline and at 6 months.
Results: Mean eplerenone dose increased significantly from baseline (28.5 ± 11.8 mg) to 6 months (31.8 ± 13.7 mg, p < 0.001); The target dose of 50mg was prescribed in 13% of patients at baseline and in 23% at 6 months. The corresponding prescription rates in patients with renal dysfunction were 15% and 17%, respectively. Heart rate decreased significantly from baseline to 6 months (72 ± 11 vs. 70 ± 8 bpm, p < 0.001), while systolic blood pressure remained stable (118 ± 18 vs. 118 ± 16 mmHg, p = 0.828). Creatinine clearance also remained stable throughout 6 months (73 ± 31 vs. 69 ± 48 ml/min, p = 0.146), while there was a small and marginally significant increase in serum potassium, which however remained within normal range (4.3 ± 0.5 vs. 4.4 ± 0.7 mmol/L, p = 0.047). Quality of life, as estimated by Kansas City Cardiomyopathy Questionnaire, improved from baseline to 6 months (p < 0.001).
Conclusions: Eplerenone was successfully titrated in HFrEF patients without adverse events. However, target dose prescription remains suboptimal. Efforts to increase adherence to Guideline recommendations are warranted.

P387
Oral sucrosomial iron improves quality of life in heart failure patients with iron deficiency: A preliminary proof-of-concept study

A Karavidas[1]; E Trogkanis[1]; D Farmakis[2]; G Georgios Papingiotis[2]; V Matzaraki[1]; A Perpinia[1]; D Balta[1]; J Parissis[2]
[1]General Hospital of Athens G. Gennimatas, Department of Cardiology, Athens, Greece; *[2]Attikon University Hospital, Second Cardiology Clinic, Heart Failure Unit, Athens, Greece*

Background: Iron deficiency is prevalent in 37-50% of heart failure (HF) patients and has been associated with reduced functional capacity and quality of life (QoL) and adverse prognosis. Intravenous iron supplementation improves functional capacity and QoL, but use of oral iron preparation has been limited by poor intestinal absorption.
Purpose: In this preliminary, proof-of-concept study, we evaluated the efficacy of sucrosomial iron (SSI), a new oral iron formulation that seems to overcome intestinal epithelial barriers, in HF patients with iron deficiency.
Methods: We studied 30 patients with chronic HF with reduced left ventricular ejection fraction (35% or less, HFrEF), New York Heart Association (NYHA) class

II or III, iron deficiency (ferritin level < 100 ng/mL or serum ferritin 100-299 ng/mL and transferrin saturation < 20%), and hemoglobin level 9.0-13.5 g/dL in females and 9.0-15 g/d in males. All patients had been on stable, evidence-based medical therapy for at least 1 month. Twenty patients received oral SSI, containing 28 mg of iron, once daily for 3 months and 10 served as controls. Clinical and laboratory parameters were evaluated at baseline and at 3 months.
Results: Patients in SSI group were strongly adherent to protocol and no drop-outs were noticed. At 3 months, SSI induced a significant increase in serum iron levels (from 43.7 ± 19.0 to 60.32 ± 16.23 mg/mL, adjusted p = 0.002), where hemoglobin levels remained stable. Quality of life, as expressed by Kansas City Cardiomyopathy Questionnaire, also improved significantly (from 55.7 ± 18.5 to 61.8 ± 20.81, adjusted p = 0.038) and there was also a trend towards a longer 6-min walked distance (from 318 ± 72 to 332 ± 74.63 m, adjusted p = 0.065).
Conclusion: Short-term oral SSI improved iron status and quality of life in HFrEF patients with iron deficiency, without causing any adverse event. A further evaluation of this form of iron warrants further investigation.

P388

Long-term follow-up of patients with dilated cardiomyopathy receiving cardiac resynchronization therapy: responders vs nonresponders -10 years single center trial

G Milasinovic[1]; MT Petrovic[2]; N Radovanovic[1]; SU Pavlovic[1]; G Nikcevic[1]; B Kircanski[1]; I Petrovic[2]; D Trifunovic[2]; J Petrovic[2]; MZ Petrovic[2]
[1]Clinical center of Serbia, Pacemaker Center, Belgrade, Serbia; [2]Clinical center of Serbia, Clinic of cardiology, Belgrade, Serbia

Introduction: Cardiac resynchronization therapy (CRT) is a validated therapy for patients with dilated cardiomyopathy (DCM) and impaired left ventricular systolic function, despite optimal medical therapy for heart failure.
Purpose: The aim of current study was to evaluate the outcome of patients with DCM after CRT, and to check a difference in survival between responders versus nonresponders to CRT.
Methods: This has been retrospective observational, single center study. The study population consisted of heart failure patients, who met standard inclusion criteria for resynchronization therapy, and in whom CRT was implanted in Pacemaker Center, Clinical Center of Serbia between August 2006 and March 2008. Ten years from the beginning of the trial, we did follow-up. Chart review, patient examination, device interrogation and telephone contact were assessed during long-term follow-up, after device implantation. We observed the efficacy of resynchronization therapy and survival. In terms of efficacy, patients with an increase in left ventricle ejection fraction (EF) of 5%, or decrease in end-systolic volume of 15% were considered as the echocardiographic responders and patients who improved at least one NYHA class or 6 minute walk test by 10% as the clinical responders to resynchronization therapy.
Results: In this study, 70 patients were included. At the beginning of the study, mean age was 59.2 ± 9.1 years and 53 (75.7%) patients were male. Forty-two patients (60%) were responders to CRT, and 28 (40%) patients were nonresponders. The mean age of responders was 60.2 ± 8.7, and of nonresponders 57.8 ± 9.6 (p>0.05). Also, there were no significant differences in gender and in therapy between responders and nonresponders. In group of responders EF before CRT was 25.1 ± 7.2% and on follow-up EF was 40.1 ± 12.1% (p < 0.01). In nonresponders the value of EF before CRT was 30.1 ± 7.3% and on follow-up was 31.3 ± 15.1% (p = 0.04). Responders showed significantly better survival than nonresponders. During follow-up, among responders 15 (35.7%) patients died and among nonresponders 19 (67.8%).
Conclusion: Results of our study have shown that a considerable percentage of patients do not have an appropriate response to resynchronization therapy, but those who are responders have a statistically significantly lower mortality during long follow-up. Our findings are consistent with the results of similar studies with shorter follow-up.

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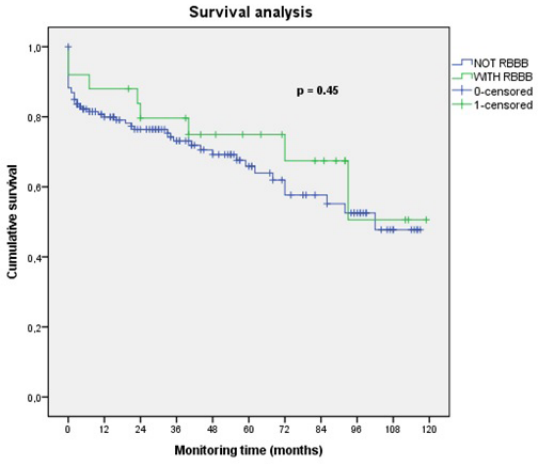
Cardiac conduction system alterations in heart transplantation recipients. prognostic implications

C Gonzalez-Portilla-Concha[1]; A Antonio Grande-Trillo[1]; D Rangel-Sousa[1]; JM Sobrino-Marquez[1]; A Abril-Molina[1]; J Rodriguez-Ortuno[1]; E Lage-Galle[1]
[1]University Hospital of Virgen del Rocio, Seville, Spain

Introduction: Right bundle branch block (RBBB), the most prevalent alteration in the conduction system after heart transplantation (HT), is not related to worse prognosis in classics studies. However, several studies correlate this alteration with cellular graft rejection. Our goal is to evaluate the prevalence of conduction system abnormalities and their prognostic implications in HT recipients.
Methods: Retrospective analysis of HT recipients in our hospital since 2007. We analyse conduction system abnormalities in the discharge electrocardiogram after HT, besides donor/recipient and surgery characteristics. We evaluate the presence of cellular rejection in first endomyocardial biopsy, pacemaker implantation in the follow up and survival rates.
Results: 194 patients were analysed (median age 52 years, range 14-69 years; 75% male). The conduction system alterations were the following: 24% incomplete right bundle branch block, 14% right bundle branch block, 4% left anterior fascicular block, 3% left bundle branch block and 55% without alterations. Differences between patients with and without RBBB are described on Table 1 and compared survival curve is showed in figure 1.
Conclusions: Presence of RBBB in electrocardiogram after HT is relatively frequent (14% in our series). Although this disturbance seems not to be related to worse survival, we obtained a value near to statistical signification when we analysed cellular graft rejection in first endomyocardial biopsy and pacemaker implantation in the follow up in patients with RBBB. Therefore, we must look out RBBB find after HT and consider it as a possible sign of cellular graft rejection to dismiss it.

	Right bundle branch block	Rest of patients	Statistical signification
Recipient Age	52 (14-69)	52 (24-68)	p = 0.78
Donor Age	45 (15-66)	43 (14-65)	p = 0.97
Weight discordance donor- recipient	4.1±15.3	4.95±12.6	p = 0.79
Ischemia time (min)	218.7±47	217±55	p = 0.888
Urgent heart transplantation	16%	26%	p = 0.2
Pacemaker implantation	12%	2.6%	p = 0.06
Cellular rejection ≥ 2	17.6%	4.9%	p = 0.08



P390

Intravenous iron therapy in chronic heart failure patients with reduced and preserved ejection fraction.

S Sergio Hernandez Jimenez[1]; G Alonso Salinas[1]; S Del Prado Diaz[1]; M Pascual Izco[1]; M Plaza Martin[1]; J Ramos Jimenez[1]; JL Zamorano Gomez[1]
[1]University Hospital Ramon y Cajal de Madrid, Cardiology, Madrid, Spain

Introduction: Intravenous iron therapy (IIT) in patients with iron deficiency and chronic heart failure (CHF) with left ventricular ejection fraction (LVEF) < 45% improves income rate due to heart failure worsening. The objective of this study is to analyse its "real life" impact, also exploring its influence in non-cardiovascular hospitalization rate and in emergency department (ED) visits.
Methods: Patients with heart failure and iron deficiency were consecutively included. Baseline characteristics, and previous-year admission rate and ED visits were retrospectively collected. During the follow-up, hospitalization rate and ED visits were registered and compared with previous-year rates according to the LVEF.

Table 1

	LVEF ≤ 45% (N = 29)	LVEF>45% (N = 27)
Age, years (m±SD)	76.1±9.5	73.4 ± 12
Female sex (n;%)	6; 20.7%	10; 37%
Chronic Kidney Disease (n;%)	15; 51.7%	10; 37%
Ischemic ethiology (n;%)	18; 62.1%	11; 40.7%

Results: 56 CHF patients with iron deficiency who were were treated with IIT, were consecutively included from August to December'17. There was a medium follow-up of 4 months. Baseline characteristics are described in table 1. Regardless LVEF, IIT reduced all-cause (0.083 (0.0 - 0.167) hospitalizations/month vs 0.0; p= 0.015) and cardiovascular (0.083 (0.0 - 0.083) Vs 0; p= 0.001) hospitalization rates. It also reduced all-cause ED visits (0.167 (0.083 - 0.333) vs 0 (0-0 - 0.143); p < 0.001) and cardiovascular ED visits (0.083 (0.0 - 0.167) Vs 0.0 (0.0 - 0.143); p < 0.001). In patients with reduced LVEF IIT improved all-cause (0.083 (0.0 - 0.167) Vs 0; p= 0.028) and cardiovascular (0.083; (0-0.083) Vs 0; p= 0.006) hospitalization rates and all-cause ED visits (0.167 (0.083 - 0.333) Vs 0 (0.0 - 0.083); p= 0.007) and cardiovascular ED visits (0.083 (0.042 - 0.167) Vs (0.0; p= 0.004). In patients with preserved LVEF, IIT reduced non-cardiovascular hospitalization rate (0.0 Vs 0.0 (0.0 - 0.04); p= 0.014) and all-cause (0.25 (0.167 - 0.417) Vs 0 (0.0 - 0.20); p= 0.005) and cardiovascular (0.167 (0.0 - 0.25) Vs (0.0; p= 0.005) ED visits. In preserved LVEF IIT did not influence cardiovascular hospitalization rate (0.083; (0-0.083) Vs 0.083; (0-0.083); p= 0.469) Conclusions. IIT improves hospitalization and ED visit rates in patients with CHF regardless LVEF. This findings are consistent with CONFIRM-HF
Conclusions: in patients with LVEF = 45%. In patients with LVEF>45% IIT reduces non-cardiovascular hospitalization rate and cardiovascular and all-cause ED visits.

P391
Hospital readmissions after left ventricular assist device implantation

P Lesny[1]; M Luknar[1]; V Simovicova[1]; M Dankova[1]; E Goncalvesova[1]
[1]*National Cardiovascular Institute, Bratislava, Slovak Republic*

Background: Left ventricular assist device (LVAD) implantation enhances survival and quality of life of end-stage heart failure patients (pts). However, unplanned readmissions are a significant cause of morbidity and reduce the potencial benefit of LVAD treatment. We analysed the causes of unplanned readmissions, their frequency, and impact on survival.
Patients and Methods: From August 2007 to June 2017, 98 pts underwent LVAD implantation (HeartMate II or III, or HearWare HVAD) at a single centre. Retrospective data analysis was performed in 81 pts, who were discharged on support. The indications were bridge to transplantation in 95% of pts and destination therapy in 5%. Mean age was 49.3 ± 10.5 years , 51% of pts were in Interagency Registry Mechanically Assisted Circulatory Support class 1 or 2. Follow-up was censored at death or transplant.
Results: Median follow-up was 11 months. Mean length of device support was 15.7 ± 11.3 months (median, 12.7 months). Fifty pts (61%) had 99 unplanned readmissions, thirty-one pts (39%) had no readmissions. Main reasons for readmission included driveline/pump-related infections (n = 25), confirmed or suspect pump thrombosis (n = 15), arrhytmias (n = 12), right heart failure (n = 11), non-device infections (n = 10), bleeding (n = 10), and neurological disorders (n = 6). Unplanned readmission predicted higher mortality (11 deaths in readmission group, vs 1 death in no-readmission group, p = 0.02).
Conclusions: Unplanned readmissions are common after LVAD implantation. The leading cause were driveline/pump-related infections. Unplanned readmission has a negative impact on survival. Multidisciplinary approach in outpatient management is required to reduce readmissions which could lead to an improved long-term survival.

P392
Decision support systems as organizing and functional part of the patient-oriented model in ambulatory stage of cardiac rehabilitation

N Nadezda Lyamina[1]; E Kotelnikova[2]; V Senchikhin[2]; T Lipchanskaya[2]
[1]*Saratov Scientific Research Institute of Cardiology, Saratov, Russian Federation*;
[2]*Research Institute of Cardiology Saratov State Medical University named after V.I. Razumovskiy, Saratov, Russian Federation*

Background: Creating of effective environment for the implementation of patient-oriented health care principles is impossible without the use of information and communications technologies (ICT). High-tech ICT devices in the format of modern communications and products of artificial intelligence are not only inferior in performance to traditional medical observation and medical mind, but in some cases surpass them, being less expensive in the future.
Purpose: User-defined reasoning about efficiency of the Decision Support System (DSS) as organizing and functional part of the patient-oriented model of cardiac rehabilitation in patients with acute myocardial infarction with ST elevation (ST-MI).
Methods: The prospective study (6 months of outpatient observation, 28 subjects with ST-MI) included use of ICT devices in the form of DSS and "Cloud" internet communications. Efficiency of DSS was assessed by the results of usability testing of 15 physicians and electronic patient reports (ePRO).
Results: Successful creation of electronic "Patient Rehabilitation Card" was demonstrated by 80% of participating physicians with an average work duration of 11 ± 4 minutes. The number of medical errors in appointing the events of cardiac rehabilitation was 4.8%. According to ePRO 53.6% of the subjects had physiological response criteria for the DSS of cardiac rehabilitation program. Remote correction of cardiac rehabilitation programs was performed in subjects with intermediate type of reaction (2.1%). Change of medical management was performed in 7 subjects (44.3%) with criteria of pathological reactions.
Conclusion: User-defined reasoning about efficiency of the DSS showed its high suitability in organizing of cardiac rehabilitation home programs. The use of ePRO in order to involve patients in treatment and rehabilitation allowed to obtain information on the safety of cardiac rehabilitation programs and to evaluate its significance for patient-oriented tactical decisions.

P393
The incidence of primary prevention ICD appropriate interventions (ATP/shock) in outpatients with severe heart failure

L Laszlo Vandor[1]; K Heltai[1]; I Osztheimer[1]; K Koltai[1]; B Merkely[1]
[1]*Semmelweis University Heart Center, Budapest, Hungary*

ICD implantation for primary prevention of sudden cardiac death is recommended in heart failure pts with >3 months optimal medical treatment (OMT) and lack of improvement of LVEF (to >35%), in ischemic heart failure with "I/A" and in non-ischemic heart failure with "I/B" level of evidence (ESC: Heart Failure Guidelines, 2016.). The role of the primary prevention ICD implantation in non-ischemic patients is also examined at the last years.
Goal: We examined the primary prevention ICD's appropriate therapy (ATP or shock) during a 4 year period. We studied the difference in ischemic and non-ischemic groups also.
Patients and Methods: Our patient are a characteristic population of heart failure, and pts on heart transplantation waiting list and pts under checkup for heart transplantation waiting list.
We retrospectively analyzed the rate of appropriate ICD therapy in 2014-2017 among our heart failure patients.
Results: 591 pts, 22% female, 78% male were observed. 62% of pts was younger than 62 y.
In 261 pts (44,2%) the underlying disease was ischemic, 92% of these patients got coronary revascularisation, 330 pts (55,8%) had non-ischemic DCM.
384 patients (65%) had EF less than 35% .
All patients received OMT before the ICD implantation.
365 patients have got ICD, of which 344 (94,2%) for primary prevention. 74 patients were observed over 4 years with appropriate ICD therapy (ATP or shock), 20,2% of the patients has got effective therapy. There was no difference between ischemic and non-ischemic pts (33 / 41 therapy).
Conclusion: Our patient population showed a higher rate of the effective primary prevention ICD therapy than the international data showes that. No difference was found between ischemic and non-ischemic patients in respect of appropriate ICD interventions. This may be partially due to the specific patient population.

P394
Usefulness of chest radiographic congestion score to predict responses to adaptive servo-ventilation

Y Nishihata[1]; N Komiyama[1]
[1]*St. Luke's International Hospital, Department of Cardiology, Tokyo, Japan*

Background: Hemodynamic effect of positive airway pressure treatment including adaptive servo-ventilation (ASV) for heart failure (HF) depends on the degree of congestion, but little has been reported on the simple marker in terms of congestion to predict efficacy of ASV.
Purpose: We assessed the usefulness of chest radiographic congestion score (CS) to predict responses to ASV.
Methods: We investigated 61 HF patients treated with ASV in our hospital between June 2009 and December 2015. We examined patient's symptoms, clinical examination, echocardiography, laboratory findings and chest roentgenogram that was blindly scored for the presence and severity of lung edema.

Results: Their mean age, LVEF, and NT-proBNP were 76 ± 13 years old, 37.3 ± 19.3% and 8666 ± 11634 pg/ml, respectively. An improvement of proportional pulse pressure and heart rate during ASV significantly correlated with patient's comfortableness in response to ASV ($p < 0.01$ and $p < 0.01$), and CS also correlated with their comfortableness at both initiation and discontinuation of ASV ($p < 0.01$ and $p < 0.05$). Among 32 patients who could continue ASV at least 1 month, there were 9 patients whose comfortableness during ASV became worse and their CS significantly decreased from initiation time of ASV (5.1 to 2.4, $p < 0.01$). Of those 9 patients, 7 stopped ASV. The other 2 patients continued ASV but they were attacked by sudden cardiac death although their NT-proBNP were improved enough. They had been enough decongested and ASV might worsened their hemodynamics.
Conclusion: Patient's comfortableness in response to ASV and lung congestion are well correlated, and they could be simple indicators about ASV therapy.

P395
Pediatric mechanical circulatory support in the presence of restrictive organ donation, single center experience.

T Tatyana Ivanova-Razumova[1]; L Mamezhanova[1]; Al Baigalkanova[1]; S Jetybaeva[2]; S Andosova[2]; GS Myrzhakmetova[2]; R Salov[3]; MS Bekbossynova[2]; S Bekbossynov[3]; Y Pya[3]
[1]National research cardiac surgery center, pediatric cardiology, Astana, Kazakhstan; *[2]National research center for cardiac surgery, cardiology, Astana, Kazakhstan*; *[3]National research center for cardiac surgery, cardiac surgery, Astana, Kazakhstan*

Objective: The objective of this study is to evaluate efficiency and safety of mechanical circulatory support (MCS) with in-core left ventricle assist devices (LVAD) using in children with end-stage heart failure.
Methods: From 2011 to 2017 year in National Research Cardiac Surgery Center (Astana, Kazakhstan) 5 MCS devices were implanted in pediatric patients. Median age - 15 years (range 9 - 17). Gender: 2 girls, 3 boys. Mean BSA was - 1,406 ± 0,5 m^2, minimal BSA was - 0,85 m^2. 4 patients were in INTERMAX II class, 1 girl - INTERMAX I. Ejection fraction of left ventricle mean - 16 ± 4,06%, mean pro-BNP level at the moment of implantation - 5967 ± 2231,6 pg/ml. Dilated cardiomyopathy were diagnosed in 4 cases, 1 boy had hypertensive cardiomyopathy, secondary to late corrected coarctation of aorta. We have evaluated basic dates, complications rate and outcomes.
Results: In 2 cases we have implanted HVAD (Heart Ware international) - 40%, in 2 cases MCS was performed with HeartMate II (Abbot) - 40% and in 1 case HeartMate III (Abbot) was implanted (20%). Driveline infection developed in 1 patient (20%), he received long-term antibiotic therapy, but 1 year late sepsis with positive blood culture was diagnosed. There were no another complications - GI bleeding, stroke, pump thrombosis, etc. One patient died after 45 days from operation due to right ventricle heart failure. 90-days survival rate was - 80%. Mean duration of mechanical circulatory support was 431,25 ± 150,13 days.4 patients, including boy with drive infection and sepsis, were successfully transplanted with adult donor hearts. 1 girl on MCS with HVAD (HeartWare international) was admitted to India (Fortis clinic) because pediatric heart transplantation is not available in Kazakhstan, and 3 weeks later she was successfully transplanted.
Conclusions: preliminary analysis of this cases revealed low rate of complications and acceptable outcomes for children with end-stage heart failure. So MCS with in-core devices is a good option for open-heart surgery center under the conditions of restrictive pediatric organ donation.

Chronic Heart Failure - Prevention

P396
Heart failure first diagnosed in the community and managed in a disease management programme (DMP) is at low risk of progression to hospitalisation

L Liam Healy[1]; R Murphy[1]; J Gallagher[1]; S Mccleland[1]; M Ledwidge[1]; S Zhou[1]; K Mcdonald[1]
[1]St Vincent's University Hospital, Cardiology, Dublin, Ireland

On behalf of: St. Vincent's University Healthcare group

Introduction: The progression of a community diagnosis of heart failure portends a poor clinical prognosis, highlighting the need to consider advanced heart failure therapies or palliative care. Defining those most at risk of syndrome progression requiring the need for hospitalisation allows heightened clinical focus on this and to focus resources on high risk patients within the framework of a disease management programme (DMP).
The purpose of this project was to define the natural history of patients diagnosed with heart failure in the outpatient setting and managed in a DMP to determine the phenotype of those most likely to progress using baseline metrics. Progression was defined as requirement of hospitalisation for acute decompensated heart failure, an accepted concerning clinical event.
Methods: A retrospective analysis of new community diagnoses of heart failure were followed over time in our heart failure unit. A rapid access clinic is provided in this centre for potentially new community diagnoses of heart failure referred in by family physicians. Subsequent confirmed cases of heart failure are followed within a cardiologist led disease management programme. Heart failure progression is defined as the need for hospital admission to manage acute decompensated heart failure.
Results: 607 patients were reviewed [age: 76.7 ± 11 years; 290 (47.8%) male; 196 (36%) heart failure with a reduced ejection fraction (HFrEF); 345 (64%) heart failure with a preserved ejection fraction (HFpEF); mean brain natriuretic peptide (BNP) 343.4 ± 465.6 pg/ml ; mean creatinine 105.7 ± 56 μmol/L].
57 (9.4%) patients demonstrated progression of HF with a mean follow up of 4.3 ± 3.3 years.
The annual incidence of progression to hospitalisation was 13 patients (2.19%).
Univariate predictors of progression included mean BNP [468.4 ± 502.2 pg/ml versus 329.7 ± 459.9 pg/ml) ($p < 0.001$)]; mean creatinine [114.2 ± 40.5 versus 104.8 ± 57.5 ($p < 0.0114$)]; E/e' [11.6 ± 4.9mmHg versus 10.1 ± 4.3mmHg ($p = 0.0467$)] in progression to hospitalisation versus non-progression respectively.
Multivariate predictors included left atrial volume index (LAVI) [66.9 ± 32.3 mL/m2 versus 47.7 ± 20.5 mL/m2 ($p < 0.001$); OR 1.03 (95%CI: 1.01, 1.05; $P = 0.014$)] in progression to hospitalisation versus non-progression respectively.
Conclusion: A Disease management programme for patients with a community diagnosis of heart failure are less likely to progress to hospitalisation affecting marginally over 2% of the population per year. The strongest indicator of risk for disease progression was left atrial size indicating that this group would likely benefit from intense follow up.

P397
Incident heart failure after myocardial infarction in regional outpatient cardiology clinic

A Klabnik[1]; J Murin[2]
[1]Outpatient cardiology clinic, Namestovo, Slovak Republic; *[2]1st Department of Internal Medicine , University Hospital Bratislava, Slovak Republic*

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Purpose: Heart failure (HF) remains serious complication of non-ST elevation (NSTEMI) myocardial infarction (MI), even in revascularization era. Comprehensive data are lacking about long-term course beyond MI hospitalization. Previous studies focused mostly on early in-hospital phase of MI, without distinguishing between cases of HF with reduced (HFrEF), mid-range (HFmrEF) or preserved (HFpEF) ejection fraction (EF) and left ventricular systolic dysfunction (LVSD) as HF stage B equivalent.
Methods: 486 consecutive patients (pts) over 45 years (without previous HF) discharged alive after first NSTEMI from January 2015 prospectively followed by regional cardiologist. Pts without revascularization procedures were excluded (recurrent MI increased HF risk dramatically).
Results: During NSTEMI was diagnosed HF in 18.7% pts (6.3% HFrEF, 10% HFmrEF and 2.4% HFpEF). After mean 23 months follow-up additional 37.2% pts developed HF within 1 year after discharge (1.8% HFrEF, 25.6% HFmrEF and 9.8% HFpEF).
Highest HF incidence was within first 6 months after MI (33.3%) and occurrence of HF markedly increased risk of death: hazard ratio (HR) 10.2, 95% CI (confidence interval) 7.7-13.5, $p < 0.0001$.
The strongest predictors of HFpEF and HFmrEF were older age (3.1%, 15.6%, and 25.6% among men and 2.2%, 18.8%, and 30.1% among women ages 45-54, 55-74, and 75-85 years, $p < 0.001$), antecedent diabetes (HR 1.67; 1.47-1.89, $p < 0.001$) and new-onset atrial fibrillation (HR 1.20; 0.99-1.46, $p < 0.01$).
Independent risk factors for HFrEF (all $p < 0.001$) included older age (for every 1 year increase in age HR 1.03; 1.02-1.04), Killip class = III (HR 5.2; 4.1-6.4), high GRACE risk score (HR 3.3; 2.8-4.1), EF= 40% (HR 2.6; 1.9-3.3).
Global LVSD (EF= 40%) was observed in 23.6% pts at discharge and 12.1% after 12 months and significant longitudinal LVSD (S' = 6.0 cm/s) had 36.8% at index MI vs 23% after one year (all $p < 0.001$).
Conclusions: Heart failure after MI occurs in a time-dependent fashion and long-term MI survivors should be monitored closely for early signs of HF beyond acute MI period.

P398

An educational program improves knowledge and awareness of heart failure irrespective of previous professional or personal experience of disease

V Vlad Damian Vintila[1]; A Vintila[2]; S Stork[3]; R Ludwig[3]; C Malsch[3]; M Lainscak[4]; D Vinereanu[1]

[1]University of Medicine and Pharmacy Carol Davila, University and Emergency Hospital Bucharest, Cardiology Department, Bucharest, Romania; [2]University of Medicine and Pharmacy Carol Davila, Coltea Clinical Hospital, Internal Medicine Department, Bucharest, Romania; [3]Comprehensive Heart Failure Center (CHFC), University of Wurzburg, Wurzburg, Germany; [4]Faculty of Medicine, University of Ljubljana, , General Hospital Murska Sobota, Murska Sobota, Slovenia

Background: Heart failure (HF) is a common pathological condition with poor prognosis. The objective of the HF Awareness Day, which represents an European annual event, is to increase the knowledge and awareness regarding this condition, by using dedicated educational programs.
Aim: To demonstrate that exposure to an educational program improves knowledge and rises the awareness of HF, irrespective of previous medical or personal experience related to this pathological condition.
Method: We analyzed a full set of questionnaires filled in by the general population from 4 European countries, during 2013 Heart Failure Awareness Day. Awareness of HF was assessed using a score computed from the correct answers. A cut-off of 6 points was considered positive. Two specific subgroups were analyzed: one subgroup of subjects employed of former employed in the medical field (group A), and one subgroup of subjects exposed to HF (either personal or through relatives) (group B).
Results: 1777 questionnaires were analyzed. After being exposed to educational program the median score of awareness changed from 7.3 ± 4.4(4-11) to 10.7 ± 4.1(8-14) ($p < 0.001$). The evolution of the 2 subgroups is shown in tabel 1. We also analyzed the change of heart failure awareness in the two groups after being exposed to an educational program. We evaluated the change of awareness through a change of the median score = 3 points. The greatest achievement of awareness was recorded in the non-exposed population, both for the professional and personal experience subgroups.
Conclusions: Professional or personal experience in a European population gives a difference in knowledge and awareness of disease. After being exposed to an educational program the subjects show a similar level of awareness of HF. The non-exposed population benefit more from that educational exposure. Such an educational program should be considered as part of treatment in any pathological condition, including HF.

HF awareness evolution through education

	Group A scoring >6	No group A scoring >6	p	Group B scoring >6	No group B scoring >6	p
Before seminar	148* (74%)	897 (60%)	<0.001	659 (71%)	301 (50%)	<0.001
After Seminar	169 (85%)	1321 (88%)	0.166	816 (88%)	546 (90%)	0.142
Change of score**	84 (42%)	831 (56%)	<0.001	437 (47%)	393 (65%)	<0.001

*valid answers ** change ≥ 3points

Group a: medical exposureGroup b: personal exposure

P399

Effect of the optimize_heart failure care (ohf) program on clinic and patients outcomes at Ho Chi Minh City (HCMC) heart institute, vietnam

PHUONG Do Thi Nam[1]; BAN Ha Ngoc[1]; DUNG Do Van[2]; HUAN Do Quang[1]; MARTIN R Cowie[3]

[1]Heart Institute, Ho Chi Minh city, Vietnam; [2]Medecine and Pharmacy University, Ho Chi Minh city, Vietnam; [3]Royal Brompton Hospital, London, United Kingdom

On behalf of: OHF Ho Chi Minh City Heart Institute
Funding Acknowledgements: Servier laboratory

Heart failure (HF) is a common public health in Europe and US but also in Asia. The HF prevalence is increasing in LMI countries with a big annual burden.
HCMC Heart Institute took part in the OHF program to improve patient's outcomes by improving HF patient's awareness, and by optimizing HF treatment.

We included all of HF patients hospitalized with left-ventricular ejection-fraction(LVEF) <50%. The patients were educated about diet, exercise, weight-control and the detection of worsening HF symptoms. The data was collected at 2 and 6 months (M2, M6) for clinical signs, treatments and outcomes (readmission and death). Patient's knowledge and practice were checked at M6 by a telephone-survey.
From Oct. 2016 until Oct. 2017, we recruited 257 HF patients hospitalized with LVEF <50%, 58% male, mean age 64.4 ± 15y.o. and BMI 22.2 ± 3.5 kg/m2. The HF etiology was ischemic heart disease(64%), cardiomyopathy(22%) and valvular heart disease(9%). The principal co-morbidities were hypertension(48%), valvular heart disease(40%), dyslipidemia(33%), arrhythmia(31%), diabetes(26%), and renal failure(21%).
The mean heart rate was improved between admission(M0) vs. discharge (97.8 ± 22.2 vs. 78.5 ± 11.7, $p < 0.001$), and M0 vs. M6 (97.8 ± 22.2 vs. 78.9 ± 13.6, $p < 0.001$). The clinical signs were improved between M0 vs. M2 and M2 vs. M6 for: dyspnea (80% vs. 36%, $p < 0.001$; 36% vs. 22%, $p = 0.002$); orthopnea (40% vs. 1%, $p < 0.001$; 1% vs. 0%, $p = 0.25$); and sign of pulmonary congestion (27% vs. 0.6%, $p < 0.001$; 0.6% vs. 0%, $p = 0.65$). The patients with NYHA class I&II rising from 45% at M0 to 97% at M2 and 99% at M6, both $p < 0.001$ compared to M0). The LVEF also increased ($36.5\% \pm 9$ at M6 vs. $33.4\% \pm 9$ at M0, $p = 0.005$).
In terms of education, 99% of patients were educated about diet (72% had knowledge, 78% practice this); 85% were educated on exercise (67% had knowledge, 62% practice this); 90% were educated about weight-control (54% had knowledge, 44% practice this); and 92% were educated for "detection of worsening HF symptoms", only 56% remembered this education.
For HF pharmaceutical treatment, we followed European guidelines, including at discharge: 91% renin-angiotensin-aldosterone system inhibitors, 33% beta-blockers (but 50% at M6), 77% mineralocorticoid-receptor-antagonist, 85% diuretics, 9% ivabradine (but 18% at M6), 33% digoxin (22% treated for atrial-fibrillation) and 16% isosorbide-dinitrate.
The readmission rate at 30 and 60 day after discharge was 8.3% and 12.5%. There was no in-hospital death. The mortality rate at 30, 60 days and 6 months was 1.2%, 2.5% and 10.4%.
The OHF Care Program could be implemented in a middle-income country without difficulty. Education was provided to a high proportion, although patient did not always retain or follow the advice. The use of drug-therapy (other than for beta-blockers) is good. Clinical-control, readmission and mortality rates appear good. Further work is underway to optimize for beta-blokade usage, and how to improve patient's behavior.

P400

Microalbuminuria is an early marker of kidney damage in cardiorenal syndrome patients

A Armine Minasyan[1]

[1]Yerevan State medical university after Mkhitar Heratsi, Surb Grigor Lusavorich Medical Center, Internal Diseases, Cardiology, Yerevan, Armenia

Background: Cardiorenal syndrome (CRS) is the term used to describe a complex disorder of the heart and kidneys, in which acute or chronic dysfunction of one organ initiates and perpetuates disease in the other. CRS is recognized as an important clinical condition that is increasingly becoming a major public health problem due to the high associated morbidity and mortality rates.
Purpose: To reveal diagnostic usefulness of microalbuminuria (MA) in CRS patients.
Methods: Echocardiographic data of left ventricular remodeling, microalbuminuria level and degree of renal dysfunction in 115 patients with CRS were examined. MA was measured with diagnostic strips, contractile function of the left ventricle (LV) - by echocardiography and glomerular filtration rate was assessed by Cockroft-Gault method.
Results: The association between MA, decreased GFR, elevated creatinine level, their association with increased LV myocardial mass and LV systolic dysfunction was revealed. Direct correlation between MA and myocardial mass index and indirect - between LV ejection fraction and MA were determined. Obtained data allow to mention the level of MA ($25,4 \pm 5,8$ ng/ml), where there is more probability of LV contractile dysfunction development. This will allow early prediction and prevention of chronic kidney diseases, therefore CRS progression. Conclusion: Presented results strengthen the diagnostic usefulness of MA in CRS patients as it develops from progressive, subclinical, structural and functional changes within the kidney and represents a sensitive marker of early renal disease. MA is independently associated with numerous modifiable cardiovascular risk (CV) factors and markers of CV disease. Physicians should measure urinary albumin excretion in patients with diabetes mellitus and hypertension routinely and be as aggressive in treating this modifiable risk factor as they do in case of blood pressure, cholesterol, or blood glucose control.

Chronic Heart Failure - Clinical

P401
Clinical pathway for heart failure management in Hospital-at-Home: Better self-care?

I Isabel Fiteni Mera[1]; M Matia Sanz[1]; M Sevil Pura[1]; C Clemente Sarasa[1]; N Martin Catalan[1]; N Alcala Rivera[1]
[1]*Hospital Royo Villanova, Internal Medicine, Zaragoza, Spain*

Background: The systematic use of a clinical pathway for a medical problem allows to minimize management variability and optimize therapy. The management of heart failure (HF) with the alternative Hospital –at-home may help a closer approach to those patients, promote their medical education and empower self-care in order to improve outcomes. Using a clinical pathway in the Hospital-at-Home (HaH) could be a tool to perform this improvement.
PURPOSE: To compare early outcome after discharge in patients with heart failure assisted by internists in HaH following a clinical pathway and those assisted in a conventional Internal Medicine Ward. We focused our study on hospital stay length, mortality and readmissions rates.
MATERIAL AND Methods: Prospective study from March to November 2017: all patients admitted to HaH, and patients admitted in IM for HF decompensation were included, excluded cognitive impairment and critically ill patients. Our clinical pathway considered therapy, adverse events control and educational schedules. Group 2 in IM were treated with usual guidelines. Self-care and quality of life were measured with validated scales the first day of admission and one month after discharge. Readmissions and visits to the Emergency Departement (ED) for HF during 3 months after discharge, Hospital stay length, side-effects (wkf, hypotension, hyperkalemia) and therapy were compared.
Results: 36 patients were enrolled, 21 patients in HaH (group 1) and 15 in IM (group 2). Baseline characteristics were similar in both groups; age, sex, cardiovascular risk factors, cardiac and non-cardiac comorbidities, NYHA class, HF etiology and causes of decompensation. In group 2 we had more patients with systolic dysfunction, but similar pulmonary hypertension and atrial fibrillation in both groups. Laboratory results were similar; NT-proBNP, hyponatremia, creatinine and ferropenia. Regarding therapy, management was similar with better fluid intake control in group 1. Patients in group 1 had less hyperkalemia during treatment (p = 0,026). At inclusion self care scores were similar in both groups with better scores in group 1 at 30 days (p= 0,005). Meanwhile there was no difference between groups for quality of life before and after hospitalization. Patients in group 2 visited more often ED than group 1 (63% vs. 18,7% respectively) and had higher readmission rates at 3 months after discharge (53,8% vs 6,6%). Both rates were similar in both groups for the 3 months previous to enrollment. Mortality was similar in both groups.
Conclusion: Implementing a clinical pathway in HaH with individual targets and instructions lead to better outcomes for patients in the 3 first months after discharge, with less ED visits and readmission rates for HF. This improvement is probably due to educational aspects more easily performed in the intervention at home. We need to continue the follow-up to observe how long the effect of this intervention persists.

P402
Iron supplementation in an acute heart failure unit

R Rita Gomes[1]; J Rodrigues[1]; F Aguiar[1]; C Graca[1]; A Torres[1]; I Araujo[1]; F Marques[1]; L Campos[1]; C Fonseca[1]
[1]*Hospital São Francisco Xavier, Heart Failure Unit, Internal Medicine Department, Lisboa, Portugal*

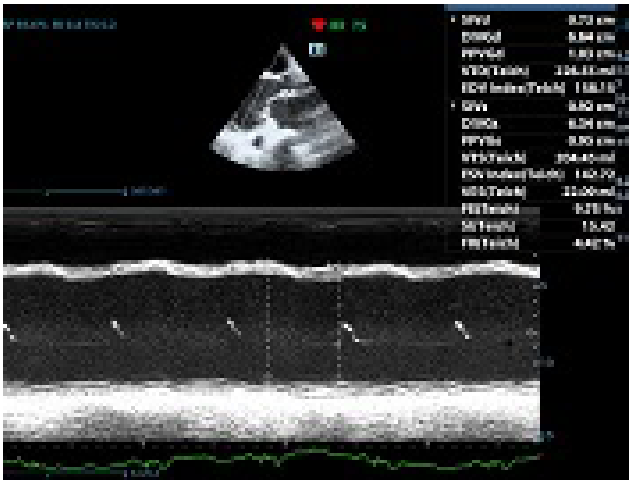
Introduction: Iron deficiency (ID) is common in heart failure (HF) and is associated with worse prognosis. Intravenous (IV) ferric carboxymaltose (FCM) is the recommended treatment. IV iron sucrose (IS) is a less expensive option. There are no published data comparing efficacy, tolerability and logistics between the administration of FCM and IS.
Purpose: to compare the burden of administration of these 2 IV iron formulations.
Methods: Consecutive patients admitted to our Heart Failure Unit (HFU) with HFpEF, HFmEF and HFrEF and ID were enrolled and randomly allocated for IV FCM or IS. Doses were determined individually according to Ganzoni's formula for IS and to the CONFIRM scheme for FCM. Follow-up was 7 months (IQR 3.5-10).
Results: 57 patients were included, 77.3 ± 9.6 years, 52.6% male. 47.4% had HFpEF, 29.8% HFrEF and 22.8% HFmEF. Hypertension (35.1%) and ischemia (26.3%) were the most prevalent etiologies. 68.4% had functional ID and 31.6% absolute ID. 59.6% had anemia (Hb 11.7 ± 2.3g/dL). 28 patients (49.1%) were given FCM and the remaining 29 (50.9%) received IS. There were no significant differences between the two treatments, except for ID type (in IS, functional ID was more prevalent (86.2%); p = 0.004) and transferrin saturation (TSat) at admission (11.8 ± 4.4% in FCM vs 15.1 ± 6.1% in IS; p = 0.024). Ferritin levels of patients with absolute ID were: at admission 53.9 ± 26.6μg/L in FCM vs 76.5 ± 30.5μg/L in IS (p = 0.163); at 6 months 493.1 ± 450μg/L in FCM vs 114.5 ± 112.4 μg/L in IS (p = 0.280). Patients with functional ID had ferritin levels: at admission of 167.2 ± 64.4μg/L in FCM vs 139.4 ± 72.4μg/L in IS (p = 0,239); at 6 month 462.3 ± 62.5μg/L in FCM vs 333.9 ± 178.9μg/L in IS (p = 0.251). TSat at admission 11.9 ± 4.9% in FCM vs 14 ± 4.7% in IS; at 6 month 24.3 ± 20.5% vs 23.6 ± 8.1% (p = 0.251). 46.4% of FCM completed the total iron dose in-hospital vs 51.7% of IS. IS had a longer hospital stay (9.4 ± 6.1days vs 8.8 ± 3.9days in FCM; p = 0.629). After 6 months, 85.4% of FCM completed the total iron dose vs 86.2% of IS. 100% in FCM vs 44.8% required only 1 or 2 administrations (p < 0.001). 7.1% in FCM and 10.3% in IS do not completed the total iron doses due to adverse reactions (p = 0.671).
Conclusions: There are no differences between the two IV iron therapies on what completing the prescribed total iron dose is concerned. At six months, all patients had ferritin and/or TSat above the normal limit, however patients who underwent FCM tended to have higher ferritin levels. FCM required a lower number of administrations and adverse events tended to be more frequent in IS. These findings suggest a reduced need for new short-term administration and related costs and a longer clinical stability with FCM, corroborating the results of the national pharmacoeconomic study recommending the use of FCM.

P403
Cardiac involvement in patients with muscular dystrophies.

N N Ali Tatar-Chentir[1]; AN Ali-Tatar Nora[1]; MT C Mt Chentir[1]; TM Tazir Meriem[1]; BY Bouhouita Yacine[1]
[1]*University Hospital Centre Mustapha, Algiers, Algeria*

On behalf of: ALI-TATAR NORA

Backround : Cardiac disease is one of the clinical manifestations of neuromuscular disorders . Heart muscle as conducting myocardial fibers may be affected in this context.



Becker dystrophy patient non responder

Purpose: To identify cardiovascular disease in patients with muscular dystrophies referred to our day hospital unit by neurologists.
Methods: We study prospectively from February 2007 to September 2017, clinical , ECG and ultrasound data according to the ESC Guidelines .
24 patients mean age 26 ± 17years (range: 6-69yrs); 22men and two women with muscular dystrophies
-9 patients were diagnosed as having Duchenne muscular dystrophy (DMD).
- 7 as having Becker muscular dystrophy (BMD) .
- 2 as having Limb-Girdle Muscular Dystrophy Type 2(LGMD2).
- 4 as having myotonic muscular dystrophy (Steinert's disease).
- One with Facioscapulohumeral muscular dystrophy (FSHD).
Results: All patients are from a first degree consanguineous marriage.
Cardiac involvement was present in 3 of 9 patients with Duchenne Muscular Dystrophy (33%) at the stage of dilated cardiomyopathy (DCM), one with left bundle brunch block (LBBB).
The occurrence of heart failure with reduced ejection fraction is observed in one of the 27-year –old brothers while his younger brother shows signs of heart failure with preserved ejection fraction (HFpEF).
Heart failure with reduced ejection fraction (HFrEF) is present in 4 of7 patients (57%) with Becker Muscular Dystrophy including two patients with cardiac resynchronization therapy (CRT) no responders. Recently one of the two CRT patients died with signs of cardio-renal syndrome.

Of the two patients with Limb-Girdle Muscular Dystrophy Type 2(LGMD2), one had premature ventricular beats that disappeared under beta-blocker treatment.
In Steiner's disease we noticed 2 LBBB, 1atrial flutter and one Left Anterior Fascicular Block (LAFB).
In Facioscapulohumeral muscular dystrophy, Echo was in the normal range.
According to the guidelines and our observations, all the patients with Duchene muscular dystrophy and Becker muscular dystrophy should began pharmacological therapy with angiotensin-converting enzyme inhibitor or angiotensin receptor blocker before the stage of DCM.
Conclusion: In addition to primary prevention aimed at discouraging consanguineous marriages, early diagnosis of myocardial involvement par strain imaging may lead to improvement of ejection fraction especially in muscular dystrophies. Further studies are needed to establish definitive occurrence of heart abnormalities in muscular dystrophies.

P404
Atrial fibrillation in heart failure with reduced versus preserved ejection fraction: Not the same thing

B T Bernadet Santema[1]; M Kloosterman[1]; IC Van Gelder[1]; I Mordi[2]; CC Lang[2]; CSP Lam[1]; JG Cleland[3]; K Dickstein[4]; H Hillege[1]; JM Ter Maaten[1]; M Metra[5]; DJ Van Veldhuisen[1]; P Van Der Meer[1]; M Rienstra[1]; AA Voors[1]
[1]University Medical Center Groningen, Cardiology, Groningen, Netherlands; *[2]Ninewells Hospital, Dundee, United Kingdom*; *[3]University of Glasgow, Glasgow, United Kingdom*; *[4]University of Bergen, Bergen, Norway*; *[5]University of Brescia, Brescia, Italy*

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Aims: The clinical correlates and consequences of atrial fibrillation (AF) might be different between heart failure with reduced versus preserved ejection fraction (HFrEF vs. HFpEF). Biomarkers may provide insights into underlying pathophysiological mechanisms of AF in these different HF phenotypes.
Methods and Results: Among 2671 patients (2149 HFrEF [EF < 40%] and 522 HFpEF [EF = 50%]) from the BIOlogy Study to TAilored Treatment in Chronic Heart Failure (BIOSTAT-CHF), 92 cardiovascular risk markers were measured (Proseek® Olink CVD III panel). Quality of Life (QoL) was assessed by the Kansas City Cardiomyopathy Questionnaire (KCCQ). AF was associated with higher levels of 78 of 92 (85%) cardiovascular risk markers compared to sinus rhythm (SR) in HFrEF; whereas in HFpEF, many more markers were higher in SR than AF. In HFrEF, AF was associated with a poorer QoL (KCCQ score of 46 vs. 52 in SR; $p < 0.001$) whereas in HFpEF, QoL was similar between AF and SR. Over a median follow-up of 21 months, AF was associated with increased mortality risk, even after adjustment for age and sex (hazard ratio [HR] of 1.24; 95% confidence interval [CI] 1.07 - 1.43, $p = 0.004$); there was no significant interaction between heart rhythm and EF group on outcome.
Conclusion: In patients with HFrEF, the presence of AF was associated with more elevated cardiovascular risk markers and a poorer QoL. In contrast, in patients with HFpEF, the presence of AF was not associated with more elevated risk markers and/or a poorer QoL.

P405
Status of vitamin D in difficult to treat cardiorenal syndrome in heart failure patients.

N Sen[1]; SONAL Tanwar[2]; ASHOK Jain[1]
[1]Narayana Hrudayalaya, Cardiology, Jaipur, India; *[2]HG SMS Hospital, Cardiology, Jaipur, India*

Background: Decreased glomerular filtration rate(GFR) is a potent predictor of cardiovascular mortality and complications. Worsening heart failure can accelerate worsening of renal function - the so-called cardiorenal syndrome. Risk factors include hypertension, diabetes, elderly age, and prior history of heart or renal failure. Aims & Objectives: To study the correlation between serum vitamin D values in uncontrolled cardiorenal syndrome and to evidential improvement in control of cardiorenal syndrome after vitamin D supplementation and correlate it with heart & renal function.
Methods: Serum vitamin D levels were assessed in 178 patients of cardiorenal syndrome in duration of 2 years (2015-2017) and we found very low level of vitamin D (average level was 16 U ng/ml) in 108 patients of difficult to treat cardiorenal syndrome between 19 -74 years of age who were uncontrolled even after courses of Betablocker, Diuretics and ACE inhibitors or Angiotensin II Receptor Blocker Neprilysin Inhibitor (ARNI) and other optimised medical therapy . These patients were treated with calcium and Vitamin D supplementation for 12 weeks and after were re-evaluated with repeat vitamin D levels, Renal function test , GFR and Cardiac functions by 2D Echocardiography .
Results: All 108 patients showed significant improvements in B-type natriuretic peptide (BNP level), Right and Left ventricular function, LVEF incresed (14+/-4%) , decreased pulmonary capillary wedge pressure and improved class of dyspnea New York Heart Association IV to class II or III. After 3 months of vitamin D supplementation 43% patients had improved GFR and serum creatinine value as compare to placebo 16% , p value(< 0.003).
Conclusion: Study showed a strong correlation between vitamin D deficiency and difficult to manage cardiorenal syndrome and good cardiorenal outcome after supplementation.

P406
Altered immune pattern of circulating endothelial cell-derived micro vesicles predicts chronic heart failure development in patients with metabolic syndrome

A E Alexander E Berezin[1]; A Kremzer[1]; T Samura[1]; T Berezina[2]
[1]State Medical University, Zaporozhye, Ukraine; *[2]Private medical center VitaCenter, Zaporozhye, Ukraine*

Background: Metabolic syndrome (MetS) is defined as risk factor clustering related to the premature development of type 2 diabetes mellitus (T2DM) and cardiovascular disease (CVD) in association with increased CV mortality in general population. The role of pattern of circulating endothelial cell-, platelet-, and monocyte-derived micro vesicles in chronic heart failure (CHF) patients with MetS is not still understood. The aim of the study was to investigate a pattern of circulating MVs in CHF patients with MetS in relation to neurohumoral and inflammatory activity.
Methods: The study retrospectively evolved 388 CHF (left ventricular ejection fraction = 43% [interquartile range: 35% to 48%]) patients (154 patients with MetS and 234 patients without MetS), 47 MetS patients without CHF, and 25 healthy volunteers, who were examined between February 2013 and November 2017. Serum N-terminal brain natriuretic peptide (NT-proBNP), high-sensitive C-reactive protein (hs-CRP), adiponectin (AND), and osteoprotegerin (OPG) were measured by ELISA. MVs were measured by flow citometry. CD41a+ was used as a more specific marker of platelets, and CD64+ was considered a more specific marker of monocytes. CD31 antigen was determined as essential marker for endothelial cells, platelets, and leukocytes. CD144+ was used to identify a pure population of endothelial cells. CD31+/annexin V+ was defined as apoptotic endothelial cell-derived MPs, MPs labeled for CD62E+ were determined as MPs produced due to activation of endothelial cells. Biomarkers were measured at baseline of the study.
Results: The results of the study have shown that number of circulating plateled-derived and monocyte-derived MPs in subjects with MetS (with or without CHF) insufficiently distinguished from the levels determined in healthy volunteers. We found significantly ($P = 0.001$ for all cases) elevated levels of CD31+/annexin V+ MPs and CD41a+ MVs, significantly lowered number of CD31+/CD144+ and CD62E+ MVs ($P = 0.001$ for all cases) in CHF patients with MetS compared to CHF individuals without MetS as well as non-CHF patients with MetS. In CHF population there was close inverse correlation between number of CD62E+ and levels of NT-proBNP ($r=-0.38$; $P = 0.001$), hs-CRP ($r=-0.34$; $P = 0.002$), AND ($r=-0.28$; $P = 0.001$), and OPG ($r=-0.34$; $P = 0.003$). In contrast, number of CD31+/annexin V+ positively correlated to NT-proBNP ($r=-0.36$; $P = 0.003$) and OPG ($r=-0.32$; $P = 0.001$). Additionally, we determined that biomarkers of biomechanical stress (NT-proBNP) and inflammation (hs-CRP, OPG) remain statistically significant predictors for decreased CD62E+ to CD31+/annexin V+ ratio, but not for decreased CD41a+ to CD31+/annexin V+ ratio in CHF patients with MetS. In conclusion, it has found that decreased CD62E+ to CD31+/annexin V+ ratio reflected altered immune phenotype of MVs and probably this fact may be discuss as surrogate marker of CHF development in MetS population

P407
Bone mineral density and metabolism in very elderly patients with congestive heart failure

SV Topolyanskaya[1]; IA Osipovskaya[2]; LS Lifanova[1]; TA Eliseeva[2]; ON Vakulenko[2]; LI Dvoretsky[1]
[1]I.M. Sechenov First Moscow State Medical University, Department of hospital therapy N2, Moscow, Russian Federation; *[2]War Veterans Hospital N3, Moscow, Russian Federation*

Background: There are few data available on the relationship of heart failure and osteoporosis in very elderly patients.
Purpose: The study purpose was investigation of bone mineral density (BMD) and metabolism in very elderly patients with heart failure.
Methods: The study enrolled 125 patients (38 men and 87 women, aged 75-98 years) hospitalized with coronary artery disease (CAD). Study group comprised 61 patients with clinically significant CHF (NYHA FC III-IV), control group - 64 CAD patients without CHF symptoms. Main exclusion criteria were any other diseases

that could cause osteoporosis and administration of medications reducing BMD. Lumbar spine and proximal femur BMD was measured by dual energy X-ray absorptiometry. Fracture risk was measured under FRAX model; osteoporosis standard risk factors were analyzed. Serum osteocalcin concentration was measured by immunochemiluminescent method, beta-Cross Laps level - by electrochemiluminescence.
Results: BMD in CHF patients was lower (both in absolute values and by the T-score) versus control group. Largest differences were recorded in proximal femur: BMD in CHF patients was 719.8 ± 188.2 mg/cm3 vs 797.7 ± 161.7 mg/cm3 (p = 0.02) in control group. Greater differences in BMD were detected in female patients (p = 0.007). Femoral neck BMD in CHF patients was 649.4 ± 137.1 mg/cm3 vs 696.2 ± 121.8 mg/cm3 (p = 0.03) in control group. There were no significant differences found in lumbar spine BMD (p = 0.4). Proximal femur BMD had normal values only in 5% of CHF patients, whilst normal BMD in control group was in 31% of cases (p = 0.003). Multiple regression analysis found that significant factors determining proximal femur BMD were CHF (ß = 0.375, p = 0.005) and female sex (ß = 0.698, p < 0.0001). Mean osteocalcin level in CHF patients was 1.2 ± 1.7 ng/ml vs 4.2 ± 4.1 ng/ml (? = 0.03) in control group. In 60.6% of CHF patients osteocalcin concentration was below the lower limit of normal (p = 0.02 vs control). Mean ß-Cross Laps level in CHF patients was 0.73 ± 0.4 ng/ml vs 0.4 ± 0.1 ng/ml (p = 0.003) in control group. ß-Cross Laps level was increased in 21.7% of CHF patients, but no one had high ß-Cross Laps values in control group (p = 0.03). There was negative correlation between ß-Cross Laps and BMD, especially in proximal femur (r=-0.4, p = 0.03). Negative correlation was found between tumor necrosis factor-a level with its serum concentration higher in CHF patients (p = 0.04) and BMD, especially in proximal femur (r=-0.9, p = 0.03). In patients with decreased leptin concentration (found only in CHF patients), BMD values were lower than in those with normal or increased serum leptin concentration (p = 0.006 for proximal femur).
Conclusion: These study findings suggest that bone mineral density in very elderly CHF patients is noticeably lower versus age-mathched patients with similar main diseases. This study has demonstrated significantly reduced osteoblast function in CHF patients and slight increase in bone resorption.

P408

Impact of nutritional status on heart failure hospitalization and mortality in nonischemic patients with implantable cardioverter defibrillator

K Kenjiro Oyabu[1]; A Suzuki[1]; T Shiga[1]; K Jujo[1]; S Higuchi[1]; Y Iwanami[1]; D Yagishita[1]; K Ejima[1]; M Shoda[1]; N Hagiwara[1]
[1]*Tokyo Women's Medical University, Cardiology, Tokyo, Japan*

Introduction: Malnutrition is associated with poor prognosis among heart failure (HF) patients. However, factors associated with malnutrition among HF patients received implantable cardioverter defibrillator (ICD) has not been fully elucidated. The aim of this study was to assess the predictive value of nutritional status in nonischemic HF patients with ICD.
Methods: We studied 165 nonischemic HF patients implanted ICD at Tokyo Women's Medical University from 2003 to 2015. Controlling nutritional status (CONUT) score was evaluated before ICD implantation.
Results: Average age was 56 +/- 15 and 112 (68%) patients were male. Median CONUT score was 1 (interquartile range 1 to 3). During a 39 [18-82] months of follow-up, 42 (25%) patients were hospitalized for HF exacerbation and 30 (18%) patients were died. By multivariate cox regression analysis with baseline characteristics, CONUT score was an independent risk for both HF hospitalization (HR 1.362, 95% CI 1.113 to 1.667, p < 0.05) and mortality (HR 1.432, 95% CI 1.139 to 1.800, p < 0.05) (Figure).
Conclusion: Our results suggested that malnutrition assessed by the CONUT score is an independent predictor of HF hospitalization and all-cause death in nonischemic HF patients with ICD.

	HF hospitalization			all-cause death		
	HR	95% CI	p	HR	95% CI	p
Men	0.682	0.338-1.376	0.285	0.463	0.191-1.123	0.089
Age ≥75	0.456	0.058-3.612	0.457	1.296	0.150-11.206	0.814
prior sustained VT or VF	0.960	0.463-1.991	0.913	2.054	0.927-4.552	0.076
eGFR <60mL/min/1.73m^2	2.299	1.160-4.557	0.017	1.516	0.620-3.708	0.362
NYHA functional class III or IV	0.670	0.295-1.519	0.337	1.579	0.615-4.055	0.342
LVEF ≤35%	2.055	0.931-4.536	0.075	2.465	0.900-6.748	0.079
Beta-blocker	0.583	0.234-1.455	0.248	1.413	0.422-4.726	0.575
ACEI or ARB	1.185	0.426-3.297	0.745	0.744	0.235-2.361	0.616
CONUT score	**1.362**	**1.113-1.667**	**0.003**	**1.432**	**1.139-1.800**	**0.002**

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; eGFR, estimated glomerular filtration; HF, heart failure; NYHA, New York Hear Association; LVEF, left ventricular ejection fraction; VT, ventricular tachycardia; VF, ventricular fibrillation.

P409

Impact of comorbidities in outpatients with chronic heart failure

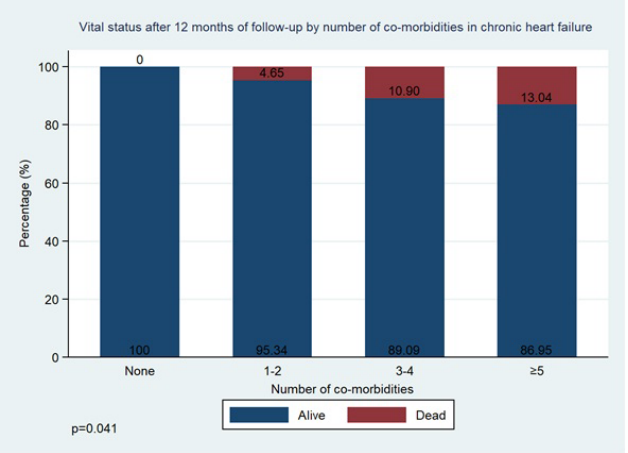
D Carrillo[1]; R Lopez-Vilella[1]; I Sanchez-Lazaro[1]; E Marques[1]; L Martinez-Dolz[1]; L Almenar[1]
[1]*Hospital Universitario y Politécnico La Fe, Heart Failure and Transplant Unit, Valencia, Spain*

Background/introduction: The comorbidities associated with chronic heart failure (CHF) adversely affect the prognosis of the disease.
Purpose: To describe the frequency of co-morbidities and mortality in the first year follow up in outpatients with CHF.
Methods: Registry of outpatients with CHF treated between April 2010 to February 2016 with follow up of 12 months. Co-morbidities as coronary heart disease with or without myocardial revascularization, malignant disease, diseases of the central nervous system (stroke, depression), diabetes mellitus, arthritis, potassium disorders, hypertension, anemia, sleep apnea, kidney dysfunction and lung disease were included. A table of frequency of co-morbidities and a bar graph of vital status by a number of co-morbidities was made.
Results: 248 patients with CHF were included (Table). Arterial hypertension, coronary heart disease, diabetes mellitus, obesity, and hyperlipidemia were the most frequent co-morbidities present (Table). There were more deaths within the first year in patients with more than 4 comorbidities compared with none (13.05% in = 5 comorbidities vs 0 in none p = 0.041) (Figure).
Conclusions: Comorbidities are very common in patients with CHF and should be aware of them and their treatment. There is a direct relationship between the number of comorbidities and mortality.

Prevalence of comorbidities in CHF

Variable	n = 248	%
Age (y), median IQR	64	54-72
Male gender	155	62.50
LVEF (%), median IQR	30	23-56
Arterial hypertension	108	43.37
Diabetes mellitus	78	31.33
Chronic kidney disease	69	27.71
Coronary heart disease	97	38.96
Sleep disorders	14	5.69
Previous or current neoplasia	15	6.02
Anemia	45	26.01
Reumatoid arthritis	1	0.40
Potasium disorders	7	4.76
Lung disease	25	10.04
Obesity	69	34.85

CHF: Chronic heart failure, IQR: Interquartile range, LVEF: Left ventricular ejection fraction



P410

Iron deficiency in patients with chronic heart failure.

M Smirnova[1]; P Chizhov[1]
[1]*Yaroslavl State Medical Academy, Department of Faculty therapy, Yaroslavl, Russian Federation*

Introduction: heart failure (HF) is an important community health problem. Prevalence and incidence of heart failure have continued to rise over the years. One of the most common co-morbidities in heart failure is presence of iron deficiency (ID) and anemia. ID affects up to 50% of HF patients, and is associated with poor quality of life, impaired exercise tolerance and higher risk of death. In the 2016 ESC guidelines for the diagnosis and treatment of HF, systematic measurement of iron parameters: serum ferritin and , transferrin saturation (TSAT) is recommended in all patients suspected of having HF. In these guidelines ID is defined as follows: 1) serum ferritin <100 mg/L (absolute iron deficiency), and 2) serum ferritin 100-299 mg/L and transferrin saturation <20% (functional iron deficiency).
Methods and Results: Serum concentrations of ferrum, ferritin and TSAT were assessed as the biomarkers of iron status in 209 patients with chronic systolic HF [age: 72,35 ± 7,04 years, men: 53, New York Heart Association (NYHA) class: 0/59/110/40] at a therapeutical departmet. All standart echocardiography and tissue Doppler echocardiography (TDE) were performed with GE Vivid 7 Medical System. Conventional measurments include left ventricle (LV) cavity dimentions, wall thickness, fraction ejection and transmitral flow velosities.
Results: patients with severe NYHA more often had many signs iron limitation of erythropoiesis (reduced haemoglobin, high red blood cells distribution width) (p <0,05). 65% patients were diagnosed with iron deficiency with low ferritin and TSAT. The level of iron and TSAT in the serum of patients with severe NYHA was significantly lower (p <0,05). The number of patients with absolute or functional ID elevates with increasing HF severity.
In patients with HF and ID were increased left ventricular cavity and reduced ejection fraction with increasing NYHA. Patients with severe NYHA with ID were observed a significant decrease of contractile ability of myocardium of the LV, which characterized low transmitral flow velosities in TDE. (p <0,05).
Conclusions: frequency of anemia becomes more higer with the increase of HF and were diagnosed most frequently in patients with NYHA 4. On the background of increasing in NYHA class there is a decrease in iron levels and hemoglobin levels, suggesting a possible latent iron deficiency in these patients. Iron deficiency in patients with HF is associated with reduced myocardial contractility. Therefore, successful management of co-morbidities ID is strongly recommended in addition to conventional therapy for HF.

P411

Relation between obstructive sleep apnea and right ventricular function

L Mathe[1]
[1]*IVth Medical Hospital, Tirgu-Mures, Romania*

Study objectives: to characterise relationships between right ventricular (RV) function and geometry and the obese and non-obese patients with obstructive sleep apnea.
Methods: Obese (n = 37, BMI 38,7+/- 7,3kg/m2) and non-obese (n = 23, BMI 24,7+/- 3,1 kg/m2) participants were founded with obstructive sleep apnea (OSA) by doing overnight polysomnography. OSA was characterized by the apnea-hypopnea index (AHI, events/hour). Function and geometry of the right heart were evaluated by tricuspid annular plane systolic excursion (TAPSE), tricuspid annular systolic velocity (TDI S'), RV myocardial performance index (TEI), RV end-diastolic (RVEDD) and end-systolic diameter (RVESD), area of the right atrium (RAA) ans systolic pulmonary artery pressure (PAPs).
Results: the 60 participants were mean 49 +/- years old (27% female). AHI was associated significantly with reduced TAPSE = 15 mm. Parameters of RV function (TAPSE 24,7 +/- 3,9 vs 24,9 +/- 3,7 mm; TDI S' 13,1 +/- 2,7 vs 13,6 +/- 2,9 mm/sec; TEI 0,23 +/- 0,11 vs 0,25 +/- 0,10) as well as geometry measurements were comparable between obese and non-obese participants with obstructive sleep apnea.
Conclusions: OSA is associated with reduced RV function. Echocardiographic measures of RV function appears to be less affected by obesity.

P412

Prevalence and prognostic value of anemia in patients with heart failure in south Indian state Kerala

A Gaskina[1]; R Rajesh[1]; S Villevalde[1]; Z Kobalava[1]
[1]*Peoples Friendship University of Russia (PFUR), Moscow, Russian Federation*

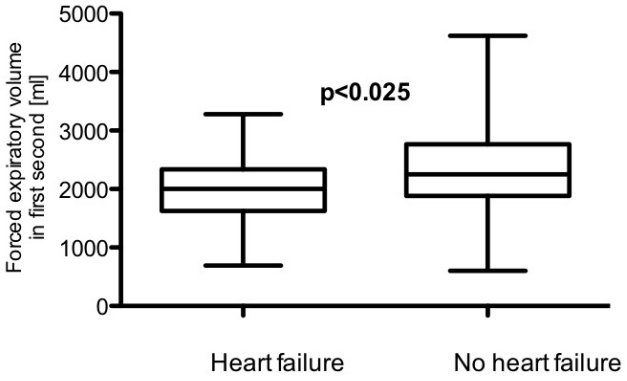
Aims: Anemia is a well-known serious comorbidity of heart failure (HF) associated with increased morbidity and mortality. The aim of the study was to evaluate the prevalence and prognostic value of anemia in patients with HF in south Indian state Kerala.
Methods: This is a single-center prospective observational study, conducted in Kerala institute of medical sciences a tertiary care hospital in the southern part of India. Patients admitted to hospital with clinical diagnosis of HF based on validated clinical criteria were included in the study. 203 patients with HF (102 male, 63,8 ± 10,1 years (M ± SD), arterial hypertension 81%, previous MI 77%, diabetes mellitus 58%, known chronic kidney disease (CKD) 28%, left ventricular ejection fraction (LV EF) (46,4 ± 14,3%) were examined. Anemia was defined as hemoglobin (Hb) < 13g/dl for males and < 12g/dl for females, based on World Health Organization definition. Mann-Whitney test and multivariate logistic regression analysis were performed. P < 0.05 was considered statistically significant.
Results: 104 (51%) patients with HF developed anemia. Patients with HF with versus without anemia were older (69 ± 13 vs 63 ± 12 years, p < 0.05), had higher baseline serum creatinine (SCr) (2,07 ± 1,15 vs 1,25 ± 0,48 mg/dl, p < 0.05), lower LV EF (37 ± 10 vs 41 ± 14%, p < 0.05). Anemia was more frequent (44.1%) in patient population with GFR = 60 ml/min/1.73 m2 (p = 0.0027). Patients with HF with versus without anemia had higher risk of 6 months rehospitalizations (59 vs 33%, p < 0.05).
Conclusions: Anemia in patients with HF and elective PCI developed in 51% of cases. Anemia in patients with HF was associated with older age, higher baseline SCr, lower LV EF. Anemia in patients with HF had negative impact on of 6 months rehospitalizations.

P413

Pulmonary function testing in heart failure patients

M Lainscak[1]; D Omersa[2]; J Farkas[1]
[1]*General Hospital Murska Sobota, Murska Sobota, Slovenia*; [2]*General Hospital Jesenice, Jesenice, Slovenia*

Background: Heart failure (HF) causes changes in pulmonary function tests that depend on volume status: restrictive pattern is observed in euvolemic patients whereas obstructive pattern is seen in volume overload. No recent studies investigated pulmonary function in HF population, characterized by echocardiography and natriuretic peptides.
Purpose: To investigate pulmonary function in HF and to evaluate influence of left ventricular function assessed by echocardiography and volume status assessed by natriuretic peptides.
Methods: The Screening Of adult urBan pOpulation To diAgnose Heart Failure (SOBOTA-HF) study is an ongoing cross sectional epidemiological study in Murska Sobota city residents aged 55 years or more. This interim report presents data for 702 participants of NT-proBNP screening; those with concentration = 125 pg/mL were invited for a detailed diagnostic visit that included echocardiography. HF diagnosis and left ventricular dysfunction were evaluated according to 2016 European Society of Cardiology guidelines. European Respiratory Society standards were used to evaluate pulmonary function.
Results: Overall, 339 participants completed diagnostic visit (age 70 ± 8 years, 35% men, NTproBNP 481 ± 936 pg/mL), 92 were diagnosed with HF and 9 had history of COPD. Average Tiffeneau index was 74 ± 9% and was < 70% in 106 participants with no higher incidence in HF patients (33% vs 31%). There was no significant correlation between Tiffeneau index and NT-proBNP, gender or age. HF and NT-proBNP significantly correlated with all other pulmonary test function parameters. Forced expiratory volume in first second was significantly lower in patients with HF (Figure).
Conclusions: In stable general population, HF and NT-proBNP are associated with lower volumes during pulmonary function testing but not with typical obstructive airway disease pattern.



P414

Utility of serum biomarkers for diagnosis of community-acquired pneumonia in patients with concomitant chronic heart failure

ZD Kobalava[1]; AA Bobylev[2]; SA Rachina[1]; SN Avdeev[3]; S Omar[1]; OT Zorya[1]
[1]RUDN University, Moscow, Russian Federation; [2]Inter-regional Association for Clinical Microbiology & Antimicrobial Chemotherapy, Smolensk, Russian Federation; [3]Sechenov University, Pulmonology Research Institute, Moscow, Russian Federation

Background: Diagnosis of community-acquired pneumonia (CAP) in patients with chronic heart failure (CHF) is associated with objective difficulties due to limited value of clinical signs/symptoms, routine laboratory and instrumental investigations.
Purpose: To assess the utility of serum biomarkers for diagnosis of CAP in patients with concomitant CHF.
Methods: Prospective observational study recruited adult hospitalized patients with suspected CAP and concomitant CHF. High-resolution chest computed tomography was used to differentiate CAP (group 1) and CHF decompensation (group 2). C-reactive protein (CRP), procalcitonin (PCT), interleukin-6 (IL-6), tumor necrosis factor a (TNFa), brain natriuretic peptide (BNP) levels were measured along with routine tests/procedures. Standard statistical tools were applied, p-value < 0.05 was considered statistically significant.
Results: Altogether 70 patients were enrolled. Groups were comparable regarding the main characteristics; only CRP, PCT and IL-6 levels were significantly higher in patients with proven CAP (table 1). AUC ROC (95% CI) was the highest for CRP - 0.91 (0.83-0.98), followed by PCT - 0.81 (0.72-0.90) and IL-6 - 0.81 (0.71-0.91). CRP value of 28.5 mg/L and IL-6 value of 27.6 pg/mL had optimal sensitivity and specificity ratio (85.7/91.4% and 82.9/71.4%, respectively). Substantial specificity reduction in sensitivity increase limited appropriate cutoff selection for PCT.
Conclusion: Serum inflammatory biomarkers such as CRP, PCT, and IL-6 can be useful to distinguish CAP and CHF worsening. It seems that CRP has the optimal diagnostic utility in this population.

Table 1. Comparison of patient groups

Characteristic	Group 1 (n = 35)	Group 2 (N = 35)	p value
Age, years/Females, %	73.9±11.4/68.6	75.1±8.7/62.9	NS
Cough, %	94.3	88.7	NS
Dyspnea, %	100	100	NS
Crepitation, %	94.3	85.7	NS
Body temperature, °C	37.0±0.6	36.6±0.5	0.0005
Chest X-ray, new infiltrates, %	80	91	NS
WBC, $\times 1000^3$/L	10.0±5.6	8.2±1.9	NS
CRP, mg/L*	74.3±55.9	17.6±11.8	<0.0001
PCT, ng/mL*	2.5±7.0	0.05±0.01	<0.0001
IL-6, pg/mL*	94.2±97.4	19.6±14.8	<0.0001
TNFα, pg/mL*	3.3±5.9	1.4±2.0	NS
BNP, pg/mL*	261.8±306.8	200.4±221.9	NS

*normal ranges: CRP 0-8; PCT < 0.1; IL-6 0-10; TNFa 0-6; BNP 0-100

P415

Markers of hypoxia and myocardial dysfunction and renal function in patients with acute decompensation of heart failure

EV Efremova[1]; AM Shutov[1]; ER Makeeva[1]; MV Menzorov[1]; ER Sakaeva[1]
[1]Ulyanovsk State University, Ulyanovsk, Russian Federation

Acute kidney injury (AKI) often complicates acute decompensated heart failure (ADHF). Early diagnosis AKI on the dynamics of serum creatinine and diuresis is difficult. That's why early diagnosis and predicting of AKI in patients with ADHF are relevant.
The aim of this study was to investigate factor-inducible hypoxia -1 (HIF-1) in patients with ADHF and the possibility of using it as a biomarker of AKI.
Materials and Methods: 84 patients (66 males, 18 females, mean age was 61,4 ± 7,1years) admitted to hospital with ADHF were studied. The main cause of ADHF was a combination of coronary artery disease and arterial hypertension.AKI was diagnosed according to the KDIGO Guidelines, 2012. ADHF was diagnosed and evaluated according to ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure, 2016. Comorbidity of patients with ADHF was c determined by Charlson comorbidity index (CCI). HIF-1, natriuretic peptide (NT-proBNP), erythropoietin were evaluated.
Results: The ??I was 6 (lower-upper quartiles: 4 - 8). The GFR was 59.8 ± 15.2 ml / min / 1.73 m2. AKI was diagnosed in 27 (32.1%) patients. In most cases, the first stage of AKI was observed (in 23 (27.4%) patients).HIF-1 was 1.27 ± 0.63 ng / ml, NT-proBNP was 2197.5 ± 1153.4 pg / ml, erythropoietin was 56,0 mIU / ml (lower-upper quartiles: 13,2 - 68,1) irrespective of AKI. A direct correlation was observed between the level of erythropoietin and the level of NT-proBNP (R = 0.44, p < 0.001).An inverse correlation was observed between GFR and the level of NT-proBNP (R = -0,51, ? = 0,005). However, there was no statistically significant association between the level of HIF-1 and GFR as well as the level of NT-proBNP and erythropoietin. Level of HIF-1 did not differ in patients with AKI and without AKI (1,21 ± 0,60 ng / ml vs. 1,30 ± 0,64 ng / ml, resp., p = 0.52).
Conclusion: AKI was diagnosed in every 3 patients with ADHF. Decreased kidney function is associated with the severity of heart failure (level of NT-proBNP). The factor-inducible hypoxia -1 (HIF-1) in patients with ADHF is not related to the kidney function.

P416

Profile of the elderly patient with heart failure admitted to cardiology department

D Daniel Enriquez Vazquez[1]; C Perez Garcia[1]; TS Luque Diaz[1]; A Travieso Gonzalez[1]; V Ruiz Pizarro[1]; C Espejo Paeres[1]; C Olmos Blanco[1]; D Vivas Balcones[1]; P Martinez Santos[1]; A Esteban[1]; J Higueras[1]; M Perez Serrano[1]; R Bover Freire[1]; I Vilacosta[1]; C Macaya[1]
[1]Hospital Clinic San Carlos, Cardiovascular Institute, Madrid, Spain

Background: Prevalence of heart failure (HF) has increased, due to the increased survival of patients. Elderly patient sometimes presents multiple comorbidities that must be taken into account when managing the patient with HF.
Purpose: The objective of this study is to know in depth this subgroup of patients more and more frequent in the usual clinical practice, as well as to study the management that is carried out in them.
Methods: Patients diagnosed with heart failure who were admitted to a cardiology department between July 2016 and March 2017 were registered prospectively and consecutively for one year.
Results: Of 336 patients analyzed, 150 patients were 80 years old or older. Baseline characteristics are summarized in Table 1. Heart rate at discharge was 81.65 vs 69.85 in those under 80 years of age. (p 0.024). In those with reduced LVEF, lower percentage of beta-blockers was used in the elderly patient (70.97% vs 84.26%, p 0.039) as well as ACE inhibitors or ARA2 (56.45% vs 72, 22%; p 0.036) and MRA (38.71% vs 62.04%; p 0.003). Devices use has been significantly lower, with 0% ICD vs 4.9% in the younger age group (p 0.007). Diuretic profile used was different, with greater use of thiazide in the elderly (6.35% vs. 1.83%, p 0.014).
Conclusion: Elderly patient with HF are mostly women, predominantly the group of HFpEF and risk factors. Drugs were used in a lower percentage according to the clinical practice guidelines, and the established objectives, such as the HR, was reached to a lesser extent, and further studies are necessary to determine the reasons for these differences. It is important to know the characteristics of this subgroup due to the increasing prevalence to improve the management of the elderly patient and improve their quality of life as well as prognosis.

Table 1

Characteristics	Elderly (>80 years)	Younger patients	p value
Mean age	84,69	68,76	<0,001
Male sex	59,3%	38,2%	<0,001
Hypertension	89,3%	75,8%	0,001
Hypercholesterolemia	68%	59,1%	0,094
Smoker	4%	14,5%	0,001
Alcohol consumption	13,9%	1,3%	<0,001
Atrial fibrillation	62,7%	48,4%	0,009
Dependent	22%	10,8%	0,019
Preserved EF	60,66%	44,62%	0,003
Diuretics at admission	69,84%	46,79%	0,003

P417

Comorbidity and prognosis in patients with chronic heart failure

EV Efremova[1]; AM Shutov[1]; ER Sakaeva[1]
[1]*Ulyanovsk State University, Ulyanovsk, Russian Federation*

Comorbidity determines the high mortality of patients with cardiovascular disease. The aim of this study was to investigate comorbidity, clinical and psychological characteristics and quality of life in patients with CHF and patients with CHF associated with chronic kidney disease (CKD).
Methods: 203 patients with CHF (130 males and 73 females, mean age was 61,8 ± 9,6 years) were studied. CHF was defined according to ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure, 2016. Glomerular filtration rate (GFR) was calculated using CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) formula and chronic kidney disease (CKD) was defined according to Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease, KDIGO 2012. Group of chronic cardiorenal syndrome (CRS) was included patients with CHF GFR < 60 mL / min / 1,73 m2 . Charlson comorbidity index was calculated. ?atients were followed up for 1 year. Psychological state, quality of life of patients with chronic cardiorenal syndrome were estimated.
Results: 89 (43,8%) patients had CKD with GFR < 60 mL / min / 1,73 m2 . CKD was the most frequent component in the structure of comorbidity of patients with CHF. Charlson comorbidity index for age was 5,0 ± 2,1 points. However, if we excluded CKD from Charlson comorbidity index. patients with CRS had a higher comorbidity (4.3 ± 1.8 vs 3.8 ± 1.7 points, resp.; p = 0.01). ?atients with CRS had a higher comorbidity. Relative risk of death of patients with high comorbidity was 1.68 (95% CI 1.35-2.09) compare with patients with low comorbidity. Patients with CRS were hospitalized due to exacerbation CHF more often than patients without CRS (1.3 ± 0.48 and 1.0 ± 0.14, resp., p = 0.01).. Patients with CRS had expressed emotional discomfort, the presence of depressive, disadaptive trends, decreased of quality of life, both in the physical and the psychological aspects.
?onclusion. CKD has a negative impact both in the clinical course and quality of life, psychological status and prognosis of patients with CHF . At the same time, patients with CRS have a high comorbidity, they are characterized by the presence of hypochondria and depression and low quality of life, which should be taken into account in the development of guidelines for the diagnosis and treatment of this group and assessment of prognosis.

P418

Heart failure and atrial fibrillation

O A Otilia Tica[1]; O Tica[2]; L Rosan[1]; MI Popescu[1]
[1]*University of Medicine of Oradea, Cardiology, Oradea, Romania*; [2]*University of Medicine of Oradea, Oradea, Romania*

Introduction: Heart failure (HF) and atrial fibrillation (AF) are two epidemics found in many patients in current daily practice. They share common risk factors and have similar pathophysiology triggers.
Purpose: The difficulty is in identifying those patients in whom AF is simply a coexisting condition and those in whom AF is an important marker in quality of life, ventricular function and long-term mortality.
Methods: A total of 318 patients admitted consecutively in our clinic were evaluated during hospitalization and after discharge periodically. Patients included had the discharge diagnosis from our clinic: heart failure and atrial fibrillation. The patients were divided into 2 groups, according their condition: if they have HF and developed AF, or have AF and developed HF. The follow-up period of 1.8 years performed included surveillance, blood test (including biomarkers) and a cardiological examination (EKG, ecocardiography and clinical examination).
Results: In our study 76 (23.89%) patients have paroxismal AF, 73 (22.95%) have persistent AF, 74 (23.27%) patients have long standing persistent and 95 (29.87%) have permanent AF. A number of 127 (39.93%) of patients developed HF first, 122 (38.36%) of patients developed AF first, and in 69 (21.69%) AF and HF occurred at the same time. The mean age is 67.4 (SD: 3.6 years; p < 0.001). Patients with higher value of NTproBNP (mean value is: 7482, SD: 3761; p>0.001) have a worse prognosis. The mean left ventricular ejection fraction is: 41, SD: 27, p < 0.02. Patients with lower ejection fraction have worse outcomes. In our study group, we had a mortality rate of 3.50% (sudden cardiac death were also included in these numbers).
Conclusion: New-onset AF in patients with established HF is proven to be an ominous sign, because it is both a sign of affected patients and because it impairs cardiac function. Patients with HF and permanent AF have a worse outcome than those in sinus rhythm, although this can be explained by age progression and HF severity.

P419

High-sensitivity cardiac troponin T and N-terminal pro-B-type natriuretic peptide in patients with hypertrophic cardiomyopathy.

M Mariusz Klopotowski[1]; K Kukula[1]; M Dabrowski[1]; A Kwapiszewska[1]; J Jamiolkowski[2]; M Spiewak[1]; Z Chmielak[1]; A Witkowski[1]
[1]*National Institute of Cardiology, Warsaw, Poland*; [2]*Medical University of Bialystok, Bialystok, Poland*

Background: High-sensitivity cardiac troponin T (hs-cTnT) and (NT-proBNP) are established biomarkers in heart failure and predict clinical outcome in patients with hypertrophic cardiomyopathy (HCM).
Aim: To assess the association between hs-cTnT or NT-proBNP and a number of demographic, clinical and echocardiographic parameters in patients with HCM.
Methods: 419 clinically stable outpatients (292 men; aged 46.7 ± 13.5 years) with HCM were included. High sensitivity troponin T and NT-proBNP measurements were performed using commercially available electro-chemiluminescence kits routinely used for diagnostic purposes during scheduled outpatient visits .
Results: The median NT-proBNP level was 659 pg/ml (IQR 288.5 - 1602.5 pg/ml). Abnormal NT-proBNP level (<125 pg/ml) was observed in 363 (86.6%) patients.
Multivariate analysis revealed an independent relationship between abnormal NT-proBNP plasma level and age (OR 1.06, 95% CI 1.02 - 1.09, p = 0.001), presence of non-sustained ventricular tachycardia (OR 3.22, 95% CI 1.51 - 6.87, p = 0.002), maximum left ventricle wall thickness (OR 1.33, 95% CI 1.21 - 1.45, p < 0.001), history or presence of atrial fibrillation (OR 3.92, 95% CI 1.22 - 12.59, p = 0.022), syncope in the past (OR 0.43, 95% CI 0.20 - 0.96, p = 0.038), and BMI > 25 kg/m2 (OR 0.28, 95% CI 0.13 - 0.63, p = 0.002)
NT-proBNP level was significantly correlated with age (r = 0.10, p = 0.038), left atrium diameter (r = 0.30, p < 0.001), maximum left ventricular wall thickness (r = 0.33, p < 0.001), maximal left ventricle outflow tract gradient (r = 0.13, p = 0.007), BMI (r = - 0.12, p = 0.016), and left ventricle ejection fraction (r = - 0.18, p < 0.001).
The median hs-cTnT level was 11 ng/ml (IQR 4 - 20 ng/ml). Abnormal hs-cTnT level (<14 ng/ml) was observed in 153 (36.5%) patients.
Multivariate analysis revealed an independent relationship between abnormal hs-cTnT level and maximum left ventricular wall thickness (OR 1.08, 95% CI 1.04 -1.12, p < 0.001), left atrium diameter (OR 1.05, 95% CI 1.02 - 1.09, p = 0.001), and left ventricle ejection fraction (OR 0.92, 95% CI 0.89 - 0.94, p < 0.001)
hs-cTnT level was significantly correlated with left atrium diameter (r = 0.22, p < 0.001), maximum left ventricular wall thickness (r = 0.24, p < 0.001), and left ventricle ejection fraction (r = - 0.19, p < 0.001).
Conclusions: Increased left ventricular wall thickness, LA diameter and lower left ventricle ejection fraction were independently associated with abnormal both NT-proBNP and hs-cTnT.

P420

Heart failure patients with depression do not only have higher symptom occurrence but also higher symptom burden

J C Van Den Berge[1]; LC Van Vark[1]; E Boersma[1]; HL Hillege[2]; I Lesman-Leegte[2]; KM Akkerhuis[1]
[1]*Erasmus Medical Center, Department of Cardiology, Rotterdam, Netherlands*; [2]*University Medical Center Groningen, Department of Epidemiology, Groningen, Netherlands*

Background: Heart failure (HF) patients with depression have higher New York Heart Association (NYHA) class than those without depression. It is unknown whether this difference might be explained by higher symptom occurrence, higher symptom burden or both.
Purpose: To compare symptom occurrence and symptom burden in HF patients with and without depression.

Methods: This Dutch multicenter study prospectively included acute HF patients. Depression was defined as = 8 points on the depression scale of the Hospital Anxiety and Depression Scale (HADS). At discharge, we asked patients to complete a questionnaire with 11 questions about HF-related symptoms. Patients were questioned on the presence (yes/no) and the burden (score 1-10) of those symptoms.
Results: We included 324 patients (72 years, 65% male, 37% depression) who completed the HADS questionnaire at discharge. Among patients with depression, NYHA class III/IV was significantly more common than in those without (57% vs. 33%, p < 0.001). Moreover, the majority of the 11 HF-related symptoms were more often present in depressive patients than in patient without depression (Table). Furthermore, patients with depression also reported higher symptom burden for most of the symptoms.
Conclusion: HF patients with depression had worse NYHA class than those without depression. Importantly, patients with depression had higher symptom occurrence and symptom burden. Therefore, both these factors may declare the difference in NYHA classification in HF patients with and without depression.

Table. Symptom occurrence and burden

	Symptom occurrence			Symptom burden		
	Depression +	Depression -	p value	Depression +	Depression -	p value
1. Ankle edema when you got out of bed	75 (69)	103 (52)	0.004	7 (6-8)	6 (4-8)	0.08
2. Ankle edema during the day	77 (71)	111 (57)	0.02	7 (6-8)	7 (5-8)	0.04
3. Troubles with falling asleep	69 (61)	112 (56)	0.41	8 (7-10)	7 (6-8)	<0.001
4. Troubles with sleeping through	95 (84)	134 (69)	0.003	8 (6-9)	7 (6-8)	<0.001
5. Decreased appetite	72 (63)	82 (43)	0.001	7 (6-8)	6 (6-8)	0.23
6. More fatigue than before	108 (95)	160 (81)	0.001	8 (7-9)	7 (6-8)	<0.001
7. Shortness of breath at rest	78 (68)	97 (50)	0.002	7 (6-9)	7 (6-8)	0.12
8. Dyspnoea d'effort	112 (97)	179 (92)	0.047	9 (8-10)	8 (6-9)	<0.001
9. Orthopnoea	82 (71)	112 (56)	0.01	8 (7-9)	7 (6-9)	0.07
10. Cough	82 (71)	127 (64)	0.21	7 (6-9)	7 (5-8)	0.01
11. Dry cough	65 (57)	89 (45)	0.04	7 (6-8)	7 (5-8)	0.01

Data on symptom occurrence reported as N (%); data on symptom burden reported as median (IQR).

P421

Role of Integrated approach of pharmacological plus non pharmacological therapy in severe chronic heart failure patients.

N Sen[1]; SONAL Tanwar[2]; ASHOK Jain[1]
[1]Narayana Hrudayalaya, Cardiology, Jaipur, India; *[2]HG SMS Hospital, Cardiology, Jaipur, India*

Background: Studies revealed non pharmacological therapy consisting of yoga, meditation ,exercise and education training, in combination with diet counselling ,stress management , Enhanced external counter pulsation machine (EECP) have good role to prevent worsening heart failure
Aim: Integrative program with focus on Integrated Medicine with life style intervention in patients with severe chronic heart failure and beneficial outcome of integrated approach.
Methods: The Observational study a 3-year outpatient : A total of 202 middle-aged men and women, chronic heart failure with Hypertension, dyslipidemia, type 2 Diabetes mellitus and obesity were enrolled. The usual care (routine allopath medicines) group A(n = 106) and the integrated approach(allopathy plus non pharmacological) with life style interventional group B (n = 96). For Group B- Education, Exercise: supervised endurance and yoga , meditation with restricted diet and aerobics: three times a week for three months with Enhanced external counter pulsation machine (EECP) four cycle weekly for 5 months.
Results: Proposed lifestyle improved after year 3 in the group A over group B. There were significant differences between groups, mean changes (and their 95% confidence intervals, CI) in waist circumference pv0.001), in waist–hip ratio p < 0.01) , decrease in HR (p < 0.01), systolic BP (p < 0.01) and diastolic BP(p < 0.05) blood cholesterol and sugar, HBA1C level . Recurrent hospitalization with congestive heart failure (CHF) in group A = 23/106, group B = 7/96(p < 0.03) . Atrial fibrillation in group A = 12/106, group B = 3/96 (p < 0.08).Ventricular tachycardia in group A = 8/106, group B = 3/96(p < 0.23). Death in group A = 18/106, group B = 6/96(p < 0.36).Post MI-CHF in group A = 9/106, group B = 3/96(p < 0.36). Post CABG-CHF in group A= 8/106, group B = 2/96.
Conclusion: Regular 3-year follow-up improvements in quality of life, decrease stress, decrease incidence of cardio-vascular events , improve Exercise Score, better reduction of heart rate, blood pressure, weight, waist circumference, three to four time decrease episodes of recurrent hospitalization , Cardiac Arrhythmias and 33% reduction of cardiovascular mortality in integrated group as compare to usual group.

P422

Comparison of depression, anxiety and perceived stress scores between patients with cardio-respiratory failure with and without cognitive impairment

M Monica Rivera Rodriguez[1]; V Pelaez-Hernandez[1]; A Orea-Tejeda[1]; A Figueroa-Herrera[1]; D Gonzalez-Islas[1]; C Chavez-Mendez[1]; C Olivo-Villalobos[1]; G Davila-Said[1]; L Castillo-Aguilar[1]; S Torres-Montiel[1]; E Perez-Cabanas[1]; R Sanchez-Santillan[1]; K Balderas-Munoz[1]
[1]Instituto Nacional de Enfermedades Respiratorias "Ismael Cosio Villegas", Heart Failure and Respiratory Distress Clinic, Mexico City, Mexico

Background: Heart failure (HF) patients have high levels of anxiety, depression and perceived stress, which may be linked with cognitive impairment in many cases. However, there is no information about patients with cardio-respiratory failure, who have major oxygenation tissue problems, which affects the brain and its functions, including those cognitive and emotional.
Objective: The purpose of this study was compare anxiety, depression and perceived stress scores between patients with cardio-respiratory failure with and without cognitive impairment.
Material and Methods: A cross-sectional study was realized. Sixty-six patients with of cardio-respiratory failure were included heart failure NYHA I-III and chronic obstructive pulmonary disease (COPD), GOLD 1-3. All participants were evaluated with the following tests: a) Hospital Anxiety and Depression Scale (HADS), with 14 items to evaluate anxious and depressive symptomatology; b) Perceived stress scale in the 10 items version, and c) Montreal Cognitive Assessment (MOCA) alternate mexican version 7.2 to determine the presence of cognitive impairment if the score is less or equal to 26 points. According to the MOCA, the participants were divided into two groups: Group 1 (G1, n = 8): without cognitive impairment, and Group 2 (G2, n = 58), with cognitive impairment. The data was analyzed with SPSS v. 21 for Windows, data didn't present a normal distribution, so the U Mann Whitney test was used.
Results: Cognitive impairment was found in the 87.87%. There were no differences in the socio-demographic variables between both groups. Patients with cognitive impairment have major scores of anxiety (G1: 3.88 ± 1.959, G2: 5.47 ± 4.168, p < 0.05) and depression (G1: 4 ± 2.777, G2: 5.97 ± 4.176, p < 0.05) according to the HADS; besides of a major perceived stress (G1: 18.50 ± 5.155, G2: 23.36 ± 6.282, p < 0.05).
Conclusions: Patients with cardio-respiratory distress has a high prevalence of cognitive impairment and poor quality of life (more anxiety and depression). The interdisciplinary evaluation and intervention as part of non pharmacological treatment is necessary.

P423

Do inflammation-associated biomarkers differ between men and women in prediction of new-onset heart failure ?

L Meems[1]; N Suthahar[1]; SJ Bakker[2]; RT Gansevoort[2]; WH Van Gilst[1]; P Van Der Harst[1]; RA De Boer[1]
[1]University Medical Center Groningen, Experimental Cardiology, Groningen, Netherlands; *[2]University Medical Center Groningen, Groningen, Netherlands*

Background: Heart failure (HF) is a heterogeneous condition that may result from various etiologies. It has become apparent that the etiology of HF in men and women is different, and chronic inflammation has been suggested to be more prominent in men. We therefore evaluated the clinical and biochemical association of inflammatory biomarkers in both sexes, and studied the associationwith new-onset HF in males and females.
Purpose: Our aim is to identify and validate in a sex-specific manner if inflammatory biomarkersdiffer between men and women, and increase our knowledge and understanding of sex differences for new onset HF.

Methods: Sex-specific new-onset HF was analysed in 7954 participants (4014 females) from the Prevention of Renal and Vascular End-stage Disease (PREVEND) cohort (free of heart failure). Baseline plasma levels of biomarkers are presented as medians (IQR). To test differences at baseline, we used Wilcoxon rank sum test, as fitted for skewed variables. Predictive value of inflammatory biomarkers (copeptin (CP), procalcitonin (PCT), plasminogen activator inhibitor (PAI)-1, Galectin (Gal)-3 and C-reactive protein (CRP)) for sex-specific new onset HF was determined by Cox regression analysis, using a multivariable model that corrects for age, eGFR, BMI, smoking, systolic blood pressure, serum glucose and plasma cholesterol. P-values < 0.05 were considered significant.
Results: There were 341 cases of new-onset heart failure. At baseline, males (M) had significantly higher plasma levels of biomarkers related to endothelial vascular damage (PAI-1: 83.5 (49.7, 136,4) vs. females (F) 60.3 (34.5, 109.9), $p < 0.001$; PCT: 1.8 (1.5,2.2) vs. F 1.4 (1.2,1.7), $p < 0.001$; CP: 6.2 (4.0, 9.4) vs. F 3.6 (2.4, 5.6), $p < 0.001$). F had higher levels of biomarkers representing macrophage and T-cell activation (Gal-3: 11.0 (9.1, 13.4) vs. M 10.6 (8.9, 12.7), $p < 0.001$; CRP: 1.33 (0.56,3.27) vs. M 1.22 (0.54, 2.72), $p < 0.001$). Nevertheless, none of the biomarkers was able to predict sex-specific new onset HF: PAI-1 M HR 1.02 (0.83-1.25): vs. F 1.16 (0.89-1.52); CRP M HR 1.10 (0.92-1.32)vs. F 1.14 (0.94-1.39); Gal-3 M HR 1.38 (0.87-2.18)vs. F HR 0.94 (0.52-1.68); PCT M HR 0.91 (0.59-1.39)vs. F HR 1.19 (0.75-1.88); CP M HR 0.92 (0.66-1.27)vs. F HR: 0.88 (0.66-1.16), p = ns for all.
Conclusion: In this study, we demonstrate that levels of inflammatory markers significantly differ in males and females. Nonetheless, none of these biomarkers displayed differential utility for predicting new-onset HF in both males and females. Future studied are needed to better understand the pathophysiological meaning of this interesting finding.

P424
Impaired skeletal muscle mitochondrial and metabolic function in patients with heart failure with preserved and reduced ejection fraction compared to healthy controls and its impact on muscle function

T Bekfani[1]; M Bekhite Elsaied[2]; SD Derlien[1]; A Hamadanchi[1]; J Nisser[2]; E Froeb[1]; D Haase[1]; T Kretzschmar[1]; UC Smolenski[2]; G Lehmann[3]; G Wolf[3]; SD Moebius-Winkler[1]; PC Schulze[1]
[1]University Hospital of Jena, Department of Cardiology, Jena, Germany; *[2]University Hospital of Jena, Institute of Physiotherapy, Jena, Germany*; *[3]University Hospital of Jena, Department of Endocrinology, Nephrology and Rheumatology, Jena, Germany*

Purpose: To elucidate exercise capacity, muscle strength and Quality of life (QoL) and the associated gene expression regulating metabolic, mitochondrial and structural characteristics among symptomatic and clinically stable outpatients with heart failure (HF) with both preserved (HFpEF) and reduced ejection fraction (HFrEF) and age-matching healthy controls (HC).
Methods: 55 participants were recruited prospectively at the University Hospital Jena: 19 HFpEF, 18 HFrEF, 18 HC (Age: 71 ± 6 vs. 68 ± 9 vs. 66 ± 7 years; sex (m/f): 8/11 vs. 15/3 vs. 7/11; BMI: 28.5 ± 4.6 vs. 27.9 ± 5.3 vs. 26.1 ± 4.3 kg/m2, respectively). All participants underwent standardized tests including echocardiography, cardiopulmonary exercise test (CPET), 6-minute walk test (6MWT), muscle function tests, blood tests, QoL assessment as well as muscle biopsies from the vastus lateralis muscle. Real-time polymerase chain reaction (Real-time-PCR). Total RNA was prepared. Expression levels of genes for carnitine palmitoyl transferase IB (CPT1B), Mitofusin (Mfn2), medium-chain acyl-CoA dehydrogenase (ACADM), RAC-beta serine/threonine-protein kinase (Akt2), peroxisome proliferator-activated receptor alpha (PPARa) were measured by Real-time PCR.
Results: Markers of oxidative fatty acid metabolism (CPT1 and ACADM) were reduced in skeletal muscle of patients with HFpEF and HFrEF compared to HC ($p = 0.001$ and 0.03 respectively) suggesting impaired transport of long chain fatty acids and reduced fatty acid oxidation. Further, MFN2 decreased in HFpEF and HFrEF patients compared to HC ($p = 0.001$). The expression of Akt2 and PPARa was found to be suppressed in HFpEF patients compared to HFrEF patients and to HC ($p = 0.001$, $p = 0.0001$, respectively). Levels of PPARa and MFN2 correlate with exercise capacity assessed by peak VO2 ($p = <0.001$, $r = 0.67$, $p = 0.007$ $r = 0.46$). Higher levels of PPARa were associated with higher values of muscle strength and QoL (peak torque right leg/muscle mass right leg: $p = 0.03$, $r = 0.38$; VAS-Score: $p = 0.01$, $r = 0.5$).
Conclusion: Patients with heart failure both with preserved and ejection fraction show impaired exercise capacity, muscle strength and quality of life and evidence of distinct abnormalities of mitochondrial and metabolic function in skeletal muscle compared to HC. These changes were found more pronounced in patients with HFpEF suggesting additional impairments of muscle function and oxidative capacity.

Chronic Heart Failure - Other

P425
Long-term changes in left ventricular ejection fraction depending on the type of heart failure

R Raquel Lopez Vilella[1]; D Carrillo Gomez[1]; J Perez Gozalbo[2]; I Sanchez Lazaro[1]; L Martinez Dolz[1]; L Almenar Bonet[1]
[1]Hospital Universitario y Politécnico La Fe, Heart Failure and Transplant Unit. Cardiology Department, Valencia, Spain; *[2]Hospital Dr. Peset, Cardiology Department, Valencia, Spain, Valencia, Spain*

Background and objective: Left ventricular ejection fraction (LVEF) classifies the type of heart failure (HF). Three types are defined in European guidelines for HF (preserved LVEF (HFpEF) = 50%, reduced LVEF (HFrEF) < 40% and mid-range (HFmrEF) 40-49%). This classification has been shown to be non-rigid, with an exchange between the three groups. How many patients change groups during their long-term evolution is not known. The purpose of this study is to know the distribution of the type of HF and its changes in a prolonged period of time.
Methods: We recruited 249 consecutive outpatients with the clinical diagnosis of HF attended in a tertiary hospital between 2012 and 2014. We excluded patients without echocardiographic studies performed in the center and patients with poor acoustic echocardiography window, those who had less than 3 months of admission for any cause and those who suffered some degree of clinical instability. We analyzed general clinical variables and etiology of HF (ischemic, non-ischemic heart disease, hypertension, valvular heart disease and others). Information on LVEF was included at the beginning and the last echocardiographic control available.
Results: From the 249 patients of the registry, 168 had LVEF initial and follow-up by echocardiography. The median age was 64 years (interquartile range [IQR] 52.5-72), 38.69% were women. The main associated comorbidities were 41.07% hypertension, diabetes mellitus 29.17%, dyslipidemia 78.20%, and 26.79% chronic kidney disease. The mean time of follow-up until the last echocardiographic control was 3.4 years (IQR 1.86-4.61). At the beginning of the study, there were 61.90% of patients with HFrEF, 7.14% HFmrEF (12/168) and 30.95% HFpEF (Table). In the last echocardiographic control, 50.60% were HFrEF, 12.5% HFmrEF and 36.90% HFpEF. 30.09% of patients with HFrEF because of dilated cardiomyopathy changed to HFpEF, 41.03% of ischemic, and 41.03% of those of valvular etiology. The overall percentage change in the category was 60.71% (102 of 168 patients). Of the total number of patients who changed, 33% had ischemic etiology, 26% had a valvular disease, 21% had idiopathic dilated cardiomyopathy, and 1.96% had hypertensive cardiomyopathy. If we divide by subgroups according to etiology, 43% of patients with dilated cardiomyopathy changed category, 65% of patients with ischemic heart disease, 73% of patients with valvular heart disease and 67% of patients with hypertensive heart disease ($p = 0.034$). The type of HF in which the most change of category of LVEF is produced is the HFmrEF, with 92% of patients that change the category of LVEF in the follow-up.
Conclusions: The most frequent etiology of HF depends on the type of HF. Staying in a group (HFrEF, HFrEF, HFmrEF) is a variable concept. The overall percentage of exchange can be relevant. The etiology that presented the most variation was valvular and hypertensive. The type of HF that suffered the most exchange was HFmrEF.

P426
Potential substitution of chronic heart failure care according to the 'Landelijke Transmurale Afspraak' (LTA)

MPM Marijke Vester[1]; SLMA Beeres[1]; LF Tops[1]; CMHB Lucas[2]; PEJ Van Pol[2]; MJ Schalij[1]
[1]Leiden University Medical Center, Cardiology, Leiden, Netherlands; *[2]Rijnland Hospital, Cardiology, Leiderdorp, Netherlands*

Background/Introduction: The prevalence of chronic heart failure is increasing due to improved medical and invasive treatment. The Dutch "national transmural agreement" (LTA) heart failure, agreed upon in 2015, aims to optimize the organization of heart failure care in the Netherlands.
Purpose: To evaluate the proportion of patients in which heart failure care can be transferred from the cardiologist to the general practitioner (GP), based upon the LTA.
Methods: A total of 200 heart failure patients (100 from a secondary and 100 from a tertiary care hospital) were evaluated at the out-patient clinic. In line with the LTA, the following patients were considered eligible for referral to the GP: 1/ Stable heart failure patients with preserved ejection fraction (HF-pEF), 2/ Stable heart failure patients with mid-range ejection fraction (HF-mEF) and 3/ Stable heart failure patients with a recovered HF-rEF (LVEF>50%).
Results: The population consisted of 57% male and mean age was 72 ± 15 years. In total, 17% of patients were considered eligible for referral to the GP. It concerned

1.5% patients with HF-pEF, 5.0% patients with HF-mEF and 10.5% patients with recovered HF-rEF. The main indications for heart failure care by a cardiologist were: recent admission for decompensated heart failure (29.5%), recent adjustment in heart failure medication (7.5%) or active cardiac disease other than heart failure (39.5%).

Conclusion: In a substantial amount of patients heart failure care can be transferred to the GP.

Subdivision heart failure patients

	Total (n = 200)	Center A (n = 100)	Center B (n = 100)	P-value
Indications secondary care				0.068
1. Unstable heart failure	74	30	44	0.040
2. Stable heart failure, active CD, LVEF <50%	53	34	19	0.016
3. Stable heart failure, active CD, LVEF >50%	26	12	14	0.674
4. Stable heart failure, no active CD, LVEF >40% or a comorbidity	13	7	6	0.774
Potential substitution				0.559
5. Stable heart failure, no active CD, preserved LVEF	3	2	1	0.561
6. Stable heart failure, no active CD, mid-range LVEF 40-50%	10	6	4	0.516
7. Stable heart failure, no active CD, recovered LVEF	21	9	12	0.489

No significant differences were observed. Unstable heart failure was the main indication for follow up at secondary care in center B, whereas an active cardiac device was the main indication in center A. CD: Cardiac Disease; LVEF: Left Ventricular ejection Fraction

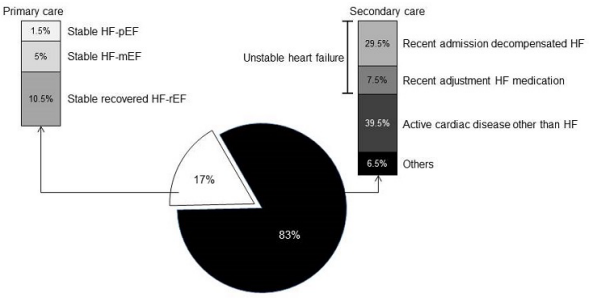


Fig. 1. Overview of patients who were eligible for referral to primary care (17%) and for who treatment by cardiologist was justified (83%) based on the 'Landelijke Transmurale Afspraak. Others includes a comorbidity or a left ventricular ejection fraction <40%. HF-pEF = Heart Failure with preserved ejection fraction; HF-mEF = Heart Failure with a mid-range ejection fraction; HF-rEF = Heart Failure with a reduced ejection fraction.

Overview of patients based on the LTA

P427

The role of right ventricular function on peak VO2 after VAD implantation in end stage heart failure patients.

PHT Timmermans[1]; L Fresiello[2]; R Buys[3]; K Vandersmissen[2]; A Belmans[4]; W Droogne[1]; F Rega[2]

[1]University Hospitals (UZ) Leuven, Cardiology, Leuven, Belgium; [2]University Hospitals (UZ) Leuven, Cardiac surgery, Leuven, Belgium; [3]University of Leuven, Rehabilitation Sciences, Leuven, Belgium; [4]University of Leuven, Biostatistics and statistical bioinformatica, Leuven, Belgium

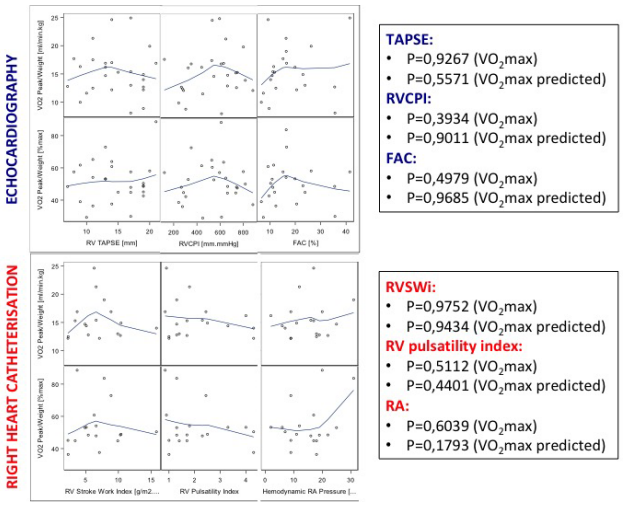
Introduction: Continuous flow LVAD therapy is not only able to improve survival in end-stage heart failure patients, but also improve excercise capacity. However, maximum excercise capacity is typically limited to around 50% of predicted VO2 max. The role of the right ventricular function on excercise capacity in VAD patients is not clear.

Purpuse: We evaluated the role of systolic RV function on excercise capacity, assessed by ergospirometry, in end-stage heart failure patients on VAD therapy.

Methods:28 patients (22 men and 6 women, mean age 54y) with end stage HF and continuous flow VAD implantation (27 HM 2, 1 HVAD) were recruted for his study, and gave written consent to participate. VAD as destination therapy and perioperative RV failure requiring temporary RV mechanical support were exclusion criteria for this analysis. All patients included underwent 3 months of ambulatory cardiac rehabilitation. All ergospirometries were conducted 4 months after device implantation. RV function was assessed pre-VAD implantation, using echocardiography parameters (TAPSE, FAC, RVCPI, PAPsystole, CVP estimations) and, if feasible, invasive measurements (full right heart catheterisation parameters and calculated vaules for right ventricular stroke work index and RV pulsatility index).

Results: Mean peak VO2 max was 15,4 ± 4,1 ml/kg.m2 or 53 ± 14% of predicted maximum, and ergospirometry parameters were compatible with cardiac limitations (mean VeVCO2 slope 42). Echocardiography was of acceptable quality to assess functional RV parameters in 26 patients (mean TAPSE 14 ± 4 mm, mean FAC 18 ± 10%, mean RVCPI 531 ± 207 mm.mmHg). Right heart catheterisation parameters were available in 18 patients (RA 15 ± 7 mmHg, mean PAP 38 ± 11 mmHg, PCWP 29 ± 9 mmHg, CI 1,7 ± 0,4 L/min.m2). Right ventricular function calculations showed a mean RV stroke work index 6,9 ± 3,5 g/m2.stroke and a mean RV pulsatily index of 2,1 ± 1,2. There was no significant correlation between any echocardiographic or invasively measured parameters of RV function (see figure).

Conclusion: There is no correlation between RV function pre-VAD implantation and VO2 max 4 months later in end-stage HF patients. Altough all patients participated in cardiac rehabilitation, mean peak VO2max was still only 53% of predicted maximum. We hypothesis that excercise capacity in patients with the of the VAD devices tested in our population is limited to the maximum output (liter per minute) these devices can generate, rather than residual right ventricular function. Further research supporting this statement is needed to further improve functional outcomes for these patients.



RV function and VO2 max correlation

P428

Differences in heart rate variability to emotional stimuli between patients with cardiorespiratory failure who suppress or reappraise their emotions

F A Figueroa Herrera[1]; V Pelaez-Hernandez[1]; M Rivera-Rodriguez[1]; SC Torres-Montiel[1]; A Orea-Tejeda[1]; D Gonzalez-Islas[1]; C Olivo-Villalobos[1]; G Davila-Said[1]; C Chavez-Mendez[1]; RN Sanchez-Santillan[1]; L Castillo-Aguilar[1]; AG Navarrete-Penaloza[1]; L Verdeja-Vendrell[1]; A Jimenez-Cepeda[1]

[1]Instituto Nacional de Enfermedades Respiratorias "Ismael Cosio Villegas", Heart Failure and Respiratory Distress Clinic, Mexico City, Mexico

Background: The management of emotions modifies the autonomic activity of healthy people and patients with cardiovascular diseases. On one hand healthy people that suppress their emotions show a decrease in heart rate variability (HRV). On the other hand, expressing and reappraising emotions have positive consequences for health. However, the effects that expression and suppression have on the HRV of patients with cardiorespiratory failure (CRF) are unknown.

Objective: To compare HRV to pleasant and unpleasant emotional stimuli during processes of expression and emotional suppression between patients with CRF that suppress or reappraise their emotions.
Method: A cross-sectional study was conducted in 18 patients with CRF. They were classified according to the Emotional Regulation Questionnaire into two groups: 1) Suppressors (G1, n = 10, 75.10 ± 8.76 years, 80% women) and 2) Reappraisers (G2, n = 8, 67.25 ± 10.33, 75% men). All the participants were evaluated with two psychophysiological profiles of 20 minutes each, one showed positive emotional images and the other negative. Each profile was divided into Baseline 1 (LB1), Expression (Ex), Inhibition (In) and Baseline 2 (LB2). In LB1 and LB2 neutral images were shown, in Ex and In the emotions evoked by the stimuli were respectively experienced or inhibited. The HRV was recorded in its bands of very low (VLF), low (LF) and high (HF) frequencies. The Mann-Whitney U test was applied to determine differences in the HRV, using SPSS version 21 for Windows,
Results: There were no statistically significant differences (p> 0.05). However, clinically there is a decrease in HRV in the G1 group compared to the G2.
Negative (BL1|Ex|In|BL2)
VLF (G1/G2): 19.87 ± 17.33 / 14.80 ± 13.08 | 20.76 ± 13.88 / 12.81 ± 12.15 | 22.74 ± 15.53 / 11.76 ± 9.77 | 21.43 ± 16.64 / 16.97 ± 14.78
LF (G1/G2): 26.07 ± 14.83 / 18.67 ± 11.63 | 25.36 ± 12.51 / 20.30 ± 10.66 | 26.67 ± 14.80 / 17.29 ± 10 | 22.75 ± 10.57 / 20.59 ± 13.33
HF (G1/G2): 42.73 ± 19.85 / 47.18 ± 14.34 | 43.25 ± 17.63 / 46.38 ± 16.18 | 40.50 ± 20.48 / 52.28 ± 9.62) | 42.81 ± 18.88 / 39.30 ± 11.13
Positive (BL1|Ex|In|BL2)
VLF (G1/G2): 31.13 ± 20.28 / 22.90 ± 8.22 | 22.87 ± 14.33 / 24.83 ± 12.61 | 28.34 ± 17.10 / 30.50 ± 20.36 | 22.13 ± 19.79 / 21.95 ± 8.20
LF (G1/G2): 25.13 ± 11.37 / 25.57 ± 10.81 | 28.11 ± 9.92 / 25.78 ± 7.04 | 27.14 ± 8.14 / 20.33 ± 6.44 | 23.97 ± 12.59 / 24.10 ± 7.26
HF (G1/G2): 36.87 ± 17.57 / 41.74 ± 11.50 | 40.57 ± 17.20 / 40.04 ± 10.81 | 36.72 ± 16.96 / 38.34 ± 13.72 | 39.46 ± 18.71 / 43.57 ± 5.47
Conclusion: Emotional suppression produces diminution of HRV in both expression and emotional inhibition, with greater magnitude in suppressive patients, translating into autonomic dysregulation before emotional stimuli and a risk factor for patients. Pleasant emotional stimuli have a positive effect on HRV. An interdisciplinary treatment that promotes emotional reappraising in patients is necessary.

P429
An audit to help establish discharge criteria for the nurse-led heart failure clinic at mater dei hospital, malta

A M Alice May Moore[1]; L Buttigieg[1]; Z Gauci[1]; J Caruana[1]; RG Xuereb[1]
[1]Mater Dei Hospital, Cardiology, Msida, Malta

Background: Local audits at the Nurse-led Heart Failure Clinic (HFC) have shown that patients with heart failure with reduced ejection fraction (HFrEF) are not reaching target or maximal tolerated doses of heart failure (HF) prognostic medications. Furthermore, up-titration of these medications is taking longer than 3 months. The main reasons for this are the increasing number of referrals to this clinic and the lack of discharges being carried out.
Purpose: To determine discharge criteria for the Nurse-Led HFC in order to focus on optimal and rapid up-titration of medical treatment of patients with HFrEF.
Method: All patients that attended nurse-led HFC from January to July 2017 were analysed. Data was collected from IT systems used in the Department of Cardiology (CVIS). The definition of optimal target doses of HF prognostic medications used is according to the 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure.
Results: 563 patients were assessed. Mean age 68 years. 70.9% males; 28.9% females. Most common cause for HF were IHD (53%) and idiopathic DCM (21.8%). The ejection fraction (EF) for each patient was recorded; 280 patients (50%) had an EF>40% whilst 280 patients (50%) had EF <40%.
Of the patients with EF>40%, only 3 patients had recorded fluid overload. 1 patient required hospital admission. 7 patients (2.5%) with were discharged from HFC. There was no documentation of why the other 97.5% were being follow-up by the nurse-led HFC.
HF medications of patients with EF <40% (280 patients) were analysed. 11 (3.9%) of these patients reached target doses of HF prognostic medications. Only 1 patient was discharged from the nurse-led HFC. The other 10 (3.5%) were given routine appointments at this clinic. No clear documented reason was given for this.
23 patients (8.2%) were on maximal tolerated doses of HF prognostic medications. 2 were discharged from the nurse-led HFC. The rest, 21 patients (7.5%), were given routine follow-up appointments at this clinic. No clear documented reason was given for this.
Conclusion: Patients with EF>40% can be discharged from the nurse-led HFC safely to GP if not fluid overloaded as HF prognostic medication, and therefore up-titration, is not indicated. The mainstay of treatment is fluid management with diuretics and treatment of underlying cause. Patients with EF <40% who are on target doses or maximal tolerated dose of HF prognostic medications, and have no other pending issues, can be discharged from the nurse-led HFC. With these criteria, 270 patients (96.4%) with EF>40% can be discharged from the nurse-led HFC as well as 34 patients (12.1%) with EF <40%.
Established discharge criteria will aid the heart failure nurses with discharges and therefore decrease burden on the HFC. This will help focus on urgent follow-up of patients who need aggressive fluid management, up-titration of HF medication and education such as fluid restriction and self-management with diuretics.

P430
Mutation spectrum of hungarian patients with hypertrophic cardiomyopathy assessed by next generation sequencing

A Tringer[1]; L Hategan[1]; V Nagy[1]; B Csanyi[1]; J Borbas[1]; Z Hegedus[2]; I Nagy[2]; T Forster[1]; R Sepp[1]
[1]University of Szeged, 2nd Department of Internal Medicine and Cardiology Centre, Szeged, Hungary; [2]Biological Research Centre of Szeged, Szeged, Hungary

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Background: Hypertrophic cardiomyopathy (HCM) is a primary disease of the myocardium most commonly caused by the mutations in sarcomeric genes. Due to the high degree of genetic heterogeneity the genetic screening of the disease is lengthy and laborious.
Purpose: We performed genetic analysis of Hungarian patients with HCM using next-generation sequencing.
Patient and Methods: We examined 103 patients with HCM (58 men, 45 women, average age: 45 ± 15 years). Familial disease was detected in 27 cases (26%). Maximal left ventricular (LV) wall thickness was 22 ± 6 mm and significant LV outflow tract gradient was observed in 28 cases. Using next-generation sequencing we screened 103 known causative cardiomyopathy genes.
Results: Genetic analysis identified 284 rare (< 1% minor allele frequency) potentially causative variants, causing either amino acid change of affecting the 'splice site' region. Pathogenic or likely pathogenic variants were identified in 68 patients (66%). Pathogenic variants most commonly affected the MYBPC3 gene (36/103, 35%), the MYH7 gene (16/103, 16%), and the TNNT2 and TPM1 genes (3/103, 3%). Rare sarcomeric gene variants, affecting the TNNI3 gene (2/103, 2%), the ACTC1, MYL2 and MYL3 genes (1/103, 1%) has also been detected. We observed the MYBPC3 p.Gln1233*, p.Pro955fs and p.Ser593fs variants in multiple cases (8, 5 and 6 cases, respectively) pointing out to a possible founder effect.
Discussion: Next-generation sequencing is appropriate for screening high number of patients. In accordance with literature data, the MYBPC3 gene seems to be the most commonly affected gene in Hungarian HCM patients.

Acute Heart Failure - Pathophysiology and Mechanisms

P431
Improvement of ventricular-arterial coupling was associated with changes of global longitudinal peak systolic strain and liver stiffness in patients with decompensated heart failure with reduced eject

O Lukina[1]; A Soloveva[1]; I Meray[1]; S Villevalde[1]; Z Kobalava[1]
[1]Peoples' Friendship University of Russia (RUDN University), moscow, Russian Federation

Objective: Ventricular-arterial coupling (VAC) represents the interaction of the heart and large arteries. VAC demonstrates mechanical efficiency in transferring the blood from the heart to the arterial system. The aim of the study was to assess correlations of dynamics of parameters of ventricular-arterial coupling and arterial stiffness in patients with decompensated heart failure (HF).
Methods: In 18 patients admitted with decompensated HFrEF (14 male, 68 ± 9 years (M ± SD), arterial hypertension 100%, previous myocardial infarction 83, diabetes 50%, NTproBNP 5462 (4219;6837) pg/ml, serum creatinine 107 (97;161) μmol/l, eGFR 59 (39;65) ± 23 ml/min/1.73m2, potassium 4.46 ± 0.59 mmol/l) arterial stiffness was assessed by applanation tonometry, parametrs of VAC by 2-dimentional echocardiography, global longitudinal peak systolic strain (GLPS) by speckle tracking echocardiography and liver stiffness (LS) by transient elastography at admission to hospital and before discharge. VAC as the ratio Ea/Ees (arterial (Ea) and end-systolic LV elastance (Ees)), optimal range was considered as 0.5-1.2. Parameters of LV efficacy were calculated. Hospital length of stay was 9.0 (7.0;10.0) days. Patients received ACEI 89%, beta-blockers 100%, aldosterone receptor antagonists 94%, iv loop diuretics 100%, iv nitrates 61%. Wilcoxon test was considered significant if $p < 0.05$.
Results: In patients with HFrEF VAC significantly decreased from 3.36 (2.98;4.00) to 2.54 (1.90;3.28) ($p < 0.05$) and Ea tended to decrease from 2.51 (1.78;3.15) to 1.63 (1.40;2.28) mmHg/ml/m2 and Ees did not change (0.63 (1.17;3.28) mmHg/ml/m2)

(p>0.05). LV efficacy (ratio stroke work/ pressure-volume area) increased from 0.49 ± 0.07 to 0.55 ± 0.10 (p < 0.05).
There were significant decrease LS from 17,6 (6,6;24,5) to 10,5 (6,3;15,7) kPa (p < 0.05). GLPS did not change significant (from -6,3 (-6,9;-3,8) to -4,8 (-8,4;-2,3)%) (p>0.05).
There was significant correlation between changes of Ea/Ees in the group of patients with HFrEF and changes of liver stiffness (R = 0.68), central pulse pressure (R=-0.64), GLPS (R=-0.82), hematocrit (R=-0.61) and hemoglobin levels (R=-0.81).
There was significant correlation between changes of LV efficacy in the group of patients with HFrEF and QRS interval duration (R = 0.79), change of hemoglobin level (R = 0.66).
Conclusion: In patients with decompensated HFrEF VAC significantly decrease due to decrease of Ea. These beneficial changes of cardiac performance was associated with changes of GLPS and liver stiffness.

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Beneficial changes of ventricular-arterial coupling during the treatment in patients with decompensated heart failure with reduced ejection fraction.

O Lukina[1]; A Soloveva[1]; I Meray[1]; S Villevalde[1]; Z Kobalava[1]
[1]Peoples' Friendship University of Russia (RUDN University), moscow, Russian Federation

Objective: The interaction of the left ventricle (LV) with the arterial system, termed ventricular-arterial coupling (VAC), is a central determinant of cardiovascular performance and cardiac energetics. Congestive heart failure (HF) modify the structure and function of both the central arteries and LV. The aim of the study was to assess dynamics of parameters of ventricular-arterial coupling and arterial stiffness in patients with decompensated HF.
Methods: In 37 patients admitted with decompensated HF (24 male, 69 ± 9 years (M ± SD), arterial hypertension 100%, previous myocardial infarction 59%, HFpEF (EF = 50%) 38%, HFrEF (EF < 40%) 49%, HFmrEF (LVEF 40-49%) 13%, diabetes 51%, NTproBNP 4219 (1402;5926) pg/ml, serum creatinine 106 (96;150) μmol/l, eGFR 52 ± 23 ml/min/1.73m2, potassium 4.56 ± 0.58 mmol/l) arterial stiffness was assessed by applanation tonometry and parametrs of VAC by 2-dimentional echocardiography at admission to hospital and before discharge. VAC as the ratio Ea/Ees (arterial (Ea) and end-systolic LV elastance (Ees)), optimal range was considered as 0.5-1.2. Parameters of LV efficacy were calculated. Hospital length of stay was 9.0 (7.0;10.0) days. Patients received ACEI 78%, BRA 11%, beta-blockers 100%, aldosterone receptor antagonists 68%, iv loop diuretics 84%, iv nitrates 46%. Wilcoxon test was considered significant if p < 0.05.
Results: Baseline Ea was 2.68 (1.89;3.14), 2.05 (1.45;2.17), 2.51 (1.78;3.15) mmHg/ml/m2, Ees 3.77 (3.06;4.69), 1.44 (1.18;1.62), 0.77 (0.51;1.01) mmHg/ml/m2 and VAC 0.78 (0.63;0.87), 1.4 (1.7;1.5) and 3.36 (2.98;4.00) in patient with HFpEF, HFmrEF and HFrEF. Changes of VAC and its components were analyzed depending EF. Dynamics of these parameters did not change significantly in all patients and in patients with HFpEF, HFmrEF. In group with HFrEF VAC significantly decreased to 2.54 (1.90;3.28) (p < 0.05) and Ea tended to decrease to 1.63 (1.40;2.28) mmHg/ml/m2 and Ees did not change (0.63 (1.17;3.28)) (p>0.05). In this group LV efficacy (ratio stroke work/ pressure-volume area) increased from 0.49 ± 0.07 to 0.55 ± 0.10 (p < 0.05). Changes of VAC were accompanied by decrease of central systolic BP from 108 ± 18 to 101 ± 13 mmHg (p < 0.05) and central diastolic BP - from 75 ± 12 to 68 ± 9 mmHg (p < 0.05).
There was a significant decrease of pulse wave velocity (PWV) (12.0 ± 3.6 vs 11.6 ± 3.7 m/s, p < 0.05), NT-proBNP level from 4219 (1402;5926) to 1924 (703;3774) pg/ml (p < 0.05), systolic and diastolic office blood pressure (130 ± 21 to 112 ± 13 mmHg (p < 0.05) and 79 ± 13 to 71 ± 6 mmHg (p < 0.05)) in all patients.
Conclusion: In patients with decompensated HFrEF VAC significantly decrease due to decrease of Ea. These changes are beneficial in this group.

Acute Heart Failure - Epidemiology, Prognosis, Outcome

P433
The inpatient costs of heart failure in Japan: evidence from the JROAD and JROAD-DPC registry

K Kanaoka[1]; S Okayama[2]; Y Saito[2]
[1]Nara City Hospital, Cardiovascular medicine, Nara, Japan; [2]Nara Medical Unibersity, First Department of Internal Medicine, Kashihara, Japan

Background: Japan is the most rapidly aging country in the world. With the aging of the population, the economic burden of heart failure is expected to increase. However, little is known about the inpatient cost of heart failure in Japan.
Purpose: Our objective was to clarify the inpatient cost of heart failure in Japan.
Methods: Using data from the Japanese Registry of All Cardiac and Vascular Diseases (JROAD) and JROAD-Diagnosis Procedure Combination (DPC) databases, we identified patients who were admitted to the hospital with common cardiovascular diseases (i.e. heart failure, acute myocardial infarction, pulmonary embolism, and acute aortic dissection) between 2012 and 2014. We evaluated the proportion of patients with heart failure out of all acute cardiovascular diseases, as well as the inpatient cost associated with heart failure. In addition, we examined how the total inpatient cost of heart failure is distributed and analysed how the cost of heart failure is distributed by age.
Results: We identified 350,636 patients with heart failure, which accounted for 61% of common cardiovascular diseases. A total of •404 billion (€3.0 billion) were spent for heart failure patients, which accounted for 49% of the cost of acute cardiovascular diseases. In heart failure patients, the median cost per patient was •775,382 (€5,730). The top 1% of spenders accounted for 8% (•33 billion [€244 million]) of all spending in heart failure, and the top 5% of spenders accounted for 25% (•99.7 billion [€736 million]) of all spending in heart failure. The cost of heart failure for patients over 70 years of age accounted for more than 75% of the total cost of heart failure.
Conclusion: The cost of heart failure is greater than the inpatient cost of any other acute cardiovascular diseases in Japan. Understanding how the total inpatient cost of heart failure is distributed may allow health providers to more effectively utilize limited resources in patients with heart failure.

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Comparison of Characteristics and 3-Year Outcomes in Patients with Acute Heart Failure with Preserved, Mid-range, and Reduced Ejection Fraction

HJ Hyun-Jai Cho[1]; WS Choe[1]; HY Lee[1]; SE Lee[2]; JO Choi[3]; ES Jeon[3]; SC Chae[4]; SH Baek[5]; SM Kang[6]; DS Choi[7]; BS Yoo[8]; KH Kim[9]; MC Cho[10]; JJ Kim[2]; BH Oh[1]
[1]Seoul National University Hospital, Department of Internal Medicine, Seoul, Korea Republic of; [2]Asan Medical Center, Department of Cardiology, Seoul, Korea Republic of; [3]Samsung Medical Center, Department of Internal Medicine, Seoul, Korea Republic of; [4]Kyungpook National University Hospital, Department of Internal Medicine, Daegu, Korea Republic of; [5]Seoul St. Mary's Hospital, Department of Internal Medicine, Seoul, Korea Republic of; [6]Severance Hospital, Department of Internal Medicine, Seoul, Korea Republic of; [7]Seoul National University Bundang Hospital, Department of Internal Medicine, Seongnam, Korea Republic of; [8]Wonju Christian Hospital, Department of Internal Medicine, Wonju, Korea Republic of; [9]Chonnam National University Hospital, Department of Internal Medicine, Gwangju, Korea Republic of; [10]Chungbuk National University Hospital, Department of Internal Medicine, Cheongju, Korea Republic of

On behalf of: KorAHF

Background: Clinical characteristics and outcomes of acute heart failure (AHF) according to left ventricular ejection fraction (LVEF) have not been fully elucidated. Especially, patients with borderline LVEF were not well represented in previous clinical trials and registries, and thus this is a grey zone with scarce data requiring further empirical characterization.
Purpose: We performed a comprehensive comparison of the epidemiology, pattern of in-hospital managements, and clinical outcomes with predictors in patients with AHF with different LVEF categories.
Methods and Results: The Korean Acute Heart Failure registry is a prospective multicenter cohort enrolling 5,320 hospitalized patients with AHF classified based on LVEF according to the 2016 European Society of Cardiology guidelines. We divided patients into three groups; LVEF < 40% as HF with reduced ejection fraction (HFrEF), LVEF = 50%, as HF with preserved EF (HFpEF) and borderline LVEF 40%–50%.as HF with mid-range EF (HFmrEF). Fifty-nine percent of patients had HFrEF, 16% had HFmrEF, and 25% had HFpEF. Compared to patients with HFrEF, those with HFpEF were older, more often female, and more likely to have non-ischemic aetiology. Patients with HFmrEF showed epidemiological profiles intermediate between HFrEF and HFpEF, and had a propensity to present de-novo HF with ischemic aetiology. Patients with lower LVEF had worse short-term outcomes; all-cause in-hospital mortality of HFrEF, HFmrEF, and HFpEF was 5.1%, 3.6%, and 3.0% respectively. Discharged patients with AHF showed poor 3-year all-cause mortality up to 38%, which was comparable between the LVEF subgroups (P = 0.623). Notably, ischemic aetiology was associated with the worst long-term outcome only in patients with HFrEF.
Conclusion: The LVEF subgroups in patients with AHF have diverse characteristics, which significantly impact clinical outcomes. These findings indicate that the outcomes of AHF are influenced by multiple factors beyond LVEF, and emphasize a focused phenotyping of each patient to tailor the management strategies and develop novel effective therapies for treating AHF.

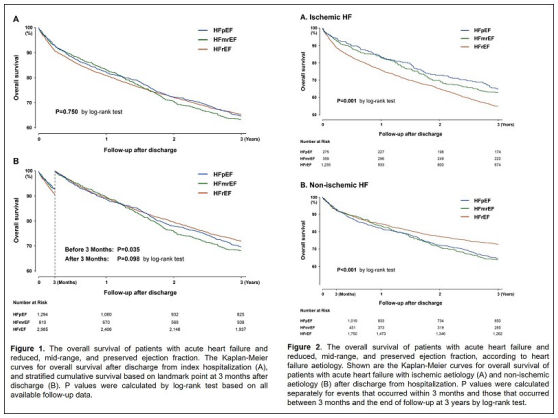

Figure 1. The overall survival of patients with acute heart failure and reduced, mid-range, and preserved ejection fraction. The Kaplan-Meier curves for overall survival after discharge from index hospitalization (A), and stratified cumulative survival based on landmark point at 3 months after discharge (B). P values were calculated by log-rank test based on all available follow-up data.

Figure 2. The overall survival of patients with acute heart failure and reduced, mid-range, and preserved ejection fraction, according to heart failure aetiology. Shown are the Kaplan-Meier curves for overall survival of patients with acute heart failure with ischemic aetiology (A) and non-ischemic aetiology (B) after discharge from hospitalization. P values were calculated separately for events that occurred within 3 months and those that occurred between 3 months and the end of follow-up at 3 years by log-rank test.

Survival

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Troponin and Lung Impedance based model for prediction 30 and 90-day Heart Failure readmission

M Michael Kleiner Shochat[1]; I Kleiner[2]; JM Weinstein[2]; A Shotan[1]; M Kazatsker[1]; A Asif[1]; I Dahan[1]; S Meisel[1]
[1]Hillel Yaffe Medical Center, Heart Institute, Hadera, Israel; *[2]Saroka Medical Center, Cardiology, Beer Sheva, Israel*

The IMPEDANCE-HF trial has shown that lung impedance (LI)-guided treatment reduces hospitalizations for heart failure (HF) and decreases HF-related mortality. The aim of the current sub-analysis was to evaluate whether troponin level elevation during admission and the degree of pulmonary congestion at discharge after HF hospitalization can predict 30 and 90-day readmission rate.

Methods Study population included 266 patients with HF and LVEF = 35% in New York Heart Association class II-IV. Noninvasive LI measurements were performed with a high-sensitive device. Assessment of the degree of pulmonary congestion was assessed by the new index ?LIR= {[1-currently measured LI/ normal baseline (calculated for each patient)] ×100}. High sensitive troponin was evaluated 6-12 hours after admission for HF. LI was performed per protocol during every admission. Pulmonary congestion assessed by ?LIR at discharge was defined as mild pulmonary congestion when 0 to -20% (compared to normal baseline LI), moderate pulmonary congestion: -20.1 to -35%, and severe pulmonary congestion: -35.1 to -60%.

Results There were 155 hospitalizations due to HF with available troponin levels (median-44 ng/ml), that were divided into 3 categories: 0-13 ng/ml- normal range, 13.1-44.0 ng/ml (mildly elevated < median), and values>44.0 ng/ml (elevated>median). The 30- and 90-day readmission rate was 37 and 45%, respectively. The probability of 30-day readmission based on troponin elevation model of lower or higher than median troponin level was associated with a Hazard Ratio (HR) = 1.7 (Confidence Interval [CI]: 0.9-3.4, p = 0.09) for <median troponin and HR = 2.6, CI: 1.4-4.8 (p = 0.003 for >median troponin). The HR for 90-day re-hospitalization rate was 1.9 (CI: 0.6-5.9, p = 0.3) for <median and 5.6 (CI: 0.7-50, p = 0.1) for >median. The HR of a 30-day readmission, based on the degree of pulmonary congestion assessed by LI, was 7.4 (CI: 3.8-14, p < 0.0001) for moderate pulmonary congestion, and 27.8 (CI: 3.9-200, p < 0.0001) for severe pulmonary congestion. The HR of 90-day readmission was 6.5 (CI: 2.2-19.2, p < 0.0001) and 78 (CI: 42-370, p < 0.0001) for moderate and severe pulmonary congestion, respectively. The predictive accuracy of the 30- and 90-day HF-related mortality based on pulmonary congestion as assessed by LI at discharge was good (p < 0.0001).

Conclusion Risk stratification for the 30- and 90-day HF hospitalizations and HF mortality was accurate if based on level of pulmonary congestion on discharge, but troponin levels were not predictive for re-hospitalizations.

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Thirty-day readmission as an important target of quality of care after discharge due to acute heart failure. The role of a more efficient hospitalization

S Mazzetti[1]; J Rossi[1]; R Abete[1]; M Chioffi[1]; P Delfino[1]; A Andrea Mortara[1]
[1]Dipartment of Cardiology Policlinico di Monza, Monza, Italy

Readmission within 30 days (Read30) after an acute heart failure (AHF) event is a marker of quality of care and hospital efficiency. In US the Read30 rate is 22.7% (Medicare data) while in Europe nearly 12-15%; this difference has been related to length of hospitalization: 5 days in US and 8-10 days in the European countries. In Italy, the Read30 rate is 14.7% with an average hospital length of stay of 10.2 days (national data from Agenas 2015, all hospital wards). The Italian "IN-HF Outcome" register showed that in cardiology departments Ria30 drops to 6.2% (average hospitalization 12 ± 10 days) but this data was limited by the mean age of the population with less comorbidities as compared to non-cardiologic wards.

The aim of this work was to evaluate the Read30 in a cardiologic center with an Heart Failure Unit and an active program of protected discharge from hospital. Between January 2010 and December 2016, 627 patients were hospitalized for AHF (excluding AHF due to STEMI and nonSTEMI) with a mean age of 77 ± 10 years and LVEF of 36 ± 13%. Etiology of AHF was ischemic in 43.1%, hypertensive in 18.8%, valvular in 16.3%, idiopathic in 13.9%, and other in 7.9%. Because of advanced age, patients had several comorbidities including chronic renal failure (47.5%), COPD confirmed by spirometry (19.1%), Anemia (44.2%), Diabetes (33.5%), dementia (5.5%).

The average length of hospitalization was 10.3 ± 5 days and overall in-hospital mortality was low, 5.4%.

At discharge, for all patients older than 80 yrs (46.5%), a program of home support and assistance to management of therapy and personal care was planned. Accordingly, in 32 patients (5.3%) a transfer to a rehabilitation center, mid or long-care ward was organized. Only 40 patients (6.7% of patients discharged alive) were re-hospitalized up to 30 days in our or other hospital wards.

In conclusion, in a cardiology department with an HF unit and an active program for a protected discharge of more fragile patients, the rate of Read30 is low, even in a population of advanced age with several comorbidities. To reduce this important indicator of quality of care, it is therefore appropriate to think of a more efficient hospital stay rather than a shorter one.

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Heart Failure Registries: Worldwide comparison including Colombia

MC Montes[1]; E Rincon[1]; JE Juan Esteban Gomez[1]
[1]Valle del Lili Foundation, Cali, Colombia

On behalf of: RECOLFACA

INTRODUCTION Different Heart Failure (HF) registries describe regional characteristics and outcomes. Few publications assess differences and similarities between registries from various geographical regions. We sought to compare relevant variables of an HF Colombian Registry (RECOLFACA) with data from other registries worldwide.

Methods: We performed a literature review to identify the leading HF registries worldwilde. We compared them with RECOLFACA data. Descriptive statistics were used to present and analyze data within and among registries.

Results: Variables of those registries are presented in table 1. Latin American (LA) registries had younger population. We found male predominance (58-63%), except in the US and Brazil. The US showed the lowest percentage of reduced LVEF (47-49%). Low reported use of devices (CRT/ICD) in all registries (9-21%).

Conclusion: In these registries, population is older and mainly men. Main ethiology worldwide was ischemic. In LA registries, the high percentage of "other etiologies" could imply endemic causes. This indicates that regional differences are significant and should be considered when developing research protocols, guidelines and recommendations.

P437 Heart Failure Registries

		RECOLFACA n = 531	ADHERE n = 187565	US OPTIMIZE n = 48612	EFICA n = 581	ESC-HF Pilot n = 1892	ATTEND n = 1110	CONAREC XVIII n = 1277	INTERN-HF n = 858	BREATHE n = 1263	RENAIC CR n = 695
		Colombia	US	US	France	Europe	Asia	Argentina	South America	Brazil	Costa Rica
		2016-2017	2001-2009	2003-2004	2001	2009-2010	2007-2009	2006	2012-2014	2011-2012	2016-2017
	Age (years), mean ± SD; median (IQR)	69±14	72±14	73±14	73±13	70±13	73±14	73 (62-82)	67±0.5	64±16	
	male,%	59	49	48	59	63	59	59	61	40	58
	LVEF <40,%	72	47	49	73¯	61	57	78°	71		81¯
	LVEF%, mean ± SD	32±14		39±18	38±15	38±14				39±16	
Etiology, %	Hypertensive	27		23	15+		18	18	20	20	43
	Ischemic	52	57	46	61	51	33	34	26	30	58
	Valvular	22			21				13	12	14
	Other	36*			4			4	25	34	26*
Comorbidities, %	Coronary artery disease	31	57	50	46			24	18	27	28
	Hypertension	71	74	71	60			80	74	71	81
	Dyslipidemia	30	36	32	30			42	49	37	54
	Diabetes mellitus	31	44	42	27	35	34	31	22	34	38
	CRT/ICD	18	21	15		9		9			

LVEF: Left Ventricular Ejection Fraction, CRT/ICD: cardiac resynchronization therapy/implantable cardioverter,*Could have more than one etiology, + Combination with hypertrofic etiology, ¯Preserved LVEF as > 45%,°Preserved LVEF as >55%

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Impact of serum levels of exocrine pancreatic enzymes in patients with acute decompensated heart failure

M Masaru Hiki[1]; T Kasai[1]; S Yatsu[1]; J Shitara[1]; H Matsumoto[1]; A Murata[1]; M Shimizu[1]; T Kato[1]; S Suda[1]; H Daida[1]
[1]*Juntendo University School of Medicine, Cardiovascular Medicine, Tokyo, Japan*

Background: In heart failure (HF), multiple organ damage in association with systemic congestion and/or impaired perfusion have been focused. However, there are no data regarding interaction between HF and exocrine pancreatic insufficiency which may impair digestion and absorption.
Methods: We assessed sAmy and sLip as a suggestive of exocrine pancreatic function in patients with (N = 102) and without (N = 35) HF. In patients with HF, we performed pancreatic function diagnostic (PFD) test, direct assessment of pancreatic exocrine function to confirm exocrine pancreatic insufficiency. Furthermore, the association between sAmy or sLip and clinical outcomes including all-cause deaths and/or re-hospitalizations.
Results: HF patients had significantly lower sAmy (54IU/L versus 68IU/L, P = 0.001) and sLip (25IU/L versus 31IU/L, P = 0.018) compared with non-HF group. In multivariable regression analyses, significant correlates of sAmy were blood urea nitrogen (BUN) (coefficient, 0.552; P < 0.001), albumin (coefficient, 0.233; P = 0.020), and B-type natriuretic peptide (BNP) (coefficient, -0.227; P = 0.024). Significant correlates of sLip were BUN (coefficient, 0.377; P < 0.001) and BNP (coefficient, -0.364, P < 0.001). In patients with ADHF, PFD test showed significantly low levels of urinary para-aminobenzoic acid excretion as compared with reference lower limit (median, 50.4% versus reference lower limit, 73.4%; P = 0.027) suggesting that patients with ADHF had exocrine pancreatic insufficiency. In the multivariable Cox proportional hazard models, exocrine pancreatic insufficiency defined as low sLip (< 18IU/L) was independently associated with long-term worse outcomes (hazard ratio [HR], 1.81; P = 0.025) whereas low sAmy (< 39IU) was not (HR, 1.12; P = 0.679).
Conclusion: In patients with HF, exocrine pancreatic insufficiency can be determined by low sLip levels which were associated with congestion and possibly poor nutrition status. Such exocrine pancreatic insufficiency can be a predictor of poor clinical outcomes in patients with HF.

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Long-term prognosis according to setting of care in elderly patients hospitalized for acute heart failure: data from the ATHENA registry

G Biagioni[1]; A Pratesi[1]; F Orso[1]; A Herbst[1]; F Fedeli[1]; A Berni[2]; G Ciuti[2]; F Bacci[2]; A Lo Forte[1]; AC Baroncini[1]; C Ghiara[1]; N Marchionni[3]; M Di Bari[1]; A Ungar[1]; S Baldasseroni[1]
[1]*Careggi University Hospital (AOUC), Department of medicine and geriatrics, Florence, Italy*; [2]*Careggi University Hospital (AOUC), Department of emergency and internal medicine, Florence, Italy*; [3]*Careggi University Hospital (AOUC), Cardiothoracovascular Department, Florence, Italy*

On behalf of: the ATHENA study group

Background: Acute Heart Failure (AHF) is a complex clinical syndrome, that typically affects elderly patients. Administrative registries show that in the "real world" most patients with HF are admitted to Internal Medicine and Geriatric wards with different epidemiological features, clinical profile and prognosis compared to patients admitted to Cardiology.
Aims: to evaluate the long-term prognosis and the predictors of mortality of elderly patients hospitalized for AHF in different settings of care (Cardiology, Internal Medicine and Geriatric wards).
Methods: ATHENA (AcuTe Heart failurE in advaNced Age) is a retrospective observational study which enrolled patients aged = 65 years) admitted with the diagnosis of AHF to the Emergency Departement (ED) of a tertiatry teaching Hospital and then transferred to three different settings of care: Cardiology, Internal Medicine and Geriatric wards. A telephone interview to evaluate vital status and functional level was conducted to obtain follow-up data.
Results: 401 patients were enrolled, 15.2% was admitted to Cardiology, 14.7% to Geriatrics and 70.1% to Internal Medicine. The mean age was 83.5 years, significantly higher in Geriatrics (86.9 years) and Internal Medicine (83.4 years) compared to Cardiology (81.0 years), p = 0.001. Females were 51%, with similar distribution in the three settings. Telephone interviews were conducted among patients discharged alive (365 patients, 91%); for 13 patients (3.6%) it was not possible to collect any information. One-year mortality was 33.2%, significantly higher for patients discharged from Geriatric ward (45.8%) and Internal Medicine (32.5%) compared to Cardiology (17.3%), p = 0.009. During the total median FU (¯21 months), mortality rate was 49.7% (47.4% for CV causes), significantly higher in Geriatric ward (60.4%) and Internal Medicine (52.0%) compared to Cardiology (32.7%), p = 0.013. More than half of patients (58.7%) were in a NYHA class III or IV and the disability rate was very high: in 33.3% of patients two or more functions of BADL were lost and in 65.5% of patients three or more IADL lost. By multivariable analysis, independent predictors of medium-term mortality were: NT-pro BNP level in ED (OR= 1.77, CI= 1.03-3.04, p = 0.039) and Charlson Comorbidity Index (OR=

1.30, CI= 1.13-1.50, p = 0.001), with a protective effect of Beta-Blockers therapy at discharge (OR= 0.53, CI= 0.29-0.95, p = 0.033) and functional status evaluated through Barthel Index (OR= 0.99, CI= 0.98-1.0, p = 0.005). Conclusion: in elderly patients with AHF long term prognosis varies significantly according to the different setting of care. The long-term mortality is very high, influenced by geriatric variables, as disability and comorbidity, in addition to cardiological variables, as NT-pro BNP level in ED and Beta-Blockers therapy at discharge.

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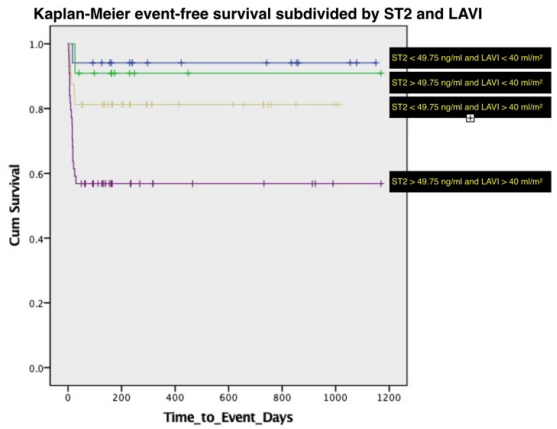
Integrated Pre-discharge Echocardiographic Parameters and Soluble suppression of tumorigenesis 2 (sST2) level to predict Outcomes of non-ischemic acute heart failure

T Sotananusak[1]; N Suvachittanont[1]; S Wattanachai[1]; M Chandavimol[1]; P Sritara[1]; T Teerapat Yingchoncharoen[1]
[1]Faculty of Medicine Ramathibodi Hospital-Department of Medicine of Mahidol University, Bangkok, Thailand

Introduction: sST2 is the circulating form of the receptor for interleukin-33, a biomarker which associated with cardiac remodeling and fibrosis. It has been demonstrated to predict heart failure hospitalization and cardiac mortality in acute heart failure especially of ischemic origin. The data on prognostic value of sST2 in non-ischemic heart failure is limited, therefore we sought to determine this value, particularly in integration with echocardiographic parameters.
Method: We conducted a prospective cohort study of patients admitted with acute heart failure during October 2014 to December 2017. Patients with recent acute coronary syndrome or coronary revascularization were excluded. All patients received regular standard treatments and were performed echocardiogram and blood test for sST2 before discharge. The patients were followed for 30-day heart failure rehospitalization or cardiac death death. Multivariable Cox regression was used to identify events association.
Results: We enrolled 104 patients in the study, 47 were male (45%), median age was 73 years old and 33 patients (31%) had atrial fibrillation. The mean follow up duration was 18.44+12.44months. The 30-day HF rehospitalization and cardiac mortality occurred in 49 patients (47%) (42 rehospitalization, and 7 cardiac mortality) during 18-month period follow-up. sST2 was associated with 30-day outcomes (HR 1.007 [95% CI, 1.003-1.011]; P < 0.001). A sST2 cut-off value more than 49.75 ng/ml was significantly associated with 30-day outcomes (HR 2.60 [95% CI, 1.097-6.172]; P = 0.03) and remains associated with the long-term outcome (HR 2.586 [95% CI, 1.387-4.821]; P = 0.003). A left atrial volume index (LAVI) of more than 40 ml/m2 was also associated with 30 days outcomes (HR 4.84 [95% CI, 1.141-20.516]; P = 0.032) but did not associate with long term outcomes (HR 1.49 [95% CI, 0.737-3.019]; P = 0.266). A combination of sST2 more than 49.75 ng/ml and LAVI more than 40 ml/m2 are the highest risk of rehospitalization and mortality.
Conclusion: In patients with non-ischemic acute heart failure, sST2 and Left atrial volume index were associated with 30-day HF rehospitalization and cardiac mortality. However, only sST2 was associated with long-term outcome. Integrated LAVI and sST2 better stratified the risk of adverse outcome in these patients.



P441

Is red cell distribution width a prognostic marker of postoperative heart failure in patients undergoing valve surgery?

P Duchnowski[1]; T Hryniewiecki[1]; M Rys[1]; M Kusmierczyk[2]; P Szymanski[1]
[1]Institute of Cardiology in Anin, Department of Acquired Cardiac Defects, Warsaw, Poland; [2]Institute of Cardiology in Anin, Department of Cardiosurgery and Transplantology, Warsaw, Poland

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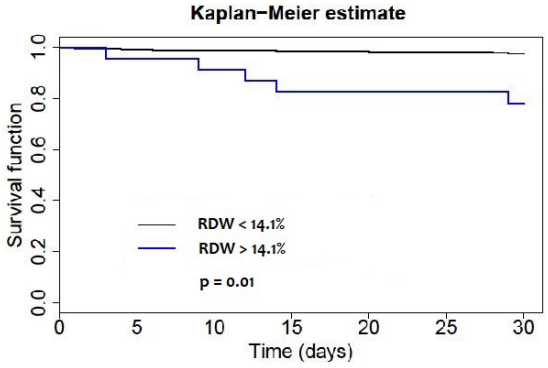
Introduction: Numerous studies have shown that elevated RDW is associated with poor outcomes in patients with myocardial infarction or stroke. The aim of the study was to evaluate the prognostic value of RDW for heart failure in the early postoperative period in patients undergoing valve surgery.
Methods: A prospective study was conducted on a group of 672 consecutive patients with haemodynamically significant valvular heart disease who underwent elective valvular surgery. The primary end-point at the 30-day follow-up was perioperative heart failure defined as the need for a supply of catecholamines more than 48 hours after completing the cardiopulmonary bypass surgery or the need to resupply.
Results: The perioperative heart failure occurred in 230 patients. At multivariate analysis: RDW (P = 0.0006), and hs troponin T (hs-TnT) (P = 0.01) remained independent predictors of the primary end-point.
Conclusions: Elevated RDW is associated with a higher risk of perioperative heart failure in patients with perioperative heart failure.



Kaplan−Meier event-free survival curves

P442

HFmrEF in elderly patients hospitalised for acute heart failure: data from the ATHENA registry.

S Parlapiano[1]; A Pratesi[1]; F Orso[1]; A Herbst[1]; G Biagioni[1]; F Fedeli[1]; AC Baroncini[1]; A Lo Forte[1]; C Ghiara[1]; F Bacci[2]; G Ciuti[2]; M Di Bari[1]; N Marchionni[3]; A Ungar[1]; S Baldasseroni[1]
[1]Careggi University Hospital (AOUC), Department of medicine and geriatrics, Florence, Italy; [2]Careggi University Hospital (AOUC), Department of emergency and internal medicine, Florence, Italy; [3]Careggi University Hospital (AOUC), Cardiothoracovascular Department, Florence, Italy

On behalf of: ATHENA Study group

Background: Recently, the European Society of Cardiology (ESC) has recognized the presence of a "gray area" of patients with ejection fraction (EF) between 40 and 49% defined "mid-range" (HFmrEF) and has redefined the specific cut off values for HF with preserved EF (= 50%, HFpEF) and HF with Reduced EF (< 40%, HFrEF).
Purpose: to better characterize patients with HFmrEF and to compare them to those with HFpEF and HFrEF in a real world setting of elderly patients hospitalised for acute HF.
Methods: data derived from the ATHENA retrospective observational study which included elderly patients (= 65 years) admitted with diagnosis of AHF to the Emergency department (ED) of a tertiary University teaching-hospital and transferred to cardiology, internal medicine and geriatric wards in the period 01.12.2014-01.12.2015.
Results: 291 patients with complete echocardiographic data composed the study population: patients with HFmrEF were 19.9%, 32.6% had HFrEF and 47.4% had HFpEF. HFmrEF and HFpEF had similar demographic characteristics, compared to patients with HFrEF: mean age of three group of patients was respectively 84.2, 84.3 and 80.3 years, p < 0.001; the prevalence of females was 43.1%, 66.7% and 30.5% for HFmrEF, HFpEF and HFrEF respectively, p < 0.001. Regarding cardiovascular risk factors, such as hypertension, diabetes and dyslipidaemia no significant difference

could be observed across the three groups, even if the patients with HFmrEF were more frequently smokers (p = 0.042). Furthermore, main non-cardiovascular comorbidities, did not differ significantly among the three groups, with the exception of chronic obstructive pulmonary disease which was more prevalent in patients with HFmrEF (p < 0.015). Considering CV comorbidities, however, we noticed that a history of coronary artery disease was more frequently reported in patients with HFmrEF (39.7%) and in those with HFrEF (35.8%) compared to patients with HFpEF (18.8%), p= 0.002. As could be expected, a significant difference could be observed in the prevalence of implantable biventricular pace maker and cardioverter defibrillators (CRT-D) with HFmrEF patients placed in an intermediate position (8.6%) respect to the other two groups of HF (20.2% for HFrEF and 2.9% for HFpEF; p < 0.001). No significant differences were found in the setting of care for HFmrEF patients who were equally distributed among cardiology, internal medicine and geriatric wards (p = 0.2). In-hospital mortality was not significantly different among the three groups of HF: 8.6% for HFmrEF, 8.0% for HFpEF and 7.4% for HFrEF (p = 0.961).
Conclusions: Our study shows that in real world setting of elderly admitted for AHF, HFmrEF patients are significantly represented, with clinical and demographic characteristics similar to patients with HFpEF, except for the ischemic feature that seems to bring them closer to patients with HFrEF. In-hospital mortality of patients with HFmrEF does not differ significantly to those with HFpEF and HFrEF.

P443

Acute pulmonary oedema as clinical presentation of acute heart failure is associated with better prognosis in patients with reduced ejection fraction

PSM Marques[1]; H Moreira[1]; MJ Pinto[1]; P Rodrigues[1]; P Bettencourt[1]; P Lourenco[1]
[1]*Sao Joao Hospital, Internal Medicine, Porto, Portugal*

Background: Acute pulmonary oedema (APO) is a possible presentation of acute heart failure (HF) and warrants prompt treatment. Prognostic implications of acute HF presentation have not been studied. We aimed to study the prognostic correlates of acute HF presenting with APO and to analyse if they differed according to the left ventricular systolic function.
Patients and Methods: We retrospectively analysed data concerning acute HF patients that had been previously included in an acute HF registry. Following the more recent European Society of Cardiology guidelines we have studied patients with ejection fraction <40% - HF with reduced ejection fraction (HFrEF) and patients with HF with preserved ejection fraction (HFpEF) when the ejection fraction was = 50%. Patients with acute coronary syndrome were not included in the registry. Patients with significant valvular disease were excluded from the analysis. Patients presenting in the emergency department with APO and those not presenting with APO, as considered by the attending emergency department physician, were characterized. Treatment was at the discretion of the attending physicians during hospital stay. Patients were followed for up to 2 years from hospital admission and the endpoint under analysis was all-cause mortality. The prognostic significance of being admitted in APO was studied using a Cox-regression analysis. Multivariate models were built. Analysis was stratified according to the ejection fraction (HFrEF and HFpEF).
Results: We studied 440 patients hospital-admitted due to acute HF; 154 (35.0%) had HFpEF and 268 (65.0%) had HFrEF; 48.6% were male; mean age was 75 years and 72 patients (16.4%) were admitted in APO - 16.2% in the HFpEF group and 16.4% in the HFrEF group. During the 2-year follow-up 210 patients died, 18 during the index hospitalization. Patients presenting in APO had very similar age and comorbidities when compared with their counterparts; BNP was lower in patients presenting in APO. Patients presenting in APO died significantly less at 2 years (31.9%) than those not presenting in APO (50.8%). The multivariate adjusted (age-,SBP (<90mmHg)-, ischemic aetiology-, atrial fibrillation upon admission- and admission BNP-) HR of 2-year mortality in patients presenting in APO was of 0.62 (95% CI: 0.40-0.96), p = 0.03; this beneficial effect of APO was only observed in the subgroup of HFrEF patients HR = 0.54 (0.31-0.95), p = 0.03 and no such protection was verified in HFpEF patients - HR = 0.75 (0.36-1.55), p = 0.43 **Conclusions:** Patients with HFrEF with acute HF presenting as APO have a 46% reduction in the 2-year mortality risk. The clinical presentation as APO in HFrEF patients probably reflects an ability to adapt to acute stress conditions that may not be present in other HF patients. This topic merits further investigation

P444

Common Precipitants of Initial Admission, 12-months Re-admissions and 30-days Mortality in Acute Heart Failure Patients within Northern Kuala Lumpur.

REF Bin Raja Shariff[1]; MK Borhan[1]; MR Yusoff[1]; C Lee[1]
[1]*Hospital Sungai Buloh, General Medicine, Sungai Buloh, Malaysia*

Background: A major contributor to the burden of heart failure (HF), is the cost associated with acute admissions. However, there is limited data on precipitants of acute HF in a Malaysian context.
Objective: To identify common precipitants of initial admissions and re-eadmissions, as well as 30-days mortality in acute heart failure patients in Northern Kuala Lumpur.
Materials & Methods: A retrospective, observational study was conducted on 418 patients admitted for acute HF, and subsequently re-admitted for acute HF within 12-months, to Hospital Sungai Buloh between 1st January 2012 to 31st December 2013. Case notes were analysed and likely precipitants to each admission and readmission were identified at 4 distinctive periods - one, three, six and twelve months from initial presentation within the study period.
Results: The mean age was 62.6 years (S.D. = 12.5), of which 234 (56%) were male. 261 (62.4%), 61 (14.6%), 89 (21.3%), and 7 patients (1.7%) were Malays, Chinese, Indians and of other races respectively. The three most common precipitants of acute HF on initial admission include non-compliance (to medication, diet or fluid restriction), acute coronary syndrome (ACS) and hypertensive emergencies (n = 188 (45.0%), n = 122 (29.2%) and n = 21 (5.2%) respectively). Other common precipitants identified include sepsis, cardio-renal syndrome and hospital-acquired pneumonia (n = 19 (4.6%), n = 15 (3.6%) and n = 14 (3.4%) respectively). One-month, three-months, six-months and twelve-months readmission rate were 16.0%, 24.0%, 25.6% and 28.5% respectively. 154 patients (36.9%) admitted within the study period had at least one subsequent re-admission within 12 months. Coincidentally, ACS, non-compliance and hypertensive emergencies were, again, common precipitants of readmissions. Mortality Rates were highest within the first month of admission (n = 60 (14.4%)), and the most common cause of deaths given was acute pulmonary oedema (n = 29 (48.0%) followed by ACS (n = 16 (27.0%).
Conclusion: This study reveals that in a multi-ethnic Asian population, ACS, non-compliance and hypertensive emergencies are major precipitants of both acute HF admissions, and subsequent readmission, highlighting the need for clinicians to address these 3 factors by identifying their risk factors.

P445

Baseline Characteristics & Acute Management of Patients Presenting with Acute Heart Failure Within Northern Kuala Lumpur: A Single-Centre Retrospective Analysis

REF Bin Raja Shariff[1]; MK Borhan[1]; MR Yusoff[1]; C Lee[1]
[1]*Hospital Sungai Buloh, General Medicine, Sungai Buloh, Malaysia*

Background: Heart failure (HF) contributes to a large proportion of acute hospital admission. Unfortunately the actual prevalence of acute HF is still unknown due to scarcity of local data.
Purpose: Our study aims to investigate the demographics, co-morbidities, acute clinical presentation and initial management received by patients within Northern Kuala Lumpur, presenting with acute HF.
Materials & Methods: A retrospective, observational study was conducted on 418 patients admitted for acute HF to Hospital Sungai Buloh between 1st January 2012 to 31st December 2013.
Results: The mean age was 62.6 years (S.D. = 12.5), of which 234 (56%) were male. 261 (62.4%), 61 (14.6%), 89 (21.3%), and 7 patients (1.7%) were Malays, Chinese, Indians and of other ethnicity respectively. 142 patients (34%) presented with de novo HF. Common co-morbidities include hypertension (n = 302 (72.2%)), coronary artery disease (n = 259 (62.0%)), diabetes (n = 254 (60.8%)), chronic kidney disease (n = 230 (55.0%)) and atrial fibrillation (n = 70 (16.7%)). 186 patients (44.5%) had reduced baseline left ventricular ejection fraction (40% or lower). The most common clinical symptoms on admission include dyspnoea, orthopnoea and paroxysmal nocturnal dyspnoea (323 (77.3%), 273 (65.3%) and 260 patients (62.2%) respectively). The most common clinical sign includes lung crepitations, peripheral oedema and raised jugular venous pressure (265 (63.4%), 246 (58.9%) and 189 (45.2%) patients respectively). The mean systolic blood pressure (SBP) and heart rate on admission were 142 mmHg (S.D. = 28) and 87 beats per minute (S.D. = 23) respectively. 83 patients (19.9%) had AF on electrocardiogram on admission. 7 patients (1.7%) presented with cardiogenic shock (systolic blood pressure less than 100 mmHg) and 48 patients (11.5%) required at least one form of inotrope and/or vasopressor for blood pressure support. Frusemide was prescribed in 397 (95.0%) of patients, of which 364 (87.1%), 26 (6.2%) and 7 (1.7%) were administered intravenously, as intravenous infusions and as tablets respectively. 38 (9.1%) patients had intravenous nitroglycerin prescribed on admission. 38 (9.1%) and 94 (22.5%) patients were admitted, at some point, to the Intensive Care and Coronary Care Unit respectively. 107 (25.6%) and 20 (4.8%) patients required non-invasive ventilation and invasive ventilation respectively.
Conclusion: To our knowledge, this is the first study looking at a Malaysian cohort of acute decompensated heart failure. It provides insight into the demography of such cohort, which could subsequently be compared with other established international registries, such as EHFSII and ADHERE, to analyse for heterogeneity.

P446

Characterization of acute heart failure hospitalizations by subgroups

L Luis Oliveira[1]; L Brochado[2]; C Serena[1]; A Fontes[1]; S Ferreira[1]; C Almeida[1]; C Machado[1]; R Dourado[1]; E Santos[1]; N Pelicano[1]; A Pacheco[1]; A Tavares[1]; F Melo[1]; D Martins[1]
[1]Hospital Divino Espirito Santo, Cardiology, Ponta Delgada, Portugal; *[2]Departamento de Ciências Biomédicas e Medicina da Universidade do Algarve, Faro, Portugal*

Introduction: Current guidelines divide heart failure (HF) in three different types according to the left ventricle ejection fraction (EF): reduced EF if < 40% (HFrEF), mid-range EF if 40-50% (HFmrEF) and preserved EF if = 50% (HFpEF). Despite the given benefits of medical treatments in patients with HF, hospitalization rates for acute HF (AHF) remain high. Also, HFpEF, with similar prognosis to HFrEF, is short on therapeutic options with proven benefit, and information on hospitalizations for AHF in this subgroup of patients is scarce.
Purpose: This study aimed to describe patients hospitalized for AHF, between types of HF and their rehospitalizations and survival rates at 5 years follow-up.
Methods: Retrospective study of patients hospitalized with AHF between June 2011 and June 2012 (index admission). All-cause mortality, HF-related mortality or rehospitalization by AHF were registered in a median follow-up time of 5.45 years (IQR 1.53-5.97).
Results: From 154 patients included, 10 were lost to follow-up and 7 died in the index admission. Of 137 patients, with a median age of 70 years (IQR 60.5-78.5), 23.4% had HFrEF, 23.3% HFmrEF and 53.3% HFpEF. On the index admission, 19.7% of patients accounted for a first episode of AHF. Main triggers were acute coronary syndrome (21.2%), arrhythmias (18.2%) and respiratory infections (18.2%). At 1 and 5 years, rehospitalization for AHF occurred in 47.4% and 77.4% of patients, all-cause mortality rates were 19.0% and 50.4% and HF-related mortality rates were 8.8% and 19.0%, accordingly.
From the readmitted patients, 55.7% had suffered at least one hospitalization apparently without any trigger. Median cumulative days of hospitalization was 23 days (IQR 10-44).
No difference in mortality, rehospitalization or cumulative days of hospitalization was found between the different types of HF. Except for gender (higher prevalence of females in HFpEF vs HFrEF - 67.1% vs 25.0%; p < 0.001), there were no statistically significant differences in the baseline characteristics of the population by subgroups.
Conclusions: Regardless of the type of HF, rehospitalizations by AHF are high. All-cause and HF-related mortality rates are high and similar between types of HF.

P447

Clinical characteristics and prognosis of patients with decompensated heart failure and preserved, mid-range and reduced ejection fraction

RM Christodorescu[1]; R Lala[2]; A Apostolescu[3]; MN Trofenciuc[4]; E Petrescu[3]; A Pop-Moldovan[2]; S Dragan[1]; D Darabantiu[2]
[1]University of Medicine Victor Babes, Cardiology, Timisoara, Romania; *[2]Vasile Goldis Western University, Cardiology, Arad, Romania*; *[3]Institute of Cardiovascular Diseases, Cardiac Rehabilitation Clinic, Timisoara, Romania*; *[4]Vasile Goldis Western University, Arad, Romania*

Background. The prognosis of patients (pts) hospitalized for decompensated heart failure(HF) regardless of ejection fraction(EF) value is poor. Recent HF guidelines introduced a new classification of HF: mid range (mrEF between 41-49%). The prognostic importance of this new classification is not clear.
Purpose: To assess the clinical profile and prognostic value of mid-range EF in patients hospitalized for decompensated HF.
Methods: This retrospective observational study included 180 consecutive HF patients admitted for decompensated HF, mean age = 67 ± 11y, female gender = 42%. The patients were divided into 3 groups according to their EF at admission: group 1 HFpEF n = 25, (13.9%), group 2 HFmEF n = 83 (46.1%), group 3 HFrEF n = 72 (40%). During follow-up at 6months all readmissions for HF aggravation and deaths were recorded. For statistical analysis we used ANOVA t test for comparison of means, Pearson x^2 test for comparison of categorical values, multivariate logistic regression for endpoint (readmission and mortality).
Results: At admission mean systolic BP was 153mmHg ± 34 in gr.1, 144mmHg ± 29 in gr.2 and 136mmHg ± 24 in gr.3, significantly higher in group 1 (p = 0.009). Mean heart rate in the 3 groups was: 82 ± 32b/min , 86 ± 20b/min and 93b ± 24/min, significanly higher in gr.3 (p = 0.049). Mean Hb was 12.3 ± 1.8g/dl, 13.7 ± 1.8g/dl and 13.5 ± 1.8g/dl , significanly lower in gr.1(p = 0.003). Mean serum creatinine was 1.34 ± 0.6mg/dl, 1.04 ± 0.3mg/dl and 1.18mg ± 0.4/dl, significanly higher in gr.1(p = 0.008). Mean serum K was 3.5 ± 1.7mEq/l, 3.8 ± 1.2mEq/l and 3.6 ± 1.5mEq/l respectively(p = 0.8). 36% pts in gr.1, 41% pts in gr.2 and 29% pts in gr.3 were readmitted. 16 deaths were recorded (20% in gr.1, 6% in gr.2 and 8% in gr.3). The predictive factors for readmission using multivariate logistic regression were hyperkalemia (p = 0.033, OR = 1.03), HFmrEF(p = 0.035, OR = 2.3) and HR (p = 0.042, OR = 1.02).
Conclusion: High heart rate at admission, hyperkaliemia and mrEF are associated with a worse outcome in patients hospitalized for decompensated heart failure. Patients with HFmrEF have a high readmission rate at 6 months and need a careful follow-up after discharge.

P448

Prognostic significance of systolic blood pressure in AHF patients

VG Samsone[1]; I Kaminskaite[2]; J Sasnauskaite[2]; V Juknevicius[3]; J Simonavicius[3]; A Mikalauskas[3]; A Mebazaa[4]; A Kavoliuniene[5]; J Celutkiene[3]
[1]Vilnius University, Faculty of Medicine, Vilnius, Lithuania; *[2]Lithuanian University of Health Sciences, Kaunas, Lithuania*; *[3]Vilnius University Santaros Clinics, Clinic of Cardiac and Vascular Diseases, Centre of Cardiology and Angiology, Vilnius, Lithuania*; *[4]University Paris Diderot , U942 Inserm, Hospital Lariboisiére, Paris, France*; *[5]Hospital of Lithuanian University of Health Sciences, Department of Cardiology, Kaunas, Lithuania*

On behalf of: The GREAT network

Introduction: Acute heart failure (AHF) is continuously increasing in prevalence and is related to significant mortality and morbidity including frequent hospitalisations. Arterial blood pressure has been shown to be a prognostic factor for short-term and long-term mortality outcomes in patients with heart failure. However, there is limited information about the prognostic significance of systolic blood pressure (SBP) in AHF patients.
Purpose: We aimed to evaluate the prognostic value of SBP in prediction of short-term mortality and readmissions in patients with AHF.
Methods. A prospective study enrolled consecutive patients admitted to the emergency department with acute dyspnea. Data of 637 patients (mean age 69.7 ± 12.1 years, 58.2% men) with adjudicated diagnosis of AHF were analysed. Patients were grouped according to the SBP quartiles. Relative risk of three-month mortality and rehospitalisations was estimated by performing logistic regression on SBP quartiles and other variables. Parameters with p < 0.1 were used in the initial multivariate analysis, which was then iteratively optimised by removing statistically insignificant parameters.
Results: 11.3% (n = 72) of patients diagnosed with AHF died and 42.7% (n = 272) were repeatedly rehospitalised in 3 months. The highest SBP quartile (156-242] was associated with significantly lower mortality risk compared to normal SBP quartile (120-135], p < 0.05. Additionally, anemia was found to be a predominant factor increasing both death and rehospitalisation risk, whereas highest mortality risk (2.41; p < 0.05) was observed in patients with acute coronary syndromes.
Conclusions: Prognostic impact of SBP at admission on short-term mortality and rehospitalisation was determined. Higher SPB was found to be a prognostic factor associated with lower mortality and less frequent three-month rehospitalisation rate in patients with AHF.

Risk analysis for death in 3 months

Variable	Univariate analysis		Multivariate stepwise analysis - Primary model		Multivariate stepwise analysis - Optimised model		
relative risk	95% CI		relative risk	95% CI	relative risk	95% CI	
SBP (70-120]	1.87	(0.99;3.52)	1.67	(0.82;3.4)	1.77	(0.9;3.47)	
SBP(135-156]	1	(0.49;2.02)	1.04	(0.48;2.25)	1.09	(0.52;2.29)	
SBP(156-242]	0.2*	(0.07;0.61)	0.28*	(0.09;0.9)	0.25*	(0.08;0.78)	
History of hypertension	0.34*	(0.2;0.6)	0.34*	(0.17;0.71)	0.34*	(0.17;0.68)	
Acute coronary syndromes	1.8*	(1.09;2.97)	2.38*	(1.27;4.46)	2.41*	(1.35;4.32)	
Chronic kidney disease	1.67	(0.99;2.82)	1.17	(0.6;2.27)			
Cancer	2.6*	(1.33;5.11)	1.79	(0.85;3.78)			
Anemia	2.52*	(1.53;4.14)	1.82*	(1.04;3.19)	1.96*	(1.15;3.33)	

* - p < 0.05; referent SBP (120-135]

P449

Impact of socioeconomic deprivation on heart failure management and clinical outcomes

S Kenyon[1]; Y C Lau[1]
[1]*Monklands Hospital, Cardiology, Airdrie, United Kingdom*

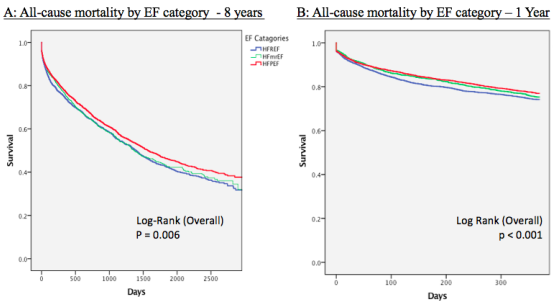
Since 1948, the NHS in UK is a publicly funded, single-payer health care system to address healthcare inequality. Heart failure results in a large healthcare burden, and is known to be more common with increased socioeconomic deprivation. Scottish Index of Multiple Deprivation (SIMD) has recently been developed to includes socioeconomic as well as other measures of deprivation (such as healthcare, education, access to housing and crime).
In this retrospective study, 96 patients admitted with Heart failure(HF) from the most deprived and least deprived tertile of Scottish Index of Multiple Deprivation (SIMD) (1 - 3, most deprived and 7 - 9, least deprived).
Between the two groups, no statistical difference exists between age, gender, haemoglobin or creatinine level; nor was there any difference in past medical history or cigarette use. Patients from the lower tertile has higher incidence of alcohol excess (16% vs 3%, p = 0.043) while higher incidence of AF for the higher tertile (55% vs 33%, p = 0.004).
Prescription of diuretics, Beta-Blocker, ACE-I or ARB were not statistically different. Patients from higher tertile is more likely to receive aldosterone antagonist (37% vs 17%, p = 0.031) and combined Beta-blocker and ACE-i/ARB treatment (42% vs 21%, p = 0.025).
6-months follow-up demonstrates composite endpoint of heart failure readmission and mortality was statistically higher among patients of lower socioeconomic tertile (p = 0.042). Stepwise multiple regression analysis also confirmed socioeconomic deprivation as an independent predictor for more adverse clinical outcome for heart failure (p = 0.003, R2 = 22%).
Summary: Despite the establishment of universal healthcare, patients from the lower socioeconomic group (based on SIMD) are still less likely to received prognostically beneficial medication and are more likely to be experience readmission for heart failure or death.

P450

Characteristics and long-term outcomes of patients with reduced, mid-range, and preserved ejection fraction following hospitalization for acute heart failure in a contemporary real world setting

I Israel Mazin[1]; D Friemark[1]; M Arad[1]; Y Peled[1]; A Gruper[1]; N Shlomo[1]; R Klempfner[1]; R Kuperstein[1]; I Goldenberg[1]
[1]*Chaim Sheba Medical Center, Tel Hashomer, Israel*

Aims: Recent ESC heart failure (HF) guidelines introduced a new mid-ranged left ventricle ejection fraction (LVEF) category. The purpose of the present study was to describe the clinical characteristics and long-term outcomes of patients hospitalized with acute HF categorized by LVEF, in large contemporary prospective tertiary center cohort.
Methods and Results: A total 7,752 patients were included in this study. Patients were divided according to the recent ESC heart failure guidelines. Patients with preserved EF (HFpEF) compared to those with mid-range EF (HFmrEF) or reduced EF (HFrEF) were older, more likely to be female, had a higher frequency of comorbidities, including hypertension, diabetes mellitus, and anemia. Kaplan-Meier survival analysis (Figure) showed increased mortality rates at 1-and 8-years of follow-up in both the HFmrEF (24% and 48%, respectively) and HFrEF (25% and 47%, respectively) groups, as compared with the HFpEF group (22% and 41%, respectively; log-rank p-value = 0.007 for the overall difference during follow-up). Consistently, multivariate analysis showed patients with HFmrEF experienced a significant higher risk for all-cause mortality (HR= 1.24, p = 0.04) and HF or death (HR= 1.2, p = 0.02) compared to the HFpEF group, and a similar risk to the HFrEF group. Systemic pulmonary artery pressure (SPAP) was an independent predictor for long-term mortality among all LVEF subgroups (HR 1.43, p <0.001).
Conclusion: Our findings suggest that acute HF patients with HFmrEF group have increased risk for long–term mortality and repeated HF hospitalization that is similar to those with HFrEF. Elevated SPAP is a powerful predictor for adverse long-term outcomes following hospitalization for acute HF.



Acute Heart Failure - Diagnostic Methods

P451

Release of mitochondrial DNA is associated with mortality in acute heart failure

KA Konstantin A Krychtiuk[1]; R Wurm[1]; S Ruhittel[1]; M Lenz[1]; K Huber[2]; J Wojta[1]; G Heinz[1]; M Huelsmann[1]; WS Speidl[1]
[1]*Medical University of Vienna, Department of Internal Medicine II, Division of Cardiology, Vienna, Austria*; [2]*Wilhelminen Hospital, 3rd Department of Internal Medicine, Cardiology and Emergency Medicine, Vienna, Austria*

Background: Inflammation is regarded as an important trigger for disease progression in heart failure (HF). Particularly in acute heart failure (AHF), tissue hypoxia may lead to cellular damage and the release of intracellular mitochondrial DNA (mtDNA), which acts as an activator of the immune system due to its resemblance to bacterial DNA. It therefore may serve as a mediator of disease progression.
Purpose: The aim of this study was to determine circulating levels of mtDNA and its association with mortality in patients with HF in different presentations.
Methods: Plasma levels of circulating mtDNA were measured in 90 consecutive patients with AHF admitted to our medical ICU as well as 109 consecutive chronic heart failure (CHF) patients.
Results: In patients admitted to our medical ICU (median age 64 (49-74) years, median NT-proBNP 4986 (1525 - 23842) pg/mL, 30-day survival 64.4%), mtDNA levels were significantly higher in patients that died within 30 days after ICU admission and patients with plasma levels of mtDNA in the highest quartile had a 3.4-fold increased risk (p = 0.002) of dying independent from age, gender, vasopressor use, NT-proBNP levels and APACHE II score. Patients with AHF showed significantly higher mtDNA levels (p <0.005) as compared to patients with CHF. In these patients, mtDNA levels were associated with NYHA functional class but were not associated with outcome.
Conclusion: mtDNA release into the circulation is associated with mortality in patients with AHF but not in patients with CHF. Release of mtDNA may therefore play a role within the pathophysiology of AHF.

P452

Decreased number of endothelial progenitor cells to apoptotic endothelial cell-derived microparticle ratio predicts atrial fibrillation in acutly decompensatede heart failure

A E Alexander E Berezin[1]; A Kremzer[1]
[1]*State Medical University, Zaporozhye, Ukraine*

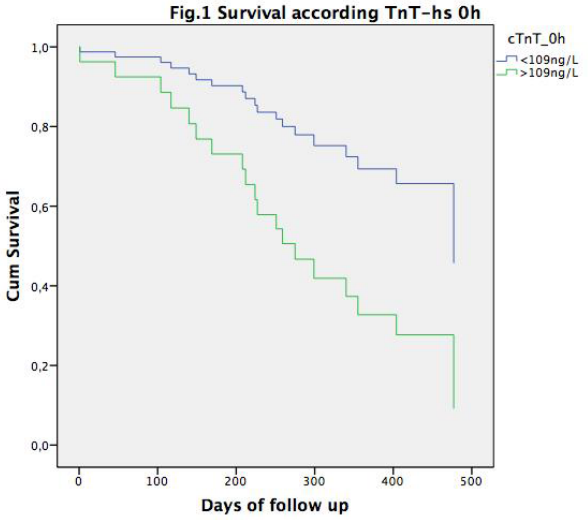
Background: Acutely decompensated heart failure (ADHF) remains a leading cause of in-hospital mortality. Atrial fibrillation (AF) associated with increased premature death rate amongst in-patinets with ADHF. The aim of the study was to investigate whether the pattern of angiogenic endothelial progenitor cells (EPCs) and apoptotic endothelial cell-derived microparticles (EMPs) would be able to predict newly atrial fibrillation (AF) in ADHF with reduced (HFrEF) and preserved (HFpEF) ejection fraction.
Methods: Two hundred fifty four ADHF subjects were retrospectively enrolled in the study. ADHF patients with global left ventricular ejection fraction (LVEF) < 40% (n = 85), LVEF = 40-49% (n = 95) and LVEF = 50-59% (n = 74) were categorized. Therefore, to compare the circulating levels of biological markers 35 control subjects without HF were included in the study. All control individuals were age- and sex-matched ADHF patients. The serum level of biomarkers was measured at baseline. The flow

cytometric technique was used for predictably distinguishing circulating cell subsets depending on expression of CD45, CD34, CD14, Tie-2, and CD309 antigens and determining endothelial cell-derived microparticles. CD31+/annexin V+ was defined as apoptotic endothelial cell-derived MPs, MPs labeled for CD105+ or CD62E+ were determined as MPs produced due to activation of endothelial cells.
Results: In multivariate logistic regression model T2DM (R2 = 0.36; P = 0.001), previous MI (R2 = 0.67; P = 0.001), galectin-3 (R2 = 0.67; P = 0.003), CD31+/annexin V+ EMPs (R2 = 0.32; P = 0.001), NT-proBNP (R2 = 0.72; P = 0.046), CD14+CD309+ cells (R2 = 0.66; P = 0.001), and CD14+?D309+ Tie-2+ cells (R2 = 0.54; P = 0.001) were found as independent predictors of AF in ADHF with LVEF < 40%. In ADHF combined cohort with LVEF 40-49% and LVEF = 50-59% previous MI (R2 = 0.52; P = 0.001), hypertension (R2 = 0.14; P = 0.001), galectin-3 (R2 = 0.68; P = 0.001), CD31+/annexin V+ EMPs (R2 = 0.57; P = 0.001), NT-proBNP (R2 = 0.62; P = 0.003), CD14+CD309+ cells (R2 = 0.52; P = 0.001), and CD14+?D309+ Tie-2+ cells (R2 = 0.48; P = 0.001) predicted AF. Using multivariate Cox-regression analysis adjusted etiology (previous myocardial infarction), cardiovascular risk factors (type 2 diabetes mellitus, hypertension) we found that CD31+/annexin V+ EMPs to CD14+CD309+ cells ratio (OR 1.22; 95% CI = 1.14 - 1.36; P = 0.001) were independent predictor for newly AF in ADHF.
Conclusion: We found that CD31+/annexin V+ EMPs to CD14+CD309+ cells ratio added to NT-proBNP, clinical data, and cardiovascular risk factors has exhibited the best discriminate value and higher reliability to predict newly AF in ADHF individuals.

P453
Single high-sensitivity cardiac troponin T measurement predicts 1-year mortality and CV events in real-world patients admitted to the emergency room with acute decompensated heart failure

M Mariana Augusto Goncalves[1]; A Tralhao[1]; C Silva[1]; C Brizido[1]; F Gama[1]; G Mendes[1]; G Rodrigues[1]; P Freitas[1]; A Oliveira[1]; M Mendes[1]
[1]Hospital de Santa Cruz, Lisbon, Portugal

Background: cardiac troponin (cTn) elevation is known to influence prognosis in acute decompensated heart failure (ADHF). However, the clinical relevance of minor increases in serum cTn is still uncertain.
Purpose: to assess the prognostic role of different high-sensitivity (hs) cTnT metrics in patients admitted to the emergency room (ER) with ADHF.
Methods: single-center retrospective analysis of patients admitted consecutively to the ER during a 6-month period (March-July 2016) with an available and positive hs-cTnT (4th generation assay, 99th percentile 0.014 ng/L). ADHF adjudication was based on discharge diagnosis according to the ICD-9. A multivariate Cox proportional hazard model was used to determine independent predictors of total mortality and major adverse cardiovascular events (cardiovascular death, myocardial infarction or stroke).
Results: 1405 patients had available hs-cTnT
Results: Of these, 201 (19%) had a final diagnosis of ADHF (age 79 ± 10 years-old, 54% female). 82% of patients had known HF and 21% had prior history of coronary artery disease. In a median follow-up of 363 days [IQR 156-427], 67 patients died and 80 had a MACE. Median hs-cTnT was 44 ng/L [IQR 26-88]. Compared to other metrics of hs-cTnT (absolute 0-3 h change, peak value and percentage change), initial hs-cTnT had the best discriminative power for total mortality (c-index = 0.636 [CI 95% 0.556-0.716], p = 0.002) and MACE (c-index = 0.676 [CI 95% 0.601-0-756], p < 0.001). Cox regression using Youden's index of 109 ng/L as the cut-off yielded hs-cTnT and age (but not NT-pro-BNP) as independent predictors of total mortality (HR 4.05 [CI 95% 1.36-12.1], p = 0.012 for hs-cTnT) and MACE (HR 3.05 [CI 95% 1.17-7.99, p = 0.023] for hs-cTnT).
Conclusions: in patients presenting to the ER with ADHF, admission hs-cTnT is a powerful prognostic marker of both mortality and MACE. Further studies are warranted to determine the potential impact of therapeutic tailoring incorporating hs-cTnT on patient outcomes.

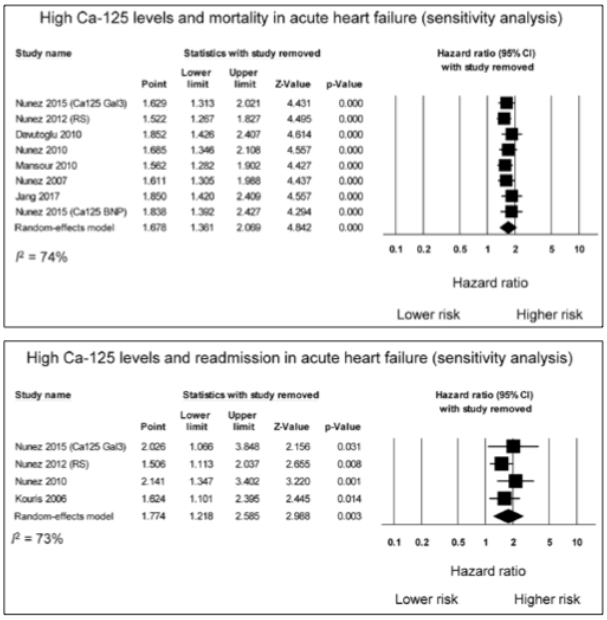


Survival according troponin 0h

P454
Cancer antigen-125 and hospital readmission and mortality outcomes in acute heart failure: a systematic review and meta-analysis

R E De La Espriella Juan[1]; G Tse[2]; M Gong[3]; G Li[3]; A Baranchuck[4]; T Liu[3]; MCS Wong[5]; A Beyes-Genis[6]; J Sanchis[7]; J Nunez[7]
[1]University Hospital Clinic of Valencia, Cardiology Department , Valencia, Spain; *[2]The Chinese University of Hong Kong, Department of Medicine and Therapeutics, Faculty of Medicine, Hong Kong, Hong Kong SAR People's Republic of China*; *[3]2nd Hospital of Tianjin Medical University, Tianjin Key Laboratory of Ionic-Molecular Function of Cardiovascular disease, Department of Cardiolo, Tianjin, China People's Republic of*; *[4]Queen's University, Department of Medicine, Kingston General Hospital, Kingston, Canada*; *[5]The Chinese University of Hong Kong, JC School of Public Health and Primary Care, Hong Kong, Hong Kong SAR People's Republic of China*; *[6]Germans Trias i Pujol Hospital, Heart Institute and Department of Medicine, Autonomous University of Barcelona, Badalona (Barcelona), Spain*; *[7]University Hospital Clinic of Valencia, Cardiology Department, INCLIVA, Department of Medicine, Valencia University, Valencia, Spain*

Background: Cancer antigen-125 (CA125) is an ovarian cancer marker but recent research work has focused on its role in risk stratification in heart failure. A recent meta-analysis examined its prognostic value in chronic heart failure. However, there has been no systematic evaluation of its role in acute heart failure (AHF).
Methods: PubMed and EMBASE databases were searched until 17th October 2017 for studies that evaluated the prognostic value of CA125 in AHF
Results: A total of 30 and 88 entries were retrieved from PubMed and EMBASE, of which 17 studies were included in the final meta-analysis. Sixteen studies were prospective cohort studies and one study was a randomized controlled trial. Our meta-analysis shows that high CA125 levels were associated with 68% increase in all-cause mortality (hazard ratio [HR]: 1.68, 95% CI: 1.36-2.07; P < 0.0001; I2: 74%) and 77% increase in heart-failure-related readmissions (HR: 1.77, 95% CI: 1.22-2.59; P < 0.01; I2: 73%). In patients with AHF, CA125 levels were higher in patients with fluid overload symptoms and signs compared to those without them, with a mean difference of 41.6 U/mL (standard error: 10.2 U/mL, P < 0.0001; I2: 82%).
Conclusion: CA125 is a significant predictor of hospital readmission and mortality outcomes in AHF. Therefore, CA125 emerges as a useful tool for risk stratification and monitoring following an episode of AHF.



High CA-125 Levels and Outcomes in AHF

P455

Thrombopoeitin as a biomarker and a regulatory mediator in acute heart failure

L Malinova[1]; N Furman[1]; P Dolotovskaya[1]; N Puchinyan[1]; T Denisova[2]
[1]Saratov State Medical University, Research institute of cardiology, Saratov, Russian Federation; *[2]Saratov State Medical University, Saratov, Russian Federation*

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Background: Recently thromboeitin (TPO) has been reported as not only a stimulator of the proliferation and differentiation of megakaryocytes, but as a possible modulator of cardiac contractility, and a factor reducing myocardial necrosis, apoptosis and decline in ventricular function following ischaemia/reperfusion. However, these finding are based predominantly on animal models.
The purpose of the study was to characterize short-term profiles of thrombopoeitin in patients with acute heart failure and to assess its potential impact on clinical course and short-term prognosis.
Methods: We report the preliminary results of the ongoing study. 40 male patients (57(47;65) y.o.) admitted with ST segment elevation myocardial infarction (STEMI) were recruited into the study. According to clinical presentation and baseline level of BNP (cut off level - 100 pg/mL) patients were divided into acute heart failure (AHF) and control (C) groups. Levels of TPO, stromal cell derived factor 1 (SCD1) and myeloproliferative leukemia virus oncogene (MPL) were measured in plasma samples obtained at admission, on the 2nd and the 7th days since STEMI manifestation with commercially available ELISA Kits. Follow-up period was 12 months after admission.

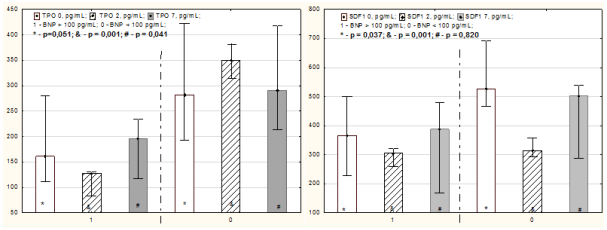


Fig.1. TPO and SDF1 dynamics

Results: Patients of both groups were comparable by age and major clinical characteristics. Symptom onset to first medical contact delay time was longer in patients with AHF: 105 (60; 180) vs 60 (30; 79) min, p = 0.018. TPO levels measured at admission, on the 2nd and the 7th days since STEMI manifestations were significantly lower in AHF patients (fig. 1). Similar situation was with SDF1 levels (fig. 1), with the only exception of the last point (7th day). MPL plasma concentrations at admission were higher in AHF patients, however this difference was non-significant. BNP and TPO levels at admission reveal negative significant correlation: Spearman R = - 0.433, p < 0.05. Early cardiovascular complications were more frequent in patients with high TPO levels at admission: 26.5% vs 8.8%, as well as incidence rate of composite endpoint (CV death + CV rehospitalisations): 25.7% vs 14.3%.
Conclusion: Received data support hypothesis of thrombopoeitin influence on cardiac function during myocardial ischaemia-reperfusion injury and acute heart failure, which may ground new diagnostic approach and pharmacological strategies in acute heart failure.

P456

The prognostic role of different renal function phenotypes in patients Hospitalized for Acute Heart Failure

A Alberto Palazzuoli[1]; G Ruocco[2]; P Pellicori[3]; E Incampo[4]; C Di Tommaso[4]; R Favilli[4]; R Nuti[2]; JM Testani[5]
[1]Santa Maria Alle Scotte Polyclinic, Siena, Italy; *[2]University of Siena, Cardiovascular Diseases Unit, Department of Internal Medicine , Siena, Italy*; *[3]University of Glasgow, Robertson Institute of Biostatistics and Clinical Trials Unit, Glasgow, United Kingdom*; *[4]Polyclinic Santa Maria alle Scotte, Cardiothoracic Department, Siena, Italy*; *[5]Yale University, Section of Cardiovascular Medicine, New Haven, United States of America*

Background: Worsening renal function (WRF) is common in patients treated for acute heart failure (AHF) and might be associated with a significant increase in blood nitrogen urea (BUN), a marker of neuro-hormonal activation.
Purpose: We aimed to evaluate the prognostic relevance of WRF according to BUN changes during hospitalisation.
Methods: We studied patients with AHF screened for Diur-HF Trial (NCT01441245). WRF was defined as an in-hospital rise in serum creatinine = 0.3 mg/dl or estimated glomerular filtration rate (GFR) reduction = 20%. BUN increase was defined as a rise in BUN = 20% during admission. Effective decongestion was defined as complete resolution of two, or more, signs of HF, or euvolemic clinical status at discharge.
Results: Of 247 patients enrolled, 59 (23%) patients experienced WRF, 107 (43%) had a BUN increase >20%, and 111 (45%) were effectively decongested during hospitalization.
During 180 days of follow-up, 136 patients died or were re-hospitalised for AHF. An increase in BUN was an independent predictor of adverse outcome, regardless of WRF (HR = 2.19 [1.35-3.54], p = 0.002 and 1.71 [1.14-2.59], p = 0.010; with and without WRF, respectively). WRF was not an independent predictor of outcome if BUN did not increase. An increase in BUN was independently associated with adverse outcome regardless of clinical congestion at discharge, whilst WRF predicted outcome only if effective decongestion was not achieved.
Conclusions: an increase in BUN>20% during hospitalization for AHF predicts a poor outcome; WRF predicts adverse outcome only if BUN increases substantially or clinical congestion persists.

P457

Carbohydrate antigen 125 and glutamic oxaloacetic transaminase as congestion markers in acute heart failure. Is there clinical association between them?

D Carrillo[1]; R Lopez-Vilella[1]; I Sanchez-Lazaro[1]; C Aguado[2]; B Laiz[2]; L Martinez-Dolz[1]; L Almenar[1]
[1]Hospital Universitario y Politécnico La Fe, Heart Failure and Transplant Unit, Valencia, Spain; *[2]Hospital Universitario y Politécnico La Fe, Clinical analysis service, Valencia, Spain*

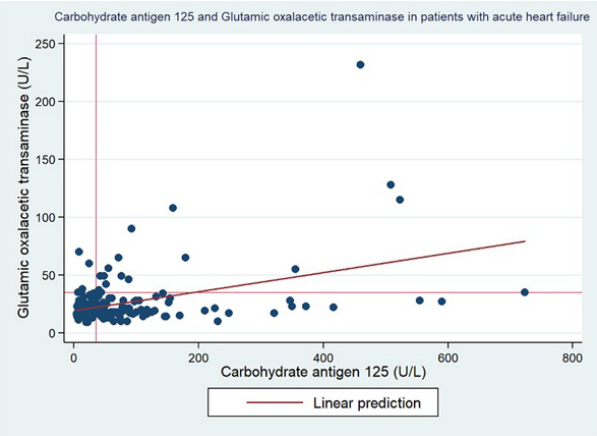
Introduction: Carbohydrate antigen 125 (CA-125) is a novel biomarker that increases when there is congestion in patients with heart failure (HF). Elevated levels require an intense diuretic treatment, while low levels are associated with acute renal failure in the case of an aggressive diuretic treatment. It might be useful to find a standardized clinical marker that correlates with CA-125 to assess the degree of congestion and help the optimization of diuretic treatment.
Purpose: To analyse the relationship between CA-125 and Glutamic oxalacetic transaminase (GOT) in patients with acute HF.
Methods: Cross-sectional study of patients admitted to hospitalization rooms of cardiology because of acute HF, between 01 august 2017 to 30 November 2017 and had, during the hospitalization, measurement of CA-125 and GOT in the same blood sample. A logistic multiple regression of GOT as dependent variable and CA-125 and BNP as independent variables were modelled.
Results: 173 patients were included. The median of age was 71 years (interquartile range IQR 61-79). 35.26% were female. Median of GOT was 19 (16-27) and 42.1 of

CA-125 (16.2-88). 10% of patients had GOT higher than 35 U/L and 3.53% more than 70 U/L. There was relation between the levels of CA-125 and GOT (Figure). Levels of CA-125 more than 35 U/L increased the probability of having increased GOT levels (OR 3.54 95% IC 1.19 to 10.54 p = 0.023) (Table).
Conclusions: There is an association between CA-125 levels and GOT values in acute heart failure. GOT could be part of the diuretic administration algorithm in AHF together with CA-125.

Logistic Regresion model of GOT

GOT elevation	Odds Ratio	95% Confidence Interval	P	
CA-125 elevation	3.54	1.91	10.54	0.023
High NTproBNP	1.01	0.34	2.89	0.99
Constant	0.068	0.02	0.19	0.00

GOT: Glutamic oxalacetic transaminase, GOT elevation >35U/L. CA-125: Carbohydrate antigen 125 35U/L. High NTproBNP >450pg/mL in < 50 years, >900pg/mL in 50-70 years, and >1800pg/mL in >70 years.



P458

Dynamics of serum lipocalin-2 concentrations in acute decompensated heart failure after levosimendan infusion

MV Lediakhova[1]; IV Zhirov[1]; SN Nasonova[1]; TM Uskach[1]; VP Masenko[1]; SN Tereshchenko[1]
[1]*National Medical Research Center for Cardiology, Moscow, Russian Federation*

Background: serum lipocalin-2 is a biomarker for early identification of acute kidney injury (AKI). Changes in serum lipocalin-2 concentrations are potentially useful for the early diagnosis of AKI in patients with acute decompensated heart failure (ADHF).
Purpose: to evaluate the value of serum lipocalin-2 concentrations in patients with acute decompensated heart failure with reduced systolic function after levosimendan infusion.
Methods: the study was a prospective, single-centre, randomized trial. We enrolled 30 patients hospitalized with ADHF. The patients had reduced systolic function (left ventricular ejection fraction (LVEF) <40%), increased levels of brain natriuretic peptide > 500 pg/mL and systolic blood pressure >125 mmHg. The exclusion criteria were: acute coronary syndrome; sustained ventricular tachycardia or ventricular fibrillation; severe aortic or mitral regurgitation; hypertrophic obstructive cardiomyopathy; restrictive cardiomyopathy; estimated glomerular filtration rate (GFR) < 30 mL/min/1.73 m2. All patients were randomized according to a 1:1 scheme to receive standard therapy or an intravenous infusion of levosimendan 0.1μg/kg/min for 24 hour added standard therapy. AKI was defined according to Kidney Disease: Improving Global Outcomes (KDIGO)
Clinical Practice Guidelines. We measured of serum lipocalin-2 concentrations by a quantitative sandwich enzyme immunoassay technique (RD systems, DLCN20, USA) at baseline, immediately after levosimendan infusion and at discharge. Statistical significance was defined as P <0.05.
Results: a total of 30 men hospitalized with ADHF were included. Average age was age 62.5 ± 9.7 years and mean LVEF was 25.0 (21.5-28.5)%. Baseline serum lipocalin-2 concentrations were similar in the two groups. We found a significant decrease of serum lipocalin-2 concentrations in the levosimendan group immediately after infusion [from 156.2 (126.4-171.2) ng/mL at baseline to 115.5 (88.9-141.5) ng/mL (P = 0.001)] and a significant increase of serum lipocalin-2 concentrations in the standard therapy group [from 164.4 (136.7-247.6) ng/mL at baseline to 185.9 (167.0-316.4) ng/mL (P = 0.047)]. At discharge, we noted a significant decrease of serum lipocalin-2 concentrations in the levosimendan group [from 156.2 (126.4-171.2) ng/mL at baseline to 128.6 (116.4-157.3) ng/mL (P = 0.041)] and a tendency to increase of serum lipocalin-2 concentrations in the standard therapy group [from 164.4 (136.7-247.6) ng/mL at baseline to 169.8 (143.4-228.1) ng/mL (P = 0.826)]. We compared the value of serum lipocalin-2 concentrations in both groups these interactions were statistically significant after infusion (P for interaction <0.001) and at discharge (P for interaction = 0.001).
Conclusion: serum lipocalin-2 concentrations are significantly reduced after infusion and at discharge in the levosimendan group in patients with acute decompensated heart failure with reduced systolic function.

P459

Endocan as a new biomarker of severity in acute heart failure

M Reina Couto[1]; JP Bessa[2]; P Serrao[2]; J Afonso[2]; R JR Roncon-Albuquerque[1]; JA Paiva[1]; A Albino-Teixeira[1]; T Sousa[1]
[1]*Sao Joao Hospital, Intensive Care Medicine, Porto, Portugal*; [2]*University of Porto, Faculty of Medicine, Porto, Portugal*

Introduction: Acute heart failure (AHF) remains a major health concern, with high mortality and re-hospitalization rates, and treatment remains largely opinion-based. Endothelial dysfunction and progression of chronic heart failure seems to be associated to increased oxidative/nitrosative stress. Although endocan is increasingly recognized as an emerging biomarker of endotelial dysfunction, it remains scarcely explored in AHF.
Purpose: To evaluate serum endocan and nitrotyrosine (a marker of redox dysfunction), and to determine the correlation between these, C-reactive protein (CRP) and high sensitivity (hs)-troponin I values in AHF.
Methods: Patients admitted to the department of intensive care medicine with the diagnosis of AHF (n = 10) and cardiogenic shock (CS) (n = 9) were included and blood samples were collected at admission and at day 3 to 5. Blood donors were used as controls (n = 10). Endocan and nitrotyrosine were measured with ELISA kits. CRP and hs-troponin I were evaluated using automated analyzers.
Results: Endocan concentration on admission was increased in patients with AHF and significantly raised in CS when compared to the values found in controls (controls: 1.9 ± 0.3; AHF: 5.2 ± 0.9 ng/mL; CS: 20.0 ± 3.8ng/mL; controls vs AHF, p = 0.0878; controls vs CS, p < 0.0001; AHF vs CS, p = 0.0441). Serum nitrotyrosine values were not significantly different between controls, AHF and CS (controls: 2.4 ± 0.4 nmol/mL; AHF: 3.4 ± 0.5 nmol/mL; CS: 3.2 ± 0.7 nmol/mL, p = 0.3623). CRP values were not different between AHF and CS groups on admission (56.8 ± 17.1 vs 116.2 ± 27.0 ng/mL, p= 0.1128). The hs-troponin I concentration was not significantly different between AHF and CS patients (19508 ± 8775 vs 67457 ± 36471 ng/mL, p= 0.356). Endocan was positively correlated with CRP (Spearman r = 0.427, p = 0.0094) but not with hs-troponin I or nitrotyrosine. Serum nitrotyrosine was positively correlated with CRP (Spearman r = 0.4101, p = 0.013) and with hs-troponin I (r Spearman = 0.6242, p < 0.0001). There were no significant differences between values of all parameters at admission and at day 3 to 5.
Conclusions: We can conclude that the extent of endothelial dysfunction is significantly higher in CS patients and is significantly associated with inflammatory status in AHF and CS. Furthermore, nitrosative/oxidative stress also seems to be associated with inflammation and myocardial damage.

P460

Endomyocardial biopsy in paediatric myocarditis and dilated cardiomyopathy may identify infectious genome presence in myocardium and guide targeted treatment

G Kourelis[1]; S Rammos[1]; GA Vagenakis[1]; K Kyriakoulis[1]; F Kakava[1]; D Rallis[1]; S C Apostolopoulou[1]
[1]*Onassis Cardiac Surgery Center, Athens, Greece*

Background/Introduction: Myocarditis and cardiomyopathy are acquired causes of heart failure with frequently infectious aetiology, complex pathophysiology and challenging management and prognosis, especially in the paediatric population.
Purpose: This study examines the role of endomyocardial biopsy in identifying infectious genome in the myocardium of children with myocarditis and cardiomyopathy, its association with histology, and its guidance on using targeted anti-infectious agents in the therapeutic management of this population.
Methods: Retrospective data collection of paediatric patients (0-18 years old) diagnosed with myocarditis and/or cardiomyopathy between 2004 and 2017 at our

institution. Data was analyzed on the basis of demographics, diagnosis, biopsy results, therapy and outcome.
Results: 80 patients (44 boys) were included in the study with diagnoses: 39 cardiomyopathy (26 dilated; 4 hypertrophic; 5 restrictive) and 43 myocarditis. Age distribution was < 0-1 year old (n = 13), 1-5 year old (n = 25), 5-16 year old (n = 37) and 16-18 year old (n = 5). Diagnosis was based on echocardiography, myocardiac enzyme levels and biopsy findings (active inflammation; necrosis; hypertrophy; fibrosis; (near) normal; other). All patients but 3 underwent endomyocardial biopsy. Overall, 27 biopsy specimens (23 of the 'myocarditis' group and 4 of the rest) were positive for viral or bacterial genetic material through polymerase chain reaction (PCR) testing. Of the positive patients, 21 received targeted antiviral or antibiotic therapy (no specific therapy was available for the remaining patients at the time of diagnosis). Intravenous immunoglobulin was administered in 20 patients and systemic corticosteroids in 4 patients based on presence of active inflammation on biopsy and positive PCR in blood or cardiac specimen. During 7.4 ± 4.7 years follow up, 51 (63%) children improved or had full recovery, 9 (11%) required prolonged medical support for heart failure, 9 (11%) received or are waiting for transplant and 11 (15 %) died.
Conclusions: Endomyocardial biopsy and PCR testing can be useful in the management of myocarditis and dilated cardiomyopathy in children identifying infectious genome in the myocardium and guiding specific anti-infectious therapy.

P461

Guided therapy in patients with acute decompensated heart failure with dilated cardiomyopathy: left ventricular diastolic filling pattern during admission and discharge

E Ersin Saricam[1]
[1]*Medicana Hospital, cardiology, Ankara, Turkey*

Background: NT-proBNP guided therapy in acute decompensated heart failure (ADHF) has been used as in-hospital guidance. Left ventricular diastolic filling pattern in transthorasic echocardiography (TTE) might provide prognosis in the patients with ADHF.
Purpose: We investigated whether left ventricular filling pattern could be used as a criteria of discharge and the success of the therapy similar to NT-proBNP target (<30% reduction from admission to discharge).
Methods: Prospective randomized study included 31 patients admitted into emergency department between March 2017 and January 2018. All of the patients had NYHA class IV, sinus rhythm, and before diagnosed dilated cardiomyopathy. The left ventricular filling pattern in admission and discharge was evaluated in the all of them by TTE. Moreover, NT-proBNP levels were analyzed in admission and discharge.
Results: The average age of the patients had 65.80 ± 4.96 years. In admission, while left ventricular pattern of all of them was restrictive (type III) diastolic dysfunction, at discharge time, 26 patients had normal left ventricular filling pattern, and 5 patients had impaired relaxation (type I) diastolic dysfuncion (Tablo).
Conclusion: Our study demonstrated that guidance of left ventricular filling pattern was succesful in ADHF therapy, similar to NT-proBNP guided therapy.

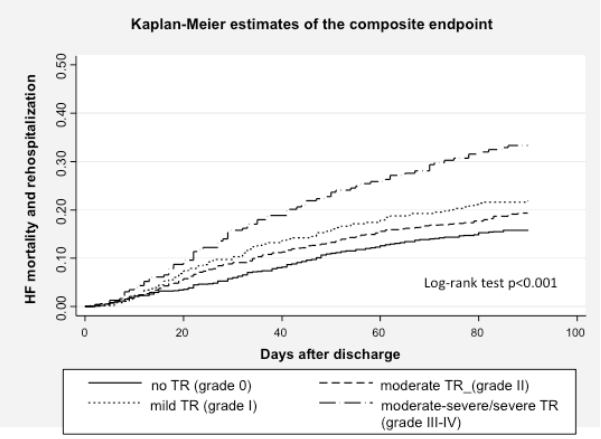
NT-proBNP levels and echocardiography	
At presentation	
NT-proBNP levels (pg/mL)	8004.75±743
Pulsed Doppler (PWD)	
E wave velocity (cm/sn)	71.18±5.85
A wave velocity (cm/sn)	28.5±3.61
Deceleration time (msec)	62.88±13.96
E/A ratio (31 patients)	2.51±0.35
E/e'	>14
At discharge	
NT-proBNP levels	1645.17±104.58
Pulsed Doppler (PWD)	
E wave velocity	59.5±5.69
A wave velocity	41.56±7.19
Deceleration time	136.64±8.81
E/A ratio (26 patients)	1.42±0.33
E/e'	<8

P462

Tricuspid regurgitation predicts short-term adverse events in acute heart failure

R De La Espriella Juan[1]; E Santas[1]; G Minana[1]; A Mollar[1]; J Gonzalez[1]; M Amiguet[1]; I Cardells[1]; J Sanchis[2]; J Chorro[2]; J Nunez[2]
[1]*University Hospital Clinic of Valencia, Cardiology Department , Valencia, Spain*; [2]*University Hospital Clinic of Valencia, Cardiology Department, INCLIVA, Department of Medicine, Valencia University, Department of Medicine,, Valencia, Spain*

Background: Although tricuspid regurgitation (TR) is a common echocardiographic finding among patients with acute heart failure (AHF), its short-term prognostic impact remains unclear. We aimed to evaluate the association between the severity of TR and short-term adverse outcomes following a hospitalization for AHF.
Methods: We prospectively included 2244 consecutive patients discharged with a diagnosis of AHF. TR was assessed using an integrated multi-parametric score that combines qualitative and semi-quantitative parameters and its severity categorized as a) none (grade 0), b) mild (grade I), c) moderate (grade II), d) moderate-severe (grade III), and severe (grade IV). The primary end-point was the composite of mortality and rehospitalization for heart failure at 90 days. Multivariate analyses were performed using Cox proportional hazards models.
Results: Mean age was 73.2 +/- 11.2 years, 50.4% were male, 31.7% had a LVEF < 40% (HFrEF), 15% between 41-49% (HFmrEF) and 53.3% >50% (HFpEF). At discharge, 792 (35.2%), 843 (37.6%), 379 (16.9%), 170 (7.6%) and 60 (2.67%) patients showed none, mild, moderate, moderate-severe and severe TR. At 90-day follow-up, 439 patients either died or were readmitted due to HF. We registered a stepwise increase in the risk of the composite endpoint from grades I to IV (p < 0.001) as shown in the figure below. After multivariable adjustment, and compared to those without TR, only patients with TR III or IV showed a significantly higher risk of reaching the endpoint (HR = 1.54; 95% CI: 1.13 - 2.08; p= 0.006).
Conclusion: In AHF setting, TR grade III-IV independently predicts the risk of short-term adverse events.



P463

Impact of load variations on systolic function of failed left ventricle under extracorporeal membrane oxygenation assessed by strain and tissue doppler imaging

N Ouazani[1]; Y Shudo[1]; K Sallam[1]; A Lee[1]; J Boyd[1]; J Teuteberg[1]
[1]*Stanford University, Cardiovascular Institute, Palo Alto, United States of America*

Introduction: Load variations have been studied in a wide range of healthy and cardiac patients. Although the diastolic conventional parameters (filling pressures) showed a load dependency, the results are controversial for systolic function assessed by Tissue Doppler Imaging (TDI) and Global Longitudinal Strain (GLS) in failing hearts. Our purpose is to assess the impact of rapid variations of flow on systolic function of left ventricle (LV) of patients under veno-arterial extracorporeal membrane oxygenation (VA ECMO) by echocardiography.

Method: The data were collected from an observational prospective study conducted in Stanford Cardiovascular Intensive Care Unit since July 2017, and included all patients under VA ECMO who met the criteria to undergo a ramp study (mean arterial pressure > 60mmhg, pulsatile waveform for 24 hours at least, normal pulmonary oxygen blood flow). This study was approved by our Institutional Review Board. The baseline clinical characteristics of patients were recorded. During the ramp, the flow was decreased by 0,5 liter every 2 minutes until the minimum value, either 1 or 1,5 liter delivered by ECMO. The following echocardiographic parameters were recorded at each step of flow: LV end diastolic dimensions (LVEDD), LV end diastolic volume and LV ejection fraction in 4 cavities (LVEDV4C and LVEF4C), velocity time integral (VTI), systolic tissue Doppler on lateral (SaL) and septal (SaS) mitral annulus, global longitudinal strain on LV (GLS LV) and GLS rate on LV (GLSr LV). To homogenize and to ensure comparison between patients, the echocardiographic parameters were analyzed at baseline, 66% and 33% of initial flow.
Results: Ten patients under ECMO whom 4 myocarditis, 1 ischemic cardiomyopathy and 1 non-ischemic cardiomyopathy underwent a complete ramp study. The median age was 37,5 years (18-64), 30% were male and the median SAPS 2 score was at 24,5. The mean arterial pressure decreased but not significantly whereas the heart rate remained stable. The median LVEF4C at baseline was severely reduced at 0,2 (0,09-0,39). The LVEDD and LVEDV4C slightly increased but not significantly. The LVEF4C and VTI increased respectively, from 0,23 to 0,29 (p <0,01) and from 9,2 (InterQuartile Range IQR : 7,8-13,2) to 14cm/sec (IQR: 11,7-16,2), p <0,00001. The GLS LV and GLSr LV changed significantly, respectively from -5.3 (IQR: -2.7 to -6.1) to -8.4% (IQR: -5.84 to -9.21, p <0,01) and from -0,4 (-0.2 to -0.6) to -0.8/sec (-0.4 to -0.9, p <0,001), as TDI SaS from 5,7 (IQR: 4,1-6,5) to 6,4cm/sec (IQR: 4,9-7,6, p <0,001). The TDI SaL remained unchanged from 6,1 (IQR: 5,3-7,1) to 6,3cm/sec (5,4-8,4), p = 0,1.
Conclusion: Based on a small study, the lateral systolic TDI parameter SaL of failed LV appeared to be load independent contrary to conventional parameters (VTI, LVEF), those derived from strain (GLS and GLSr) and TDI measured on septal mitral annulus. These data need to be validated in a larger sample.

P464
Prognostic significance of in-hospital coronary angiography in patients hospitalized with acute heart failure -results from REALITY-AHF-

E Eiichi Akiyama[1]; M Konishi[1]; T Okumura[2]; K Kida[3]; S Oishi[4]; S Suzuki[5]; M Yamamoto[6]; T Kitai[7]; Y Matsue[8]
[1]Yokohama City University, Division of cardiology, Yokohama, Japan; *[2]Nagoya University , Nagoya, Japan*; *[3]St. Marianna University, Kawasaki, Japan*; *[4]Himeji Cardiovascular Center, Himeji, Japan*; *[5]Fukushima Medical University, Fukushima, Japan*; *[6]Tsukuba University, Tsukuba, Japan*; *[7]Kobe City Medical Center General Hospital, Kobe, Japan*; *[8]Kameda Medical Center, Chiba, Japan*

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Background: Coronary artery disease (CAD) is a major cause of heart failure (HF). Urgent coronary angiography (CAG) is recommended for patients with acute HF (AHF) complicated with acute coronary syndrome (ACS); however, clinical usefulness of in-hospital CAG in AHF patients without ACS remains unknown.
Purpose: To investigate the association between in-hospital CAG and all-cause mortality at 1-year after hospital discharge.
Methods: From the REALITY-AHF study, 1344 patients hospitalized with AHF were enrolled in this study and followed up for 1-year after hospital discharge.
Results: In our AHF cohort, 511 patients (38%) underwent in-hospital CAG. CAG group was younger, more likely to be male, had higher prevalence of HF with reduced left ventricular ejection fraction (< 40%), de novo HF, and diabetes mellitus compared with non-CAG group (all P < 0.01). The history of CAD was similarly observed in both groups. CAG group had lower creatinine levels and higher hemoglobin levels compared with non-CAG group (both P < 0.001). Unadjusted risk of death at 1 year was lower in CAG group than in non-CAG group (hazard ratio [HR] 0.30, 95%-confidence interval [CI] 0.21-0.43, P < 0.001). Likewise, CAG group was associated with lower mortality compared with non-CAG group after adjustment for MAGGIC score (HR 0.45, 95%-CI 0.29-0.70, P < 0.001) and in propensity-score matched 296 pairs (HR 0.60, 95%-CI 0.37-0.98, P = 0.04).
Conclusions: In patients hospitalized with AHF, in-hospital CAG was associated with a better long-term survival.

Acute Heart Failure - Treatment

P465
Effect of serelaxin on worsening heart failure when added to standard therapy in European patients with acute heart failure: Results from the RELAX-AHF-EU study

A P Maggioni[1]; J Lopez-Sendon[2]; M Aalamian-Mattheis[3]; J Hallen[3]; Y Wang[4]; O W Nielsen[5]; G Ertl[6]
[1]Associazione Nazionale Medici Cardiologi Ospedalieri Research Center, Florence, Italy; *[2]University Hospital La Paz, Madrid, Spain*; *[3]Novartis Pharma AG, Basel, Switzerland*; *[4]Novartis Pharmaceuticals Corporation, East Hanover, United States of America*; *[5]Bispebjerg University Hospital, Copenhagen, Denmark*; *[6]Comprehensive Heart Failure Center (CHFC), Wurzburg, Germany*

Funding Acknowledgements: Novartis pharma AG, Basel, Switzerland

Background: About 10-30% of patients with acute heart failure (AHF) develop in-hospital worsening heart failure (WHF). Serelaxin, a recombinant human relaxin-2 hormone with vasodilatory properties, improved dyspnoea and clinical outcomes in AHF patients in a phase III clinical trial. However, a larger trial, RELAX-AHF-2, reported neutral effects on WHF and 6-month cardiovascular mortality.
Purpose: RELAX-AHF-EU study (CT.gov identifier: NCT02064868) primarily assessed the effect of serelaxin added to standard of care therapy (SoC) on WHF or all-cause death through Day5 in patients hospitalised for AHF.
Methods: This prospective, randomised, open-label, blinded-endpoint evaluation study, enrolled hospitalised AHF patients at 494 sites across 26 European countries. Within 16 hours of presentation with dyspnoea, pulmonary congestion, elevated natriuretic peptide levels, mild-to-moderate renal impairment and systolic blood pressure = 125mmHg, eligible patients were randomised (2:1) to receive 48-hour intravenous infusion of 30µg/kg/day serelaxin+SoC or SoC. The primary endpoint was time to adjudicated WHF/all-cause death through Day5. Secondary endpoints included WHF/all-cause death/rehospitalisation for heart failure (HF) through Day14, persistence of HF symptoms and renal deterioration (= 0.3mg/dL increase in serum creatinine) through Day5, index length of hospital stay (LoS) and safety through Day30.
Results: Of a target of 3183 patients, 2666 were randomised when the study was terminated early by the sponsor due to the neutral RELAX-AHF-2 **Results:** Adjudicated WHF/all-cause death through Day5 was significantly reduced in the serelaxin+SoC vs SoC group (5.0%vs.6.9%; hazard ratio [HR] 0.71; 95% confidence interval [CI] 0.51-0.98; P = 0.017), but when all events reported by the investigator (not adjudicated) were considered, the difference between treatment groups was not significant. No significant difference between treatment groups was observed for the rate of WHF/all-cause death/HF rehospitalisation through Day14 (HR 0.79; 95%CI 0.61-1.02; P = 0.063) and for the LoS during index hospitalisation (P = 0.139). The rate of persistent HF signs/symptoms was significantly lower in the serelaxin+SoC vs SoC group at each visit until Day4. Fewer patients experienced renal deterioration through Day5 in the serelaxin+SoC vs SoC group (17.1%vs.23.6%; P = 0.0001). Overall incidence rates of treatment-emergent adverse events (AEs) through Day5 (serelaxin+SoC,58.1% vs SoC,56.0%), serious AEs through Day14 (12.4%vs.12.0%) and all-cause deaths through Day30 (3.3%vs.4.3%) were comparable between treatment groups. Hypotension and haemoglobin/haematocrit decreased more frequently in the serelaxin+SoC group.
Conclusion: The primary endpoint was met indicating serelaxin reduces adjudicated WHF when added to SoC, but due to early study termination and lack of power, efficacy analyses should be considered as exploratory. The incidence of AEs was comparable between groups.

P466
Targeted interventions reducing late maternal death due to heart failure

F Feriel Azibani[1]; J Baard[1]; A Osman[2]; L Zuhlke[3]; A Lachmann[2]; E Libhaber[4]; A Chin[1]; M Ntsekhe[1]; P Soma-Pillay[5]; MR Johnson[6]; J Roos-Hesselink[7]; J Anthony[2]; K Sliwa[1]
[1]University of Cape Town, Medicine, Cape Town, South Africa; *[2]University of Cape Town, Obstetrics & Gynaecology , Cape Town, South Africa*; *[3]University of Cape Town, Paediatrics, Cape Town, South Africa*; *[4]University of the Witwatersrand, Soweto Cardiovascular Research unit, Johannesburg, South Africa*; *[5]University of Pretoria, Obstetrics & Gynaecology , Pretoria, South Africa*; *[6]Imperial College London, London, United Kingdom*; *[7]Erasmus Medical Center, CARDIOLOGY, Rotterdam, Netherlands*

Background: Late maternal mortality (up to 1 year postpartum) is poorly reported globally and is commonly due to cardiovascular disease (CVD). We reported previously on the spectrum of disease, mode of presentation, maternal and fetal outcome in patients referred to a dedicated Cardiac Disease and Maternity Clinic (CDM), identifying excellent survival outcome rates in pregnant mothers with complex diseases,

but a high 6-month postpartum mortality. The aim of this study was to investigate two targeted interventions aimed at reducing peripartum heart failure admission and late maternal death.
Methods and Results: Women presenting with CVD in pregnancy, or within 6 months postpartum, were studied in a single-centre, prospective ongoing study over a period of 6 years. Both CDM Group I (152 women assessed in 2010-2012) and Group II (117 patients assessed in 2013-2015) were attended to by a dedicated cardiac-obstetric team, with input by other specialists, at the CDM clinic while pregnant. CDM Group II patients routinely received additional targeted interventions: 1. Early (2-6 weeks) postpartum follow-up at the CDM clinic and immediate referral to dedicated CV specialist clinics, remaining under close supervision and care by the CDM team for a period of 1 year. 2. Beta-blocker therapy was continued in women with left ventricular ejection fraction <45% while pregnant, or immediately started postpartum. Follow-up data on maternal mortality and re-admission was collected over a period of 1 year post diagnosis.
Of the 269 consecutive women (mean age 28.6 ± 5.9), 213 (79%) presented prepartum, 22% in NYHA Classification group III-IV and 79% in modified World Health Organization (WHO) Group III-IV (high risk). Patients were diagnosed with congenital heart disease (30%, 25 operated previously), valvular heart disease (25%, 15 operated previously), cardiomyopathy (31%) and other (14%).
There were no significant differences between the groups in age, gravida, diagnosed condition, NYHA, modified WHO Group, blood pressure, heart rate and HIV, but patients in CDM Group II had a higher rate of previously known CVD (p <0.0001), as well as a lower rate of being nulliparous (p < 0.0005). Nine patients (6%) from CDM Group I died within the 12-month follow-up period. Eight of the 9 patients died >42 days postpartum. Group 2 had one death occurring 132 days postpartum (p = 0.029). Peripartum heart failure leading to admission was 32% (n = 48) in CDM Group I versus 14% (n = 16) in CDM Group II (p = 0.0008), with CDM Group II having a significantly higher beta-blocker use in the peripartum period (p = 0.0002). Perinatal death occurred in 1/152 in group I and 5/117 in group II (p = 0.088) - translating to a perinatal mortality rate of 22/1000 live births. Conclusion: Early follow up in a dedicated CDM clinic with targeted interventions, continuation of beta-blockers when indicated and timely referral led to a significant reduction in peripartum heart failure admission and mortality.

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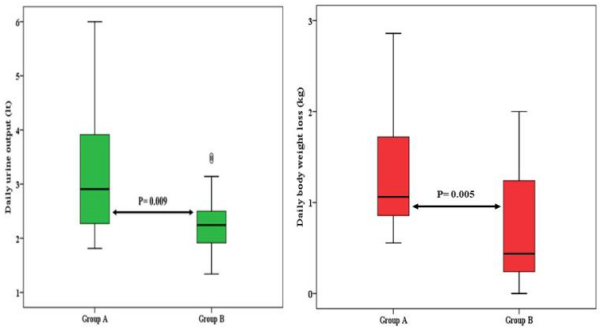
Association between high-dose spironolactone and decongestion in patients with acute heart failure

C Chris Kapelios[1]; M Bonou[1]; P Vogiatzi[1]; P Mantzouratou[1]; S Vakrou[1]; K Malliaras[1]; D Dambasis[1]; M Chalikos[1]; LH Lund[2]; J Barbetseas[1]
[1]Laiko University General Hospital, Athens, Greece; *[2]Karolinska University Hospital, Stockholm, Sweden*

Background: Acute congestive heart failure (ACHF) is a state of severe, secondary hyperaldosteronism. Relief of congestion has prognostic implications. High doses of spironolactone have been proposed as a potential measure to increase diuresis in ACHF with diuretic resistance.
Purpose: Our aim was to assess associations between high-dose spironolactone and a) decongestion and b) safety in patients with ACHF.
Methods: Twenty patients who were hospitalized with ACHF and received high doses of spironolactone (75-300 mg daily, Group A) on top of standard of care (SOC) treatment were studied and compared with twenty matched patients who received SOC treatment alone (Group ?).
Results: The two groups were similar as per their baseline characteristics. Mean daily spironolactone dose was 143 ± 56 in group A vs. 25 ± 25 mg in group B (P < 0.001). Patients of group A demonstrated significantly greater daily urine output (2.9 [2.3, 3.9] vs. 2.2 [1.9, 2.5] L/day, P = 0.009, figure 1), daily weight loss (1.1 [0.9, 1.7] vs. 0.4 [0.2, 1.2] kg/day, P = 0.005, figure 1), total body weight loss (10.5 [7.3, 13,8] kg vs. 3.8 [3.0, 6.0] kg, P < 0.001) and percentile body weight loss (12.8 ± 4.9 % vs 5.7 ± 4.6%, P < 0.001) compared with patients of group B. The incidence of worsening renal function (15% vs. 30%, P = 0.451), hypokalemia (10% vs. 25%, P = 0.212) and hyperkalemia (5% vs. 10%, P = 0.548) were also similar among patients of group A and group B, respectively. Nineteen out of twenty patients in group A (95%) were prescribed spironolactone (50 [25, 125] mg) at discharge as compared with 14/20 (70%) in group B (25 [0, 25] mg) (P = 0.037 for comparison of prescription rates and P = 0.004 for comparison of spironolactone dose at discharge). One case of hyperkalemia (potassium levels of 6.2 mmol/L) was noted in the HPODS group. At the 3-month follow-up 1/20 (5%) patients in Group A vs 5/20 (25%) patients in Group B had been rehospitalized (P = 0.077).
Conclusions: In patients with ACHF administration of high doses of spironolactone on top of SOC treatment appears safe and is associated with greater decongestion than SOC alone.



P468

Time to Furosemide Treatment and Outcomes in patients admitted for Acute Heart Failure

D David Cabrita Roque[1]; D Candeias Faria[1]; J Augusto[1]; J Baltazar Ferreira[1]; A Sacchetti[2]; L Melo[2]; J Simoes[1]; C Morais[1]
[1]Hospital Prof Fernando da Fonseca EPE, Cardiology, Amadora, Portugal; *[2]Hospital Prof Fernando da Fonseca EPE, Internal Medicine, Amadora, Portugal*

Introduction: Acute Heart Failure (AHF) is a life-threatening disease requiring urgent treatment. The most recent ESC Guidelines established the concept, previously well known for acute myocardial infarction, of time to treatment in this group of patients.
Purpose: The aim of this study is to evaluate the association between time-to-diuretic treatment and clinical outcomes in patients admitted in the Emergency Department for AHF. We also aim to evaluate if the total dose of diuretic in the first 24 hours of hospitalization has an impact on outcomes.
Methods: Retrospective study of 258 consecutive patients admitted in the emergency department for ADHF, defined by the presence of = 2 signs or symptons of heart failure. Admission, maximum and discharge values of creatinine (Cr) were collected, along with other clinical, laboratory and therapeutic variables. The HF profile was assessed as according to the ESC guidelines. Furosemide was considered as the standard diuretic since is the only endovenous diuretic in our hospital pharmacy.
Results: We evaluated 258 patients with ADHF (45.7% male, mean age of 74.6 ± 16.6 years). The median time for the administration of Furosemide was 16 (5-100) minutes. We further divided the patients in two groups: the early treatment group (= 60 minutes until the first administration of IV Furosemide, 68.6%) and the nonearly treatment group (< 60 minutes until the first administration of IV Furosemide, 31.4%). Median baseline Cr was 1.29 (0.94-1.92) mg/dl, maximum Cr was 1.49 (1.14-2.13)mg/dl and discharge Cr was 1.21 (0.96-1.71)mg/dl. The death rate during hospitalization was 8.1% (n = 21); 1-month readmission rate was 18.2%% (n = 47). The patients in the early treatment group were more likely to have na emergente admission (52.4 vs. 15.6%, p < 0.001) and to have a higher blood pressure at admission (median 150 vs 141mmHg, p = 0.042). There was a tendency to better clinical outcomes in terms of in-hospital death (7.1% in the < 60 minutes groups vs. 9.1%, p = 0.0612), but no difference in terms of nadir GFR (p = 0.823). The median diuretic dose in the first 24h was 80 (60-100mg) and patients that received > 60mg of Furosemide in the first 24h had higher systolic blood pressure at admission (median 155 vs 133mmHg, p < 0.001), were more likely to have an emergent admission (45.7 vs 33.0%, p = 0.049) and had lower peak Cr values (mean 0.95 vs 1.34mg/dL, p = 0.049)
Conclusions: This study establishes that time to treatment in patients admitted for acute heart failure should be an important parameter when evaluating the way, we treat our patients, since the time to first administration of IV furosemide (using a cut-off of 60 minutes in this study) shows a tendency to be associated with worse clinical outcomes, namely in-hospital mortality. Besides that, although it's more likely that patients admitted through the emergency room and those that have higher blood pressure to be treated early, all patients should be early evaluated and treated.

P469

Use of levosimendan in the real world over the last 10 years - what to expect?

S Sofia Alegria[1]; AC Gomes[1]; A Marques[1]; AR Pereira[1]; D Sebaiti[1]; MJ Loureiro[1]; I Rangel[1]; AR Almeida[1]; OS Simoes[1]; H Pereira[1]
[1]*Hospital Garcia de Orta, Cardiology, Almada, Portugal*

Introduction: Levosimendan is an inodilator drug that has emerged as a new cardioprotective inotropic. In addition it acts in other tissues, such as the coronary vascular endothelium, kidney and brain.
Purpose: To characterize patients treated with levosimendan, analyze its impact on kidney function, natriuretic peptides, functional class and days of hospitalization, as well as to identify predictors of mortality in this population.
Methods: Retrospective study including all patients treated with levosimendan during the last 10 years in a Cardiology Department of a tertiary center.
Results: 80 hospitalizations were identified in 61 patients, 77% male, mean age 60 years (IIQ 55-72). 72% were in NYHA class IV, LV ejection fraction (EF) was 22 ± 8% and 57% had RV systolic dysfunction.
The majority of patients were admitted from the emergency department and the outpatient clinic (50 and 44%, respectively). The main reason for initiating levosimendan was decompensated heart failure (HF) in advanced functional class and symptoms of low cardiac output (83%). It was also used in the setting of acute myocardial infarction with cardiogenic shok (11%) and previous to hemodynamic evaluation by right heart catheterization (6%). The mean blood pressure (BP) before starting levosimendan was 100/61 mmHg (minimum 74/34 mmHg), the maximum dose reached was 0.13 ± 0.06 ug/kg/min and adverse effects occurred in 5% of the cases. During hospitalization, 19% needed vasopressors and 29% dobutamine.
There was a significant improvement in kidney function (serum creatinine (Cr) 1.6 vs 1.3 mg/dl), NT-proBNP (7702 vs 3157 pg/dl), functional class (74% with improvement >= 1 class), and a reduction in the number of days of hospitalization in the subsequent 12 months compared to the previous 12 months (median 16 vs 0 days) ($p < 0.05$ in all). In the echocardiogram performed after treatment with levosimendan (median 96 days), 26% presented EF improvement (defined as >5% and final EF >30%) and 31% recovered RV function.
30-day mortality was 21%, 1-year mortality 38%, and the overall mortality at follow-up (median 575 days) was 61%. In the patients admitted for decompensated HF, the predictors of 1-year mortality were: use of metolazone before hospitalization (HR 4.54, $p = 0.018$), need for vasopressors or dobutamine (HR 2.69, $p = 0.041$, and HR 7.08, $p < 0.001$, respectively), maintenance of NYHA class IV or absence of functional class improvement (HR 78.22, $p < 0.001$, and HR 11.04, $p = 0.003$, respectively), baseline Cr >1.5 mg/dl (HR 3.06, $p = 0.034$), Cr decrease < 0.4 mg/dl (HR 3.53, $p = 0.028$) and lowest NT-proBNP after levosimendan >4500 pg/dl (HR 4, 96, $p = 0.011$).
Conclusion: The use of levosimendan in this population was well tolerated, even in patients with low BP profile, and was associated with improvement of functional class, kidney function, NT-proBNP and reduction of days of hospitalization. Despite this, the mortality rate remains very high in these patients.

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Impact of levosimendan in the renal function of heart failure patients: data from a 10-year cohort

S Sofia Alegria[1]; A Marques[1]; AR Pereira[1]; AC Gomes[1]; D Sebaiti[1]; A Briosa[1]; MJ Loureiro[1]; AR Almeida[1]; OS Simoes[1]; H Pereira[1]
[1]*Hospital Garcia de Orta, Cardiology, Almada, Portugal*

Background: Impairment of renal function (RF) is common in heart failure (HF) patients and is associated with high morbidity and mortality. Levosimendan (LVS) is a calcium sensitizer and ATP-dependent potassium channel opener developed for treating acute HF. Timely intervention with LVS may reverse renal dysfunction through several protective mechanisms.
Purpose: To analyze the impact of treatment with LVS in the RF of patients with HF, as well as to identify predictors of improvement in RF and its association with one-year mortality.
Methods: Retrospective study including all patients treated with LVS during the last 10 years in the Cardiology Department of a Tertiary Center. Improvement of RF was defined as decrease in serum creatinine (Cr) = 0.3 gr/dl.
Results: 80 hospitalizations were identified in 61 patients (77% male, median age 60 years (IQR 55-72). 72% were in NYHA class IV and mean EF was 22 ± 8%.
The main reasons for initiating LVS was decompensated HF in advanced functional class and with signs of low output (83%) and acute myocardial infarction with evolution in cardiogenic shock (11%). In the remaining patients, it was used previous to hemodynamic evaluation by right heart catheterization (6%). The maximum dose reached was 0.13 ± 0.06 ug/kg/min and adverse effects occurred in 5% of the cases. During hospitalization, 19% needed vasopressors and 29% dobutamine.
In 58.1% of patients RF improved after treatment with LVS (Cr 1.89 ± 1.05 vs 1.35 ± 0.55 mg/dl; $p < 0.001$), with the lowest value of Cr obtained 4 days after starting the perfusion. However, this improvement was not significant at 6 months (Cr 1.51 ± 0.66 mg/dl). Patients with CRT, AFib, adverse reaction to LVS or that required treatment with vasopressors or dobutamine were less likely to improve renal function; on the other hand, patients with diabetes or chronic kidney disease (CKD) were more likely to improve renal function ($p < 0.05$ for all). There was no difference between ischemic or non-ischemic etiology of HF regarding improvement in RF with the use of LVS.
After adjusting for confounding variables, the only predictor of improvement of RF at 6 months was the reduction of Cr in the days after treatment with LVS (OR 8.75; $p = 0.015$).
All-cause mortality was 21% at 30 days, 38% at 1 year and 61% at the end of follow-up (median 575 days). In patients admitted for decompensated HF, both the baseline RF (Cr >1.5 mg/dl) and the lowest Cr after treatment with LVS >1.05 mg/dl were predictors of 1-year mortality (HR 3.06, $p = 0.034$; and HR 6.01, $p = 0.019$, respectively).
Conclusion: This study shows that in this population the use of LVS was associated with improvement in RF, and that kidney injury is associated with higher mortality. Nevertheless, LVS seems to have less benefit in more critical patients, although it has good results in patients with previous history of CKD or risk factors for CKD, like diabetes.

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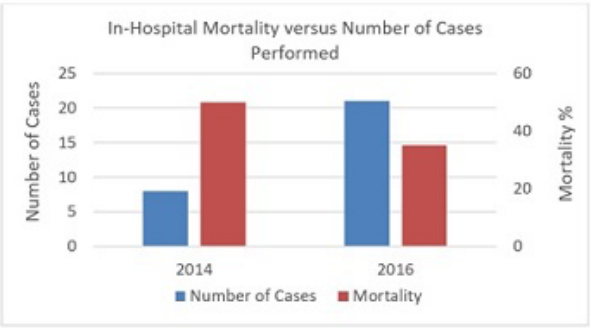
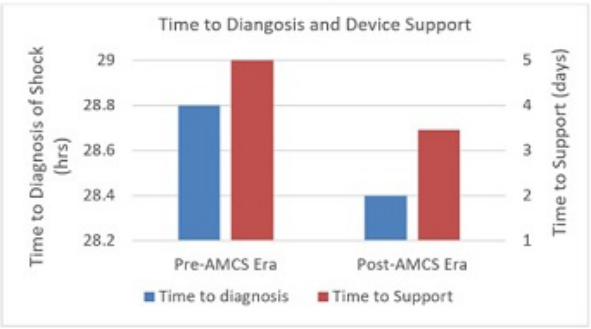
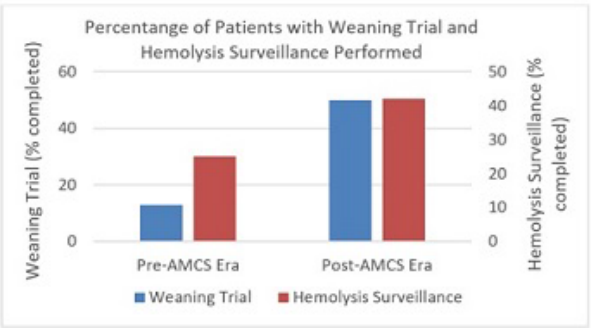
Value of multi-disciplinary systematic evaluation of acute mechanical circulatory support for cardiogenic shock in a regional non-transplant LVAD center

K Gobeil[1]; V Grewal[1]; F Katsikeris[1]; J Hernandez-Montfort[1]; E Lau[1]; M Slawsky[1]; G Valania[1]; D Engelman[1]; D Deaton[1]; A Haider[1]; P Robinson[1]; A Islam[1]; C Donaldson[1]
[1]*Baystate Medical Center, Springfield, United States of America*

Background: Cardiogenic shock (CS) remains a disease entity with an unacceptably high mortality. Early recognition provides the possibility of instituting therapies that can promote myocardial recovery and/or safer transition to a durable solution such as left ventricular assist device or heart transplant.
Purpose: The complexity and heterogeneity of CS patients requires expertise and longitudinal coordination of care. Early recognition and timely intervention remains paramount in this subset of patients. The aim this research is to examine the benefits of implementing a systematic approach to CS patients directed by a multidisciplinary team.
Methods: We conducted a retrospective chart review of 43 patients receiving acute mechanical circulatory support (ACMS) via Impella (CP or 5.0) with or without VA-ECMO for the indications of CS during a period from 2014 to 2016 at Baystate Medical Center. In September 2015, an AMCS/CS team initiated a systematic care program based on integration of clinical, hemodynamic and echocardiographic profiling.
Results: From January 2014 to December 2016, time to device implant went from an average of 5.4 days to 3.4 days. The number of cases performed per calendar year increased from 8 in 2014 to 21 in 2016. Patient profiling, namely echocardiographic assessment, right heart catheterization and weaning trails with hemolysis surveillance, increased from 50% to 85%; 2014 and 2016 respectively. Mortality during this time trended down from 45% in 2014 to 33% in 2016. Lastly, involvement of advanced heart failure specialist increased yearly (20% in 2014 and 85% in 2016). The purpose of the study is descriptive, additional time and patient enrollment will allow for future assessment of statistical significance.
Conclusion: We aim to highlight the importance of a multi-disciplinary systematic approach to CS patients, involving both early recognition and intervention. The importance of timely invasive strategies requires expertise and coordination of care amongst cardiovascular specialties and front-line clinicians. Implementation of a multidisciplinary AMCS/CS team resulted in streamlined care and profiling of optimal patient selection allowing earlier intervention. Through longitudinal care, we were able to drastically increase the volume of patients cared for with earlier MCS intervention, ultimately providing a trend towards mortality improvement. Multi-center prospective registry data will help define clinical and socioeconomic profiles associated with myocardial recovery.







Graphic Representation

P472

Cardiac autonomic nerves stimulation improves hemodynamics: a pilot study in advanced heart failure patients

MPC Michael Cuchiara[1]; CM Marin Y Kall[2]; JB Boehmer[3]; MC Cowie[4]; AM Mebazaa[5]; TD Diaz[6]

[1]NeuroTronik, Clinical Research, Durham, United States of America; *[2]University of Miami, International Medicine Institute, Miami, United States of America*; *[3]Milton S. Hershey Medical Center, Hershey, United States of America*; *[4]Imperial College London, National Heart and Lung Institute, London, United Kingdom*; *[5]University Paris Diderot , Paris, France*; *[6]Hospital Punta Pacifica, Panama City, Panama*

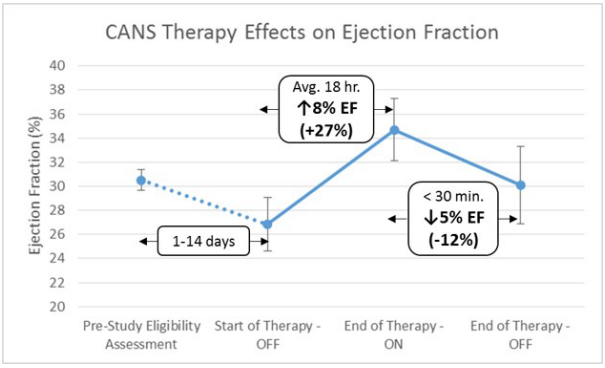
Background: Despite therapy advances in the management of heart failure, symptomatic congestion in acute heart failure is a leading cause of mortality and morbidity. An electrode catheter-based technology is being investigated to transvenously stimulate cardiac autonomic nerves to control left-ventricular contractility and heart rate (HR) in order to improve hemodynamics.

Purpose: The purpose of this study was to investigate transvenous cardiac autonomic nerve stimulation (CANS) effects on in-hospital hemodynamics and signs and symptoms of congestion.

Methods: The present study was a single-center, observational, clinical investigation of CANS. Five (5) subjects with reduced left ventricular ejection fraction (LVEF < 40%), who presented with at least two signs and symptoms of congestion were consented and enrolled. A purpose-built electrical stimulation catheter was placed percutaneously, under fluoroscopic guidance, in the left brachiocephalic vein via left subclavian vein access. A purpose-built neurostimulator was then connected to the catheter and used to deliver CANS therapy bedside, for an allowed duration up to 24 hours. Hemodynamic effects and measures of signs and symptoms of congestion were observed over the stimulation period.

Results: The majority of the subjects were male (3/5), had a mean age of 65 years, mean body mass index of 34, mean NT-proBNP of 3622 pg/mL and a mean Pulmonary Capillary Wedge Pressure (PCWP) of 30 mmHg. CANS was provided for a mean of 18 hours and was well tolerated. There were no safety concerns or adverse events reported. LVEF increased in all subjects (mean +8% from 27% to 35%) over the stimulation period. LVEF acutely decreased a mean of -5% (from a mean of 35% to 30%) in direct association with stimulation cessation. In three (3) subjects, CANS directly modulated arterial pulse pressure (12% average change) with a neutral heart rate effect (< 1% average change) over the stimulation period. PCWP decreased in all subjects (mean reduction of 10 mmHg from 30 to 20 mmHg) over the stimulation period. PCWP improvements were accompanied by improvements in dyspnea and edema from pre-study to discharge. The hemodynamic and clinical improvements occurred in the presence of minimal changes to concomitant medical therapy.

Conclusion: Alongside concomitant medical therapy, CANS directly improved hemodynamics and was associated with improved signs and symptoms of congestion in advanced symptomatic heart failure patients. These improvements, coupled with a positive safety profile, demonstrate that CANS holds promise as a tool to improve in-hospital hemodynamics and congestion. As the present study included stimulation of limited duration, in a specific patient phenotype, with a limited number of subjects, future study is warranted to investigate CANS Therapy for longer stimulation duration, in expanded patient phenotypes, in more subjects.



P473

Add-on immunoadsorption shortly-after optimal medical treatment further significantly and persistently improves cardiac function and symptoms in recent-onset heart failure

K Karolina Weinmann[1]; J Werner[1]; W Koenig[1]; W Rottbauer[1]; D Walcher[1]; M Kessler[1]

[1]University of Ulm, Department of Medicine II, Ulm, Germany

Background: Immunoadsorption and intravenous immunoglobulin administration (IVIG) can have beneficial effects in dilated cardiomyopathy patients with end-stage heart failure (HF).

Purpose: We investigated the effect of immunoadsorption with subsequent intravenous immunoglobulin (IVIG) administration on cardiac function and symptoms in patients on optimal medical heart failure treatment (OMT) with recent-onset cardiomyopathy in long-term follow-up.

Methods: Thirty-five patients with recent-onset of HF symptoms received intensive guideline-recommended medical HF therapy (OMT) for 5.2 months. Subsequently, all patients received a single cycle of immunoadsorption for five days subsequent IVIG administration. In a 28-month follow-up NYHA functional class, left ventricular ejection fraction (LVEF) and N-Terminal pro Brain Natriuretic peptide (NT-proBNP) were evaluated. Changes in quality of life (QoL) were assessed using the Minnesota Living with HF Questionnaire.

Results: During the period of 5.2 months on OMT, NYHA-class improved from median NYHA-class 3.0 to 2.0, whereas LVEF remained unchanged (LVEF 27.0%). Subsequently, all patients received immunoadsorption and subsequent IVIG administration. At first follow-up, three months after immunoadsorption treatment, NYHA-class further improved to 1.5 ($p < 0.005$) and LVEF significantly increased to from 27.0% to 39.0% ($p < 0.0001$). Long-term follow-up of 28 months showed a stable NYHA-class and a further moderate increase in LVEF from 39.0% to 42.0%

($p < 0.0001$) accompanied by a significant improvement of NT-proBNP and QoL scores.
Conclusion: Immunoadsorption and subsequent IVIG administration further enhances LVEF, HF symptoms, QoL and biomarkers in patients with recent-onset HF on optimal medical treatment.

P474
The inspection of usefulness judging from the view point of physical therapist about clinical pathway with early use of tolvaptan for congestive heart failure cases

T Teruaki Kubo[1]; K Kuroiwa[1]; H Wake[1]; J Inoue[1]; N Kajiwara[1]; K Kimura[1]; Y Kato[2]; M Hasegawa[2]; Y Nakano[2]; A Takaishi[2]
[1]Mitoyo General Hospital, Rehabilitation, Kanonji, Japan; *[2]Mitoyo General Hospital, Cardiovascular Center, Kanonji, Japan*

Background: In Japan, the patients with congestive heart failure(CHF) continue increasing rapidly in recent years. The mean age of them was usually over 80 years old, so the hospitalization period tend to be prolonged by the deterioration of dementia or lowering of activity. And they are often readmitted with exacerbation of CHF within short duration. For the resolution of these problems we introduced the original clinical pathway for CHF cases(CP) in which early use of Tolvaptan and early start of physical therapy ware provided after admission.
Purpose: We inspected the clinical usefulness about CP judging from the view point of physical therapist(PT).
Method: We enrolled 334 CHF patients admitted in our hospital between April 2011 and July 2017 who had not been admitted with CHF within past 1 year and left our hospital to own home directly(mean age 80 ± 10 years old, male/female 178/156). And we divided them to two groups, NCP-group (the cases who ware admitted before introduction of CP: 207 cases) and CP-group(the cases who ware applied CP after admission:127 cases. We investigated their characteristics and clinical course from the view point of PT and examined the difference about them between two groups.
Results: Between CP-group and NCP-group there was no difference about mean age(79.6 ± 10.2 vs 79.7 ± 10.0 years old), the ratio of male to female(95/62 vs 106/101), the prevalence of dementia(30 vs 39%) or the ejection fraction of left ventricle with echocardiography(48.3 ± 18.3 vs 50.4 ± 17.6%). In CP-group compared with NCP-group, the mean hospitalization period(15.7 ± 11.6 vs 23.8 ± 15.7 days; $p < 0.0001$) was shorter, the starting time of cardiac rehabilitation after admission was shorter(3.2 ± 1.5 vs 6.2 ± 6.1 days; $p < 0.0001$), the enforcement rate and mean duration of continuous infusion ware lower(65 vs 96%; $p < 0.0001$) and shorter(3.7 ± 2.7 vs 8.8 ± 8.6 days; $p < 0.0001$) and the enforcement rate and mean duration of urethral catheterization was also lower(41 vs 63%; $p < 0.0001$) and shorter(4.8 ± 7.6 vs 9.0 ± 8.0 days; $p < 0.0001$). In most cases of CP-group, the activities level of daily living at discharge had recovered to that before admission(99 vs 92%; $p < 0.01$). But there was not significant difference about readmission rate with CHF between CP-group and NCP-group(21 vs 31%; NS).
Conclusion: By introduction of original clinical pathway set early use of Tolvaptan and early start of rehabilitation for congestive heart failure, the enforcement of efficient medical care without waste was achieved, and this change led great shortening of their mean hospitalization period and keeping their activity level of daily living. But we could not verify the effect of prognostic improvement after discharge about this clinical pathway. We thought that the comprehensive and continuous instruction for prevention of heart failure re-exacerbation should be necessary after discharge.

P475
Multiprofessional team on acute heart failure improves short-term outcomes: results from a cohort

LCSP Luiz Carlos Passos[1]; ML Mota[2]; WN De Carvalho[2]; JCL Macedo[2]; TM Trindade[1]; VRS Souza[3]; NFC De Oliveira[4]; EOM Andrade[3]; YM Lira[4]; EL Garrido[3]; AMP De Lima[2]; AGQ De Jesus[2]; AMAF De Jesus[2]; PPC Camara[2]
[1]Federal University of Bahia, Internal Medicine, Salvador, Brazil; *[2]Ana Nery Hospital, Salvador, Brazil*; *[3]Federal University of Bahia, Faculty of Nursing, Salvador, Brazil*; *[4]Bahiana School of Medicine and Public Health, Salvador, Brazil*

Background/Introduction: Acute heart failure treatment requires specialized efforts in order to improve quality of life and reduce lethality associated to its natural prognosis. An interdisciplinary approach is one of the milestones of a high quality level of care.
Purpose: The aim of this study was to compare drug treatment and clinical outcomes before and after the initiation of a multiprofessional approach focused on acute heart failure cases in a tertiary cardiac referral centre.
Methods: Cohort data from 295 patients admitted in a tertiary cardiac referral centre for acute decompensated heart failure treatment between 2016 and 2017. Multiprofessional approach care model was defined as the initiation of a bed-to-bed clinical surveillance by a heart failure specialist staff composed by a cardiologist, a nurse and a clinical pharmacist. All the data was collected from medical records. Heart failure was defined according to the European Society of Cardiology (ESC) guidelines. All patients were submitted to a 30-day post-discharge telephone follow-up in order to investigate symptoms of decompensation, degree of drug therapy adherence and new hospitalizations or death.
Results: A sum of 295 patients was analyzed. Most of the patients were of ischaemic (34.9%) or chagasic (20.7%) etiology. Drug treatment at discharge showed significant increase over the prescription of essential heart failure pharmacologic therapy as seen by frequencies of spironolactone (56.6% vs 74.5%; $P = 0.02$), angiotensin converting enzyme inhibitor (43.4% vs 65.6; $P = 0.03$), and betablockers (77.3% vs 94.5%; $P = 0.04$). At the 30-day post-discharge telephone follow-up, patients underwent the multiprofissional approach during their hospital stay showed better therapeutic adherence (Morisky-Green scale) (75.5% vs 94.4%) and had less hospital readmissions (29.7% vs 9.4%; $P = 0.03$). Conclusion: Multiprofessional intensive surveillance significantly improved the standard of care quality as expressed by improved rates of heart failure therapy prescription and better rates of therapeutic adherence and re-hospitalizations during the shot-term post-discharge period.

P476
Clinical effectiveness and cost analysis between treatment methods of hyponatremia in acute decompensated heart failure

SP Sirait[1]; R Soerarso[1]; N Hersunarti[1]; BB Siswanto[1]
[1]National Cardiovascular Center Harapan Kita, Cardiology and Vascular Medicine, Jakarta, Indonesia

Background: Hyponatremia, defined as sodium level below 135 mEq/L, is found in 15-20% of emergency unit admissions. Hyponatremia is independently associated with adverse outcomes in patients with heart failure. High-dose diuretics for the management of congestion and edema due to heart failure may exacerbate hyponatremia caused by the loss of free water and electrolytes, including sodium and potassium. Therefore, the use of AVP receptor antagonists, which are agents that can increase free water excretion without the loss of electrolytes, may be considered in the management of heart failure. Adverse outcomes due to hyponatremia also affect health funding, and this is a potential target for intervention to decrease health costs.
Purpose: This study aims to evaluate the clinical effectiveness of treatment methods of hyponatremia in heart failure and to analyze total direct medical costs between these methods.
Methods: This is a cross sectional study in National Cardiovascular Center Harapan Kita (NCCHK) - Jakarta, Indonesia, on acute decompensated heart failure patients with hyponatremia from January 2014 until May 2017. Baseline characteristics, clinical data during hospitalization, and direct medical cost data was acquired from medical records.
Results: 128 subjects were analyzed, with 71 (55.5%) subjects treated with conventional therapy added with AVP receptor antagonist and 57 (44.5%) subjects treated with conventional therapy only. We found a significant difference ($p = 0.041$) in sodium increase after three days of therapy (median of 4 (-8 - 26) in patients receiving AVP receptor antagonist and 3 (-16 - 16) in those without), and also a significant difference ($p < 0.0001$) in length of stay (though longer in patients receiving AVP receptor antagonist, with a median of 10.50 (3-40) days, compared to 6 (3-71) days in those without). Multivariate analysis showed that day of AVP receptor antagonist initiation has the strongest correlation with length of stay ($p < 0.0001$). Partial cost analysis showed no significant difference in average daily cost with the addition of AVP receptor antagonist.
Conclusions: There is a significant difference in sodium increase after three days of therapy, yet a longer length of stay was seen in the AVP receptor antagonist group, with a strong association between length of stay and day of AVP antagonist receptor initiation. There is no significant difference in cost with the addition of AVP receptor antagonist.

P477
Shining a light on acute inpatient care experiences during an exacerbation of heart failure.

SELINA Jarvis[1]; TOM Sandford[2]; LIHUA Wu[3]; VIVEK Srivastava[1]
[1]St Thomas' Hospital, Acute Medicine , London, United Kingdom; *[2]Royal College of Nursing, London, United Kingdom*; *[3]University of Manchester, Manchester, United Kingdom*

Background: Acute Heart failure (AHF) is associated with frequent emergency hospital admissions and these may be distressing for patients. Good patient experiences have the potential to impact favourably on treatment adherence,

readmission rates and confidence after an admission. Initiatives to evaluate patient experience such as the National Patient Survey Programme (NPSP) exist but the inpatient survey asks generic questions posed which may not be relevant to patients presenting in an acute setting and are not disease tailored. Learning more about the HF patients' experience in this dynamic and acute setting may provide evidence of what is important to HF patients and help provide better care.
Purpose: (1) To understand patient experiences and care priorities during the acute inpatient stay (2) compare data acquired from qualitative interviews to a structured inpatient care experience tool, the 'AHF patient specific questionnaire (AHF-PSQ)'.

Methods: A concurrent triangulation mixed methods design was used, which included the use of qualitative semi-structured interviews to explore aspects of the acute care admission alongside data collected from the AHF-PSQ. Interviews elicited spontaneous descriptions of patient experience with AHF, which were transcribed, manually coded and a thematic analysis undertaken. In conjunction with this we compared the responses collected from the AHF-PSQ.

Results: 27 patients were interviewed with a mean (SD) age of 72.6 (12.3) yrs of age. After a thematic extraction using a hybrid method of both deductive and inductive approaches, 3 key themes that were elicited from the interviews (i) a desire to have better communication with health care staff (ii) more participation in care but through better awareness of heart failure condition and (iii) Fears about being readmitted to hospital. This data correlated with relevant items on the AHF-PSQ and also provided evidence that patients wanted more information/education about their condition and medications. 78% of patients requested more information about their 'aftercare' when leaving hospital in order to avoid readmission.
Conclusions: Qualitative approaches reveal important insight about the experiences of presenting with AHF. We also confirm that questions posed in our structured questionnaire which were deemed 'very important' to patients correlated with qualitative data. Use of a disease-focused assessment questionnaire may be a more appropriate approach to assess experience of HF patients in the acute setting which may elicit their care needs.

Acute Heart Failure - Clinical

P478
Inpatient heart failure management - cardiology participation helps improve patient care with shorter length of stay

S L Su Ling Tee[1]; GJ Ong[1]
[1]*Queen Elizabeth Hospital, Cardiology, Adelaide, Australia*

Introduction: Inpatient heart failure (HF) management is extremely complex and is often compounded by co-existing acute medical issues. Past evidence suggested that HF patients had improved outcomes when they were managed by the Cardiology team. Due to an increasing number of patients who are diagnosed with decompensated heart failure (DHF) with other acute issues in hospital, many of them are now being treated by teams other than Cardiology.
Purpose: To investigate whether admission under a different team other than cardiology would influence patient management and outcomes.
Methods: This retrospective observational study included 186 patients admitted to the local hospital over a 6-month period with a primary diagnosis of DHF under different subspecialties. Important parameters, such as length of stay, readmission rates, background medical therapy, treatment of atrial fibrillation and iron deficiency as well involvement of cardiology or heart failure nurse follow-up were obtained.
Results: Out of the 186 admissions, 133 (72%) were admitted under Cardiology. 75 (40%) of the included patients had Heart Failure with Preserved Ejection Fraction (HFpEF), 71 (38%) had Heart Failure with Reduced Ejection Fraction (HFrEF) and 24 (13%) had Heart Failure with Mid-range Ejection Fraction (HFmEF). The majority of these patients were aged 80-89 years. 127 patients (68%) had atrial fibrillation (AF), of whom 104 (82%) of them were anticoagulated. Those admitted under Cardiology had a shorter length of stay [median (interquartile range, IQR) = 5 days (IQR 3-6) vs 6 days (IQR 3-11); p = 0.02] and were more likely to receive appropriate HF therapy. In patients with HFrEF specifically, 78% (46) received cardioselective beta-blockers and 61% (35) received a mineralocorticoid receptor antagonist (MRA), compared to 58% (7) and 42% (5) (p = 0.03 and 0.01 respectively) admitted under a different team. Patients were also more likely to be followed up by HF nurse and a Cardiologist on discharge if admitted under Cardiology.
Conclusion: Inpatient HF management is challenging and optimisation of appropriate HF therapy needs further improvement. Involvement of specialist care may refine overall care with shorter length of stay and better ongoing follow up.

Medications / Follow Up	HFrEF (71)		HFmEF (24)		HFpEF (75)	
	Cardio	Others	Cardio	Others	Cardio	Others
ACE-I / ARB	49/59 (83%)	5/12 (42%)	11/20 (55%)	1/4 (25%)	28/51 (55%)	16/24 (67%)
Cardioselective Beta-Blockers	46/59 (78%)	7/12 (42%)	13/20 (65%)	3/4 (75%)	-	
MRA	36/59 (61%)	5/12 (42%)	10/20 (50%)	1/4 (25%)	16/51 (31%)	2/24 (8%)
IV Iron Therapy	15/31 (48%)	4/7 (57%)	4/13 (31%)	0/1 (0%)	8/22 (36%)	6/18 (33%)
HF nurse referral	25/59 (42%)	0/12 (0%)	3/24 (12%)	0/4 (0%)	5/51 (9%)	2/24 (8%)
Cardiology follow up	52/59 (88%)	4/12 (33%)	20/24 (83%)	0/4 (0%)	21/51 (41%)	6/24 (25%)

HF Therapy - Cardiology vs Other Teams

P479
Factors influencing extended length of hospital stay in patients with heart failure with preserved ejection fraction

C Delcea[1]; CA Buzea[1]; A Dima[2]; A Tocitu[3]; A Andrus[3]; A Breha[3]; GA Dan[1]
[1]*University of Medicine and Pharmacy Carol Davila, Colentina Clinical Hospital, Bucharest, Romania*; [2]*University of Medicine and Pharmacy Carol Davila, Bucharest, Romania*; [3]*Colentina University Hospital, Bucharest, Romania*

Introduction: Heart failure with preserved ejection fraction (HFpEF) is a clinical entity with increasing incidence as well as morbidity and mortality, accounting for up to 50% of patients diagnosed with heart failure. While cardiovascular mortality rates seem to be lower in this subset compared to reduced ejection fraction, the incidence and length of hospitalizations are reported to be similar.
Purpose: Our aim was to assess the clinical and biological profile of patients with HFpEF that require extended hospitalization.
Methods: We retrospectively analyzed data from HFpEF patients admitted to our clinic from January 2011 to December 2014. New patients with a cardiac ultrasound evaluation and an NTproBNP level on admission were prospectively included. We excluded patients with acute coronary syndromes, pulmonary embolism, infections. We classified patients into quartiles according to the length of stay (LOS). We defined an extended LOS a period equal to or greater than 7 days, the limit for the forth quartile.
Results: Our sample consisted of 347 HFpEF patients with a mean age of 67.1 ± 11.1 years. 219 patients (62.6%) were female. Mean length of stay was 4.78 ± 2.12 days. 59 patients (17%) had an extended LOS.
Longer LOS was observed in female compared to male patients (4.94 ± 2.27 vs 4.50 ± 1.80 days, $p = 0.05$), acute decompensated HFpEF compared to stable HFpEF (6.24 ± 2.40 vs 4.34 ± 1.83 days, $p < 0.001$), class IV HYNA compared to classes I-III (7.90 ± 2.88 vs 4.69 ± 2.03 days, $p < 0.001$), class III NYHA compared to classes I-II (5.54 ± 2.30 vs 4.43 ± 1.86 days, $p < 0.001$), atrial fibrillation (AF) compared to sinus rhythm (5.48 ± 2.37 vs 4.59 ± 2.01 days, $p = 0.001$), diabetes mellitus (DM) compared to no DM (5.36 ± 2.28 vs 4.57 ± 2.02 days, $p = 0.002$), reduced eGFR < 60ml/min compared to Egfr > 60 ml/min (5.91 ± 2.58 vs 4.55 ± 1.91 days, $p < 0.001$) and anemia vs normal hemoglobin levels (5.41 ± 2.25 vs 4.63 ± 2.07 days, $p = 0.004$).
In ROC curve analysis, NTproBNP was the best predictor for a prolonged LOS with an AUC of 0.769 (95%CI 0.729-0.809), $p < 0.001$. Other parameters with significant prognostic value were age with an AUC of 0.664 (95%CI 0.620-0.708, $p < 0.001$), hemoglobin with an AUC of 0.617 (95%CI 0.573-0.662, $p < 0.001$), and eGFR with an AUC of 0.656 (95%CI 0.614-0.698, $p < 0.001$).
In multiple logistical regression, only hemoglobin ($p = 0.023$) and NTproBNP ($p = 0.05$) were independent predictors of an extended LOS, irrespective of age, sex or NYHA class.
Conclusion: NTproBNP and hemoglobin levels on admission are independent predictors of an extended hospitalization in patients with HFpEF. Age, sex, NYHA class, AF and eGFR are also important parameters to be considered in anticipating a longer length of hospital stay.

P480

Platelet function parameters assessment by multiplate aggregometry in patients with acute coronary syndrome and heart failure

M Mirjana Isailovic-Kekovic[1]; P Kekovic[1]; S Apostolovic[2]; P Cvetkovic[2]
[1]Hospital Dr Aleksa Savic, Prokuplje, Serbia; *[2]Clinical Center of Nis, Nis, Serbia*

Background: The term acute coronary syndrome (ACS) refers to any group of clinical symptoms compatible with acute myocardial ischemia and includes unstable angina (UA), non-ST-segment elevation myocardial infarction (NSTEMI), and ST-segment elevation myocardial infarction (STEMI). Platelets play a pivotal role in atherogenesis and its thrombotic complications such as those occurring in patients with ACS which is a platelet-driven process.
Purpose: To study platelet function parameters assessment by Multplate aggregometry in patients with ACS and heart failure.
Methods: A total of 70 patients with acute coronary syndrome (ACS) (28 STEMI patients, 33 NSTEMI patients and 9 UA patients) were considered for entry into the study. Platelet function parameters-response to acetylsalicylic acid(ASPI test),clopidogrel(ADP test) and thrombin receptor activating peptide(TRAP test) were assessed by the Multiplate platelet function analyzer. We measured ratio ASPI/TRAP and ADP/TRAP (cut off value < 0.50 is for good therapy response on dual antiplatelet therapy-arachidonic acid and clopidogrel). Value of left ventricular ejection fraction (LVEF) was measured by echocardiography.
Results: 70 patients were entered into the study (45 males,25 females) .In this group were 12 patients with left ventricular ejection fraction (LVEF)= 40% and clinicaly manifest heart failure (Killip II and Killip III)-group I and 58 patients with LVEF>40%-group II.
Mean age of patients in group I was 73.00 ± 8.32,while in group II was 65.15 ± 10.26. (P < 0.05).
In I group value of ASPI test was 405.92 ± 110.75 AU*min,in II group ASPI test was 385.26 ± 210.76 AU*min. (NS). In I group value of ADP test was 641.33 ± 191.84 AU*min,in II group it was 496.22 ± 183.79 AU*min. (P < 0.05). In I group value of TRAP test was 1162.50 ± 301.55 AU*min,but in II group it was 1000.14 ± 228.96 AU*min. (P < 0.05). In I group ratio ASPI/TRAP was 0.36 ± 0.09,while in group II was 0.40 ± 0.21 (NS). In group I ratio ADP/TRAP was 0.56 ± 0.13,in group II was 0.49 ± 0.14 (P < 0.05). 53 patients have good therapy response on arachidonic acid-ASPI/TRAP < 0.5,while 35 patients have good therapy response on clopidogrel-ADP/TRAP < 0.5.
Conclusion: Patients with ACS and LVEF = 40% were oldier than patients with ACS and LVEF>40%. Patients with ACS and LVEF = 40% had higher values of ASPI,ADP and TRAP test and ratio ADP/TRAP than patients with ACS and LVEF>40%. Patients with ACS and LVEF = 40% had lower ratio ASPI/TRAP than patients with ACS and LVEF>40%.

P481

Takotsubo syndrome as a form of an acute variant of primary microvascular angina

I A Leonova[1]; S Boldueva[1]; O Zakharova[1]; V Feoktistova[1]; A Lipunova[1]; M Kolesnichenko[1]
[1]North-Western Sate Medical University named I.I. Mechnikov, St-Petersburg, Russian Federation

Acute primary microvascular angina (MVA) is an unstable form, variant to acute coronary syndrome. It can occur as new-onset angina with little physical exertion or it may be characterized by recurrent attacks of pain at rest. The diagnosis is confirmed by ECG signs of myocardial ischemia appeared to regression of changes, normal coronarography (CAG) and in some cases a slight increase in cardiac enzymes. There is no doubt that in these situations should be excluded conditions such as spasm of epicardial coronary artery (CA), coronary embolism and spontaneous thrombolysis in the non-occlusive atherosclerotic plaque and other possible causes. As in the basis of acute primary MVA lies coronary microvascular dysfunction, it is needed evidence of the latter. In recent years, it expressed the view that Takotsubo (TT) cardiomyopathy refers to primary acute MVA due to generalized microvascular spasm. The proposed idea is supported by following facts: TT develops mainly in pre- and postmenopausal women, on the background of stress; patients are characterized by anxiety. Perhaps genetic polymorphisms rho-kinase are considered the causes of the general incidence of coronary vasospasm in different level of coronary vasculature. The purpose of this study to evaluate the development of various forms (acute and chronic) in patients with microvascular angina.
11192 CAG data for 2012-2017 were analyzed, of which unchanged CA were found in 12 % of cases (1343 pts.). After excluding cases of secondary MVA and type 2 myocardial infarction, 223 patients with previous diagnosis of primary MVA were selected. PET with cold test was performed to confirm the diagnosis of patients (impaired endothelium-dependent vasodilation - an increase of MBF < 25 %). Based on all diagnostic criteria in 118 patients primary MVA was diagnosed. In the analysis of the available data, it was revealed that 10 (8.5 %) patients (all women in perimenopause) were hospitalized with primary diagnosis of acute coronary syndrome. Upon further observation of patients, it was found that in 6 (5.1 %) patients myocardial infarction due to microvascular dysfunction was diagnosed, that was confirmed by the presence of hypoperfusion zones according to PET. At the same time in 4 patients (3.4%) on the basis of data of ECG, echocardiography, PET (reversible disorders of contractility and perfusion), a proved connection with severe stress situation TT syndrome was diagnosed.
Conclusion: Most patients with primary MVA have chronic form of disease, at the same time, there is less than 10 % of patients whose disease is debuted as an acute coronary event, including such variant as TT cardiomyopathy. The main pathogenetic mechanism is microvascular spasm of different severity.

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Inpatient management of acute decompensated heart failure (ADHF) under general medical teams remains suboptimal despite specialist input

J Mc Cambridge[1]; C Keane[1]; M Walshe[1]; P Campbell[1]; PR Kalra[2]; MR Cowie[3]; JP Riley[3]; R O' Hanlon[1]; M Ledwidge[1]; J Gallagher[1]; K Mc Donald[1]
[1]St Vincent's University Hospital, Heart Failure Unit, Dublin, Ireland; *[2]Portsmouth Hospitals NHS Trust, Portsmouth, United Kingdom*; *[3]Royal Brompton Hospital, London, United Kingdom*

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Introduction: Many patients presenting with ADHF are admitted under the general medical team (GM) on call, even though it is well established that these patients have better outcomes when treated under the care of cardiologists. It is unclear if access to an inpatient HF service for GM can bridge this gap in inpatient care.
Purpose: To analyse the number of patients with ADHF admitted under GM and the differences, if any, in clinical care between these patients and those admitted under cardiology in a hospital which has a dedicated HF service.
Method: This analysis is from a single centre in an ongoing multicentre, observational study evaluating care pathways in patients admitted with ADHF. It focuses on the inpatient period; specifically, the differences in care under GM versus the cardiology/HF service. Every patient under GM had input from the HF service on a consultation basis during admission. The number and frequency of further reviews by the HF service was decided on clinical grounds. A p value < 0.05 was taken as statistically significant.
Results: A total of 114 patients were admitted with ADHF: 57 had a new diagnosis of HF (de novo, DN) and 57 had a known history of HF (recurrent admissions, RA). Of these 114 patients, 83 (73%) were admitted via the emergency department (ED). The remaining 31 (27%) were admitted directly under cardiology from the community or were transferred from another hospital/inpatient service, bypassing the ED. Of the 83 patients admitted via the ED, 60 (72%) were referred to cardiology and 23 (28%) were referred to GM. Patients referred to cardiology had an older median age (76 vs. 73, p= 0.97) and a fewer median number of comorbidities (3 vs. 4, p= 0.15) compared to patients referred to GM. Those referred to cardiology were more likely to have a background of ischaemic heart disease (50% vs. 36%, p= 0.28), whereas those referred to GM were more likely to have a background of COPD (36% vs. 13%, p= 0.02). There was no significant difference between the percentage of DN and RA admitted under GM (26% vs. 31% respectively, p= 0.62). Patients admitted under GM were more likely to spend > 24 hours in the ED (52% vs. 16%, p= 0.001), have a longer median inpatient stay (days, 8.5 vs. 6, p= 0.21) and have a time to clinical stability > 7 days (50% vs. 31%, p= 0.125) compared to those under cardiology. DN admitted medically were more likely to wait = 3 days for an echocardiogram from the time of admission compared to DN under cardiology (73% vs. 31% respectively, p= 0.012).
Conclusion: Over a quarter of patients admitted with ADHF via ED were admitted under GM in a hospital with a dedicated inpatient HF service. These patients experienced suboptimal quality of care when compared with those under cardiology, despite input from the HF service. This underlines the need for patients with ADHF to be cared for primarily under the cardiology service.

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Impact of cardio-renal anemia syndrome in de novo acute heart failure and acutely decompensated chronic heart failure

M Al Jarallah[1]; R Rajesh[1]; I Al Zakwani[2]; R Dashti[1]; B Bulbanat[1]; M Ridha[3]; J Al Suwaidi[4]; K Sulaiman[5]; P Panduranga[5]; W Almahmeed[6]; K Alhabib[7]; H Amin[8]; N Bazargani[9]; A Al-Motarreb[10]; A Al-Saber[11]
[1]Sabah Al Ahmad Cardiac Center, Al Amiri Hospital, Cardiology , Kuwait, Kuwait; *[2]Sultan Qaboos University , Department of Pharmacology & Clinical Pharmacy, College of Medicine & Health Sciences, Muscat, Oman*; *[3]Adan Hospital, Cardiology, Kuwait, Kuwait*; *[4]Hamad General Hospital, Cardiology, Doha, Qatar*; *[5]Royal Hospital, Cardiology, Muscat, Oman*; *[6]Sheikh Khalifa Medical City, Cardiology, Abu Dhabi, United Arab Emirates*; *[7]King Fahad Cardiac Center, Riyadh, Saudi Arabia*; *[8]Mohammed Bin Khalifa Cardiac Centre, Bahrain, Bahrain*; *[9]Dubai Hospital and Rashid Hospital, Cardiology, Dubai, United Arab Emirates*; *[10]Sana'a University, Cardiology, Sana'a, Yemen*; *[11]Kuwait Technical College, Statistics , Kuwait, Kuwait*

On behalf of: Gulf CARE
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Aim: To study the impact of Cardio renal anemia syndrome (CRAS) in de novo acute heart failure (de novo-AHF) and acutely decompensated chronic heart failure (ADCHF).
Subjects & Methods: Patients were categorized into de novo-AHF patients with CRAS (A1) and ADCHF patients with CRAS (A2). Chi-square test of independence was utilized for A1 and A2.
Results: In hospital cardiogenic shock, intubation, stroke were reported almost same in both groups. In hospital major bleeding was seen more with de novo-AHF group 4.1% (25/608) p = 0.019. Mortality rate was seen slightly higher with ADCHF group 8.3% (61/735) while de novo-AHF group had 6.9% (42/608) p = 0.016.
Conclusions: In the setting of acute heart failure de novo-AHF CRAS patients were more prone towards in-hospital major bleeding compare to those ADCHF CRAS patients. Incidence of in-hospital mortality was seen higher with ADCHF CRAS patients.

Demographic and clinical characteristics

Characteristics	Cardiorenal Anemia Syndrome		
De novo AHF n = 608	ADCHF n = 735	P-Value	
Gender (Male)	397 (65.3%)	468 (63.7%)	0.536
Age, Years	62.59 ± 14.51	66.49 ± 13.08	0.001*
Hypertension	375 (61.7%)	499 (67.9%)	0.017*
Type 2 DM	269 (44.2%)	396 (53.9%)	0.001*
CAD	316 (52.0%)	435 (59.2%)	0.008*
Dyslipidemia	208 (34.2%)	315 (42.9%)	0.001*
Smoking	94 (15.5%)	64 (8.7%)	0.001*
LVEF %	37.31 ± 14.40	34.79 ± 12.91	0.001*
Intubation ventilation	59 (9.7%)	57 (7.8%)	0.206
Cardiogenic Shock	47 (7.7%)	58 (7.9%)	0.913
Stroke TIA	63 (10.4%)	89 (12.1%)	0.314
Major Bleeding	25 (4.1%)	19 (2.6%)	0.019*
AF	39 (6.4%)	50 (6.8%)	0.776
Calcium Channel Blocker	81 (13.3%)	137 (18.6%)	0.009*
Anti-arrhythmics	10 (1.6%)	28 (3.8%)	0.017*
Statin	331 (54.4%)	456 (62.0%)	0.005*
IV diuretics	351 (57.7%)	486 (66.1%)	0.002*
Mortality	42 (6.9%)	61 (8.3%)	0.016*

Coronary Artery Disease - Pathophysiology and Mechanisms

P484
Cardiogenic shock in myocardial infarction: role of beta-blocker therapy

M J Maria Joao Nobre De Matos Pereira Vieira[1]; D Durao[1]; A Belo[2]; K Domingues[1]; N Craveiro[1]; M Saraiva[1]; B Saldanha Santos[1]; M Alves[1]; M Leal[1]; RNSCA Investigadores Do Registo Nacional De Sindromes Coronarios Agudos[2]
[1]Hospital Santarém, Cardiology, Santarém, Portugal; *[2]Sociedade Portuguesa de Cardiologia, Lisboa, Portugal*

On behalf of: Registo Nacional dos Sindromes Coronarios Agudos da Sociedade Portuguesa de Cardiologia (RNSCA)

Background: Beta-blockers (BB) are one of the most widely therapy used in the context of myocardial infarction (MI). In the past its benefit was demonstrated with a significant reduction in mortality. However, in the era of percutaneous revascularization, conflicting data have emerged on the association of BB and the development of cardiogenic shock (CS).
Purpose: To evaluate the association between in-hospital BB therapy and the development of cardiogenic shock.
Methods: We performed a retrospective study including 16587 patients (age 66 ± 13 years, 74% men), from the Portuguese Registry on Acute Coronary Syndromes (RNSCA) with the diagnosis of myocardial infarction (MI) admitted between 01/10/2010 and 03/01/2018. The population was divided into two groups: Group A (A), with in-hospital oral beta-blocker therapy (n = 13635) and Group B (B), without in-hospital BB oral therapy (n = 2952). The primary outcome was the development of CS during hospital staying. Demographic, clinical, electrocardiographic, echocardiographic and angiographic data were evaluated. Multivariate analysis was conducted by logistic regression.
Results: Significant differences were observed between groups regarding age, smoking habits, previous history of diabetes mellitus, chronic kidney disease, previous myocardial infarction, type of myocardial infarction at admission, left ventricular ejection fraction, use of angiotensin-converting enzyme inhibitors (table). Cardiogenic shock was observed in 359 pts (2,2 %) with significant differences between groups (A 1,2% vs B 6,5%; OR = 0,18; P < 0,001). The use of BB therapy was also associated with lower occurrence of mechanical complications (A 0,4% vs B 1,3%; OR = 0,3; P < 0,001), lower development of congestive heart failure (A 10,7% vs B 20,1%; OR = 0,48; P < 0,001), lower need for intra-aortic balloon (A 0,3% vs B 0,9%; OR = 0,36; P < 0,001) and invasive ventilation (A 0,7% vs B 2,7%; OR:0,26; P < 0,001), lower onset of sustained ventricular arrhythmias (A 1,2 vs B 1,9%;OR = 0,41; P < 0,001), lower cardiorespiratory arrest (A 2,3 vs B 3,5%; OR = 0,63; P < 0,001) and lower all causes intra-hospital death (A1,4 vs B 7,2%; OR = 0,19; P < 0,001).
In the multivariate analysis, beta blocker was an independent predictor of CS, assuming a protective role in this setting (OR: 0,32; 95% CI: 0,23-0,45; P < 0,0001), regardless of whether the presentation was STEMI (OR: 0,18; 95% CI: 0,14-0,24; P < 0,0001) or NTEMI (OR: 0,17; 95% CI: 0,11-0,26; P < 0,0001).
Conclusions: In this study the use of BB therapy in patients with MI decrease in-hospital mortality and the incidence of CS. The benefits were observed both in STEMI and NSTEMI patients. The benefits of beta-blocker therapy were widely described in long-term follow up period studies, but its effects in in-hospital outcomes have been scarcely described.

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Positive stress test at myocardial scintigraphy and obstructive coronary artery disease: is associated factors match?

A N Alexey Sumin[1]; EV Korok[1]; AA Korotkevitch[1]; EN Kachurina[1]; AN Kokov[1]; OL Barbarash[1]
[1]RAMS Scientific-Research Institute for Complex Studying of Cardiovascular Diseases, Kemerovo, Russian Federation

Background: The detection rate of non-obstructive coronary arteries (CA) in patients with suspected coronary artery diseases (CAD) accounts for 58.4% according to the European registries. Recent Russian studies report the rate of 55.6%. They pay particular attention to a low performance of non-invasive stress tests before coronary angiography (CAG), while in the European and American clinical practice this figure reaches 64%. The question arises: why this does not affect the improvement of the detection of obstructive coronary artery lesions of the coronary arteries during CAG. Apparently, the relationship between the results of non-invasive tests and structural changes in the coronary arteries requires further investigations.
Purpose: To compare the factors associated with positive stress tests with single photon emission computed tomography (SPECT) and the presence of hemodynamically significant CA stenoses during invasive CAG.
Methods: The retrospective analysis included 107 patients who were examined and treated at the clinic KPSSZ Research Institute during 2012-2015 with previously diagnosed CHD or hospitalized for CHD exclusion. To identify hemodynamically significant stenoses CA all the patients underwent coronary angiography and SPECT, the time interval between the studies did not exceed 3 months.
Results: In the analysis of the studied sample observed the predominance of males, the average age of 61 year. A quarter of the patients represented by smokers, most often suffer hypertension, had angina. The typical clinical picture of angina is more common than atypical and cardialgia and angina functional class (FC) II prevailed. Myocardial infarction (MI) in history was observed in 56.1% of patients, Chronic Heart Failure - in 91.6%. Coronary revascularization in the whole group was subjected to 51.4% of patients. At the same time the average pre-test probability of the CHD presence was quite high (77 [58; 84]). Positive results of pharmacological stress testing with SPECT detected in 28% of cases, obstructive lesions of CA with invasive coronary angiography - in 56% of patients. Independent clinical predictors of a positive stress test with SPECT and significant CA stenoses were male gender and the presence of angina (with SPECT - angina FC II, and at CAG - angina IV FC). Conclusion. The results of this study it is advisable to consider when developing diagnostic approaches to identify obstructive coronary artery disease, in particular when using a stress test with SPECT.

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The level of C-reactive protein and major artery elasticity in patients with ischemic heart disease

O V Oleg Ilyukhin[1]; MV Ilyukhina[1]; DL Tarasov[1]; DI Dorashenko[1]; YM Lopatin[1]
[1]State Medical University, Volgograd, Russian Federation

Methods: the study included 52 patients with coronary artery disease, all men, the average age was 54 ± 1.58 years, I-III angina and functional class (FC) I-III heart failure (NYHA). Major artery elasticity was evaluated by pulse wave velocity (PWV). The reactivity of the major arteries (a. radialis) in response to increased blood flow was measured using the test with reactive hyperemia (RH). The concentration of CRP was quantified by ELISA.

Results: the figures were compared elasticity and reactivity of the main arteries, depending on the level of CRP. A significant correlation between pulse wave velocity for elastic arteries and the concentration of CRP (r = 0.34; p = 0.018). In the study of endothelium-dependent reactivity we detected significant changes in the arteries of muscular type of reaction in response to increased blood flow in the test of the RH. See example reduction in sample, an average of CAD patients was only 12.4% in the control group and 19.7% (p < 0.05). The level of CRP was highly significant correlation with a decrease in PWV in response to increased blood flow (r = 0.49; p = 0.0005).
Conclusion: the increase in the level of CRP in blood plasma in patients with coronary artery disease may be associated with significant changes from the elasticity of the main arteries and simultaneous assessment of lipid spectrum and CRP enhances diagnostic significance of each index separately.

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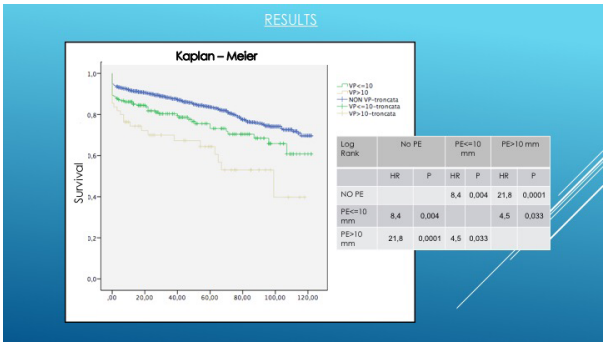
Long term prognostic relevance of small pericardial effusion after an ST elevation myocardial infarction

S Stefano Albani[1]; L Falco[1]; D Stolfo[1]; E Fabris[1]; S Santangelo[1]; A Perkan[1]; G Sinagra[1]
[1]*Postgraduate School in Cardiovascular Sciences, Cardiovascular Department, University Hospital of Trieste, Trieste, Italy*

Background: Although the presence of moderate (<10 mm detected by echocardiography) pericardial effusion (PE) after ST elevation myocardial infarction (STEMI) increases the risk of short term mortality at 30 days, data concerning the impact on long-term prognosis of small pericardial effusion (SPE) after STEMI in the current era of primary percutaneous coronary interventions (PCI) are lacking.
Objective of the study and Methods: The aim of this study was to evaluate the potential association between different degrees of PE and long-term survival in a large cohort of STEMI patients treated with primary PCI. The presence of PE was assessed by transthoracic echocardiography within 3 days after the hospital admission.
Results: We evaluated 1728 patients affected by STEMI from 2/2007 to 3/2017, mean follow up 6,7 years. Patients were divided in 2 groups: PE group (244 patients - 14,2%) and patients without PE (NPE, 1483 patient, 85,8%). PE patients were older (67,7+/-12 vs 65 +/-12 P = 0,008), more frequent woman (31,8% vs 24% P = 0,006) more frequent they were affected by anterior MI (65,7% vs 39,8%,p = 0,0001) and less frequent inferior MI (28,5% vs 52%,p = 0,0001) compared to NPE patients. PE patients were further divided in SPE (> = 10 mm: 195 patients, 79,6%) and moderate-severe PE (MSPE) (PE > 10 mm and < = 20 mm: 43 patients, 17,6%, and PE > 20 mm: 7 patients, 2,9%). The univariate analysis showed a clear association of PE and all cause mortality (HR 1,89, IC 1,38-2,57, p < 0,0001). The only different variable between the 2 groups was the Killip class at the admission that was higher in MSPE than SPE (24,5% - 13 pts vs 10,5% - 20 pts, p < 0,008). At the multivariate analysis PE is still a risk factor for all cause mortality in patients with reduced ejection fraction (IC 95% 1,05-2,46, p < 0,027) and SPE was an independent risk factor to all cause mortality in patients with preserved ejection fraction at discharge (IC 1,20-2,51, p < 0,003). Kaplan-Meier curves for all cause mortality showed a significant worse survival for each subgroup of PE compared to NPE (log rank test, p = 0.004) and for MSPE compared to SPE (log rank test P = 0,0001)
Conclusion: The study showed that the presence of PE after primary PCI was independently associated to increase long term all cause mortality, however in a multivariate model without considering ejection fraction, also the presence of only a SMP after primary PCI was associated to increase long term mortality compared to patient without PE.



Survival Kaplan Meier curves

Coronary Artery Disease - Treatment

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Frailty is associated with mortality and hemorrhagic risk in elderly patients with acute coronary syndrome

N N Nino Soseliya[1]; L Babaeva[1]; N Bagmanova[1]; S Villevalde[1]; Z Kobalava[1]
[1]*Peoples' Friendship University of Russia (RUDN University), Moscow, Russian Federation*

Background: Frailty is a high-priority issue in cardiovascular medicine because of the aging of patients. It reflects the complex functional disorders and is associated with high morbidity and adverse outcomes. Estimation of the risk of mortality and bleeding in patients with acute coronary syndrome (ACS) = 75 years remains ambiguous. In the widely used GRACE and TIMI scales age is one of the main factors if risk grading. The CRUSADE scale includes comorbidity, decreased glomerular filtration rate (GFR), which frequency increases with age. The aim of the study was to examination prevalence of frailty, its associations with mortality and hemorrhagic risk in elderly patients with ACS.
Methods: In 130 patients = 75 years (83 ± 5 years, arterial hypertension (AH) 92%, previous myocardial infarction (MI) 32%, atrial fibrillation 32%, diabetes mellitus 27%, chronic heart failure (HF) 77%, acute HF (Killip I - 60%, II - 29,2%, III - 10%, IV - 0,8%), left ventricular ejection fraction (LVEF) 43,1 ± 10,6%, admitted with MI (75%) or unstable angina (25%), frailty (national validated questionnaire), mortality (GRACE, TIMI scales) and hemorrhagic risk (CRUSADE scale) were assessed.
Results: Frailty was revealed in 66% of patients. 68% of patients had >140 points on GRACE scale (high mortality risk), 53% >5 points on TIMI (high mortality risk), 73% >40 points on CRUSADE (high hemorrhagic risk). Patients with frailty were more likely women (72 vs 59%; p < 0,05), had higher incidence of AH (94 vs 86%; p < 0,01), MI in this hospitalization (86 vs 55%; p < 0,05), GFR < 60 ml/min/1,73 m2 (71 vs 48%; p < 0,05). Patients with frailty had higher risk of bleeding (47 ± 10 vs 41 ± 10 points on CRUSADE scale, p < 0,001) and mortality (162 ± 36 vs 144 ± 22 points on GRACE scale, 4,9 ± 1,1vs 4,5 ± 1,1 points on TIMI scale, p < 0,001). More pronounced frailty score was revealed in patients with TIMI >5 points (3,3 ± 1,1 vs 2,5 ± 0,5 points, p < 0,001), ?RUSADE >40 points (3,1 ± 1,0 vs 2,0 ± 1,4 points, p < 0,001), ST-segment elevation MI vs unstable angina (3,5 ± 0,9 vs 2,9 ± 1,2 points, p < 0,01). Frailty score correlated with heart rate (r = 0,27), troponin (r = 0,294), GRACE score (r = 0,187), TIMI score (r = 0,216), serum creatinine (r = 0,198), urea (r = 0,194), p < 0,05 for all. Duration of hospitalization was higher in patients with frailty (9,6 ± 3,8 vs 9,1 ± 2,2 days, ?2 = 36.3, p < 0,01). In-hospital mortality occurred only in patients with frailty (1,16%), 6-month mortality was not significantly higher (24,6 vs 16,2%) in this group. Conclusion. Frailty occured in 66% of elderly patients with ACS, was associated with MI during index hospitalizathion, higher score risk of mortality and bleeding

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Geriatric syndromes are common and associated with ischemic and bleeding risk in elderly patients with acute coronary syndrome

N Soseliya[1]; B Lobzhanidze[1]; N Bagmanova[1]; S Villevalde[1]; Z Kobalava[1]
[1]*Peoples' Friendship University of Russia (RUDN University), Moscow, Russian Federation*

Background: Elderly patients with acute coronary syndrome (ACS) can experience a wide spectrum of geriatric conditions that aggravate their prognosis. Older age is universally considered as a risk factor, but geriatric conditions are not usually evaluated. The aim of the study was to assess the prevalence and associations of geriatric syndromes in elderly patients with ACS.Methods.In 130 patients = 75 years (83 ± 5 years, arterial hypertension(AH) 92%, previous myocardial infarction (MI) 32%, atrial fibrillation 32%, diabetes mellitus(DM) 27%, chronic heart failure (HF) 77%, acute HF (Killip I - 60%, II - 29,2%, III - 10%, IV - 0,8%, left ventricular ejection fraction (LVEF) 43,1 ± 10,6%, admitted with MI (75%) or unstable angina (25%) physical disability (Barthel index), functional mobility, nutritional status (Mini Nutrition Assessment), cognitive function (Mini Mental State Examination), mortality (GRACE, TIMI scales) and hemorrhagic risk (CRUSADE scale) were assessed.Results.Disorders of functional mobility were revealed in 93,1% of patients (mild 57,7%, moderate 30,8%, severe 4,6%). 13,8 and 60,8% of patients had mild and moderate physical disability of daily living. The risk of malnutrition was revealed in 53,8% of patients, two (1,5%) patients were malnourished. 31,5% of patients had cognitive dysfunction (mild 13.8%, moderate 17,7%).More pronounced cognitive dysfunction was revealed in patients with GRACE >140 points (26,6 ± 5,0 vs 29,9 ± 1,9 points, p < 0,05), with MI vs unstable angina (26,7 ± 4,9 vs 28,7 ± 3,1 points, p < 0,05), with vs without DM (25,7 ± 4,3 vs 27,7 ± 4,6 points, p 0,01). Higher physical disability of daily living was revealed in women (87,7 ± 11,1 vs 91,2 ± 11,8 points, p 0,014) patients with TIMI >5 points (86,9 ± 9,4 vs 95,2 ± 5,1, p < 0,001), ?RUSADE >40 points (89,3 ± 8,9 vs 98 ± 1,2 points, p < 0,001), MI vs unstable angina (86,8 ± 12,1

vs 95,2 ± 5 points, p < 0,001), More disorders of functional mobility had patients with GRACE >140 points (34,0 ± 3,6 vs 37,1 ± 1,2 points, p < 0,01) and ?RUSADE >40 points (34,4 ± 3,4 vs 38,2 ± 1,1 points, p < 0,01). Barthel index correlated with BMI (r = 0,19), age (r=-0,21), TIMI score (r=-0,23), troponin (r=-0,24), total cholesterol (r=-0,18), glucose (r=-0,2). There was significant correlation between cognitive function and LVEF (r = 0,31), troponin (r=-0,32), glucose (r=-0,29), total cholesterol (r = 0,2), serum creatinine (r=-0,22), hemoglobin (r=-0,2), p < 0,05 for all. Functional mobility correlated with BMI (r=-0,3), systolic blood pressure (BP) (r = 0,28), diastolic BP (r = 0,25), troponin (r=-0,29), serum creatinine (r=-0,22), hemoglobin (r=-0,2), p < 0,05 for all.Conclusion.Geriatric syndromes are common in elderly patients with ACS. Disorders of functional mobility were revealed in 93,1% of patients, physical disability of daily living in 74,6%, disorders of nutritional status in 55,1%, cognitive dysfunction in 31,5%. Geriatric syndromes were associated with MI during index hospitalization, DM, higher risk of mortality and bleeding

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Impact of prior exposure to aspirin on prognosis after acute coronary syndrome: a multicenter portuguese registry

C Catarina Ruivo[1]; F Montenegro Sa[1]; L Santos[1]; J Correia[1]; J Morais[1]
[1]*Hospital Santo Andre, Cardiology, Leiria, Portugal*

On behalf of: Portuguese National Registry of Acute Coronary Syndromes

Background: Despite the known protective cardiovascular effect of aspirin, former studies identified its prior exposure to an acute coronary syndrome (ACS) as an independent risk factor for adverse events. However, those studies did not reflect contemporary approaches. In the current study, we determine whether patients exposed to aspirin before an ACS have a worse cardiovascular risk profile and if it predicts higher risk of recurrent cardiovascular events or mortality.
Methods: A cohort of patients enrolled in a national registry of ACS was analyzed according to prior exposure to aspirin. A propensity score standardized patients according to baseline comorbidities. Multivariable COX regression analysis was performed in unmatched and matched populations for a primary endpoint (composite of all-cause mortality and/or cardiovascular rehospitalization) and two secondary endpoints (all-cause mortality and cardiovascular rehospitalization, separately) at 1-year follow-up.
Results: Among 5533 ACS patients, 1763 were previously exposed to aspirin. They were older and had more comorbidities; contemporary approaches, both coronary angiography and percutaneous coronary angioplasty were less likely to be performed. Before matching the population, prior exposure to aspirin was an independent predictor of primary composite endpoint (p = 0.002) and cardiovascular rehospitalization as the secondary endpoint (p = 0.001). There were no statistically significant differences between both groups in the multivariable model for the primary or secondary endpoints after matching.
Conclusions: Previous exposure to aspirin identified ACS patients with worse baseline characteristics, establishing its role as a cardiovascular risk marker. However, our data do not support including aspirin pretreatment in risk stratification scores as an adverse prognostic variable.

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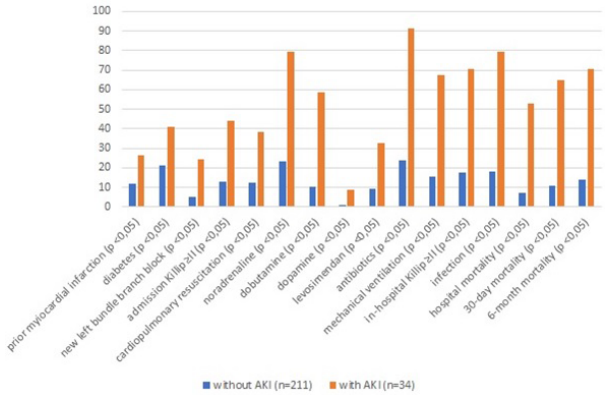
Acute heart failure is among significant predictors of acute kidney injury in patients with acute ST-elevation myocardial infarction

K Masnik[1]; M Mihevc[1]; A Andreja Sinkovic[2]
[1]*University of Maribor, Medical faculty, Maribor, Slovenia*; [2]*University Medical Centre Maribor, Maribor, Slovenia*

Background/introduction: Acute kidney injury (AKI) is defined as a rapid decline of renal function due to a decrease of glomerular filtration rate, followed by an increase of serum urea and creatinine. One of the most important causes of AKI in STEMI patients is myocardial necrosis, which causes systolic or diastolic dysfunction of the left ventricle leading to renal hypoperfusion and initiation of inflammation. Other risk factors for AKI are hypovolemia, dehydration, toxic effect of contrast media, nephrotoxic drugs, etc.
AKI develops in up to 30% of patients with STEMI and represents an important risk factor for complications and mortality of STEMI patients.
Purpose: The aim of our study was to evaluate the incidence of AKI in STEMI patients, its relation to the treatment outcome, and risk factors for AKI.
Methods: 245 STEMI patients (67,3% men and 32,7% women, mean age 63,9 ± 11,9 years) treated at the Department of medical ICU of University clinical centre Maribor between December 2014 and December 2015 were studied retrospectively.
AKI was defined as a 1,5-fold increase in baseline levels of serum creatinine in 24-48 hours after presentation. Heart failure was defined as Killip-Kimball classes = II. Collected data were compared using chi-squared test and t-test. Significant variables were tested in a model of binary logistic regression.
Result: Primary percutaneous coronary intervention (PPCI) was performed in 92,2% of STEMI patients. AKI developed in 13,9% of patients after PPCI.
In patients without and AKI significant difference in admission and in in-hospital acute heart failure was found. Patients with AKI had significantly more often prior myocardial infarction (MI), diabetes, new left bundle branch block, and were more likely resuscitated. They were significantly more often treated with noradrenaline, dopamine, dobutamine, levosimendan, and antibiotics. Furthermore, there was a significant difference in mechanical ventilation (MV), infection, and in-hospital, 30-day and 6-month mortality (Picture 1).
Patients with AKI in comparison to STEMI patients wihad significantly higher mean peak CRP (69,1 ± 81,8 vs. 198,9 ± 123,0 mg/L, p <0,001), mean peak NT-proBNP (881,3 ± 1186,2 vs. 2757,4 ± 1565,9 pmol/L, p <0,001), and lower ejection fraction (41,41 ± 14,9 vs. 24,34 ± 10,9%, p <0,001).
Using logistic regression, we proved prior MI (OR 8,69; 95%CI 1,82 to 41,58; p = 0,007), MV (OR 5,29; 95%CI 1,37 to 20,34; p = 0,015), infection (OR 7,15; 95%CI 2,12 to 24,05; p = 0,001), and in-hospital heart failure (OR 3,73; 95%CI 1,21 to 11,45; p = 0,021) to be the most significant independent predictors of AKI in STEMI patients.
Conclusion: AKI was observed in 13,9% of patients. Most significant independent predictors of AKI were prior MI, MV, and infection. Acute in-hospital heart failure proved to be the fourth most important predictor of AKI in STEMI patients. AKI was a significant risk factor of mortality of STEMI patients.



Significant differences in parameters

P492

Drug-eluting balloon catheters in the endovascular treatment of patients with true left main bifurcation lesions

Z KH Shugushev[1]; D A Maximkin[1]; OO Safonova[1]; AG Chepurnoy[1]
[1]*RUDN University, Moscow, Russian Federation*

Aim: to evaluate the effectiveness of drug-eluting balloons in patients with Left Main (LM) bifurcation stenosis.
Material: 128 patients with true bifurcation lesions of the LM were included in the study. All patients underwent 'Provisional T' stenting of the LM coronary artery with the final kissing-dilatation technique. Depending on the balloon catheters used for the final kissing, the patients were randomized into 2 groups. Group I (n = 64) included patients who had a kissing-dilatation performed with traditional NC balloon catheters, and group II included patients (n = 64) who had a kissing-dilatation of the main bifurcation artery with a traditional NC balloon catheters, and a side branch - with drug-eluting balloon catheters. In addition, patients from group II also underwent kissing-predilatation with drug-eluting balloon catheters. All interventions were culminated with vascular imaging using IVUS or OCT.
Results: all patients were implanted with drug-eluting stents. Survival of patients after PCI was 100% in both groups. All interventions are performed without complications. 6-month results were analyzed in all patients. After 6-months no cases of MACE were observed. In 3 patients (4.7%), group I showed signs of new-intima hyperplasia (restenosis up to 50%), repeated interventions were not performed. 12-month results were followed in 52 patients from group I and 48 patients from group II. In 1 patient (1.9%) from group I, and 1 patient (2.1%) from group II (p> 0.05) there was a recurrence of angina. Myocardial ischemia is confirmed by stress tests, coronary angiography revealed stent restenosis up to 80%. Both patients underwent repeated interventions. Restenosis of the side branch of less than 50% according to QSA was detected in 5 patients (9.6%) from group I and in 4 patients (8.3%) from group II (p>0.05). In patients from group I, the average MLA in the side branch (LCX) after 12 months was 5.58 ± 1.34 and 4.21 ± 1.21 mm, respectively (p <0.05), compared with data after PCI; in the ostium of the side branch (LAD) - 6.34 ± 1.56 and 5.28 ± 1.14, respectively (p <0.05). In patients from Group II, the average MLA at the end of PCI and after 12 months were, respectively, 5.38 ± 1.24 and 5.11 ± 1.44 mm

for the ostium of LCX (p> 0.05) and 6.68 ± 1.75 and 6.46 ± 1.22 mm for the ostium of LAD (p <0.05). All patients had complete stent endothelization, with no signs of malapposition. There were no cases of late thrombosis of the stents.
Conclusion: the use of drug-eluting balloon catheters to perform 'Provisional T' stenting of true LM bifurcation stenoses is highly effective and safe, as evidenced by a significant low incidence of restenosis of the side branch according to intravascular imaging methods without affecting the MACE frequency and can be considered as an alternative two-stent strategy of bifurcation stenting.

P493
How do we treat patients diagnosed with Myocardial Infarction with Non Obstructive Coronary Arteries?

C Carmen Collado Moreno[1]; I Valiente-Aleman[2]; RF Garcia-Gonzalez[1]; D Castro-Sanchez[3]; S Blasco-Turrion[1]; I Lobo-Torres[1]; A Gomez-Juanatey[1]; P Gonzalez-Perez[1]; FJ Morales-Ponce[1]
[1]Puerto Real Hospital, Department of Cardiology, Puerto Real, Spain; *[2]Puerto Real Hospital, Critical Medical Medicine, Puerto Real, Spain*; *[3]University of Cadiz, Cadiz, Spain*

Background: Myocardial Infarction and NonObstructive Coronary Arteries (MINOCA) is an important subtype of MI type 1 where epicardial vessel shows a stenosis < 50%. The aim of this study is to describe prevalence, clinical features, management and prognosis of patients diagnosed with MINOCA.
Methods: A prospective observational study of patients admitted to Intensive Care Unit with diagnosis of acute MI was performed between January 1st 2007 and December 31 st 2016. Data were extracted from the ARIAM Andalucia registry. All patients underwent coronary angyography. Patients with MI and no were diagnosed as MINOCA. Follow-up data were obtained from DIRAYA.
Results: A total of 1676 patients with diagnosis of acute MI were registered but only 54 patients fulfilled inclussion criteria for MINOCA disease.
The prevalence of MINOCA was 3.2 % with a mean age of 60.59. MINOCA was more frequent in women than in men. Most frequent cardiovascular risk factors were hypertension (55.6%), smoking (51.9%) and hyperlipemia(35.2%). Median risk score GRACE was 123 ± 32.68 and CRUSADE 27.4 ± 16.07. Left ventricular ejection fraction (LVEF) was preserved in 59.39%, mildly reduced in 24.1%, moderately reduced in 11.1% and severely reduced in 5.5% patients. Preferred treatments at discharge were aspirin (96%), statins (86%), ACEI/ARBs (80%), beta-blockers (70%) and DAPT (64%). One patient died at 3 month follow-up (1.85%).
Conclusions: MINOCA disease has an important prevalence and short-term mortality. Diagnostic work-up of these patients is often suboptimal so its management is not completely accurate. Therefore more studies on etiology and management of MINOCA are needed.

P494
Does intra-aortic balloon add value to cardiogenic shock therapeutics?

D Daniela Carvalho Silva[1]; D Bento[1]; J Guedes[1]; N Marques[2]; W Santos[2]; J Mimoso[1]; P Gago[1]; I Jesus[1]; A Belo[3]
[1]Faro Hospital, Cardiology, Faro, Portugal; *[2]DCBM, UAlg, Faro Hospital, Cardiology, Faro, Portugal*; *[3]Portuguese Society of Cardiology, Lisbon, Portugal*

On behalf of: ProACS

Introduction: Cardiogenic shock (CS) is a frequent complication in acute coronary syndromes (ACS). In addition to myocardial revascularization, there are few therapeutic arms with proven efficacy in reducing in-hospital mortality (IHM), which remains high.
Purpose: To characterize, in a population of patients (P) with ACS complicated by CS, the differences between P who underwent the use of intra-aortic balloon (IAB) and those who were not, as well as the predictive factors (PF) of the use of IAB. To evaluate if the use of IAB was associated to differences in complications and IHM, in univariate (UA) and multivariate (MA) analyzes.
Methods: Retrospective, descriptive and correlational study, with P included in a national registry of ACS, between October 1, 2010 and September 19, 2017, with ACS complicated by CS. They were divided into 2 groups - in group 1 (G1) were included the P not submitted to IAB and in group 2 (G2) those that were. Baseline characteristics, acute episode, therapeutic (TX), complications and IHM were assessed in UA using SPSS 19.0. In MA, PF were evaluated for the use of IAB and if it was independent predictor of IHM and other complications.
Results: 703P, 624 (88.8%) in G1 and 79 (11.2%) in G2 were included. In UA, were associated with the use of IAB (p < 0.05): younger age; absence of history of valvular disease, heart failure, peripheral arterial disease and COPD; ACS with ST segment elevation and, among them, the anterior location; lower systolic blood pressure (SBP), hemoglobin minimum level and HDL; TX in admission with acetylsalicylic acid, clopidogrel, gp IIb / IIIa inhibitors and unfractionated heparin; TX reperfusion TX, but greater door-reperfusion and door-balloon time; coronary angiography and angioplasty; common left main (CLM) significant stenosis or culprit, anterior descending occlusion, 2-3 vessels disease, indication for myocardial revascularization surgery; CLM angioplasty; use of thrombectomy devices; lower left ventricular ejection fraction and emergent transfer to another center. There were no differences in complications or IHM. In MA, the PF of IAB use were lower diastolyc and SBP. The diagnosis of non ST elevation myocardial infarction was independent predictor of non-use of IAB. There were no differences in IHM and complications.
Conclusions: The IAB was used in younger P, with more severe presentation. There were no differences in complications and mortality. In this context, the decision on the use of IAB should be individualized.

P495
The ASSAIL-MI trial: a Norwegian multicentre, randomised controlled trial designed to assess the effect of tocilizumab on ischaemia reperfusion injury in ST-elevation myocardial infarction

AK Anstensrud[1]; S Woxholt[2]; K Sharma[3]; K Broch[4]; B Bendz[1]; JK Damaas[2]; BH Amundsen[5]; O Kleveland[2]; AK Opdahl[4]; NE Kloew[6]; I Seljeflot[7]; G Andersen[3]; R Wiseth[2]; P Aukrust[8]; L Gullestad[1]
[1]Oslo University Hospital, Department of Cardiology, Rikshospitalet and University of Oslo, Institute of Clinical Medicine, Oslo, Norway; *[2]St Olavs Hospital, Department of Cardiology and Norwegian University of Science and Technology, Trondheim, Norway*; *[3]Oslo University Hospital, Department of Cardiology, Ullevål, Oslo, Norway*; *[4]Oslo University Hospital, Department of Cardiology, Rikshospitalet, Oslo, Norway*; *[5]St Olavs Hospital, Department of Cardiology, Trondheim, Norway*; *[6]Oslo University Hospital, Department of Radiology, Ullevål and University of Oslo, Institute of Clinical Medicine, Oslo, Norway*; *[7]Oslo University Hospital, Ullevål and University of Oslo, Institute of Clinical Medicine, Oslo, Norway*; *[8]Oslo University Hospital, Rikshospitalet, Oslo University Hospital, Institute of Clinical Medicine, Oslo, Norway*

Background: Interleukin-6 (IL-6) may be involved in plaque destabilisation and ischaemia-reperfusion injury following revascularisation during myocardial infarction (MI). We have recently shown that IL-6 inhibition by tocilizumab attenuates systemic inflammation and troponin T-release in patients with non-ST elevation MI (NSTEMI). Experimental studies suggest that IL-6 inhibition can also limit infarct size through anti-inflammatory mechanisms. We have recently started enrolment in the ASSAIL-MI trial, designed to address this issue in ST-elevation MI (STEMI) patients.
Purpose: To examine whether a single administration of the IL-6 receptor antagonist tocilizumab can reduce myocardial injury in patients presenting with an acute STEMI.
Methods: In this three-centre, randomised, double blind, placebo-controlled trial, 200 patients with first-time STEMI scheduled for acute PCI within 6 hours from the onset of chest pain will be randomised to receive one dose of intravenous tocilizumab or matching placebo prior to PCI. The patients will be followed-up for 6 months.
The primary endpoint is the between-group difference in the myocardial salvage index measured 3-7 days post-PCI by cardiac magnetic resonance imaging (CMR). Secondary endpoints are plasma markers of myocardial necrosis (e.g., troponins), systemic inflammation and extracellular matrix remodelling, and final infarct size at 6 months assessed by CMR. Efficacy and safety assessments during follow-up include physical examination, blood sampling, cardiac imaging and recording of clinical adverse events.
Results: Trial enrolment has started at all participating sites. Demographics of the first 40 patients are presented in Table 1.
Summary: The ASSAIL-MI trial is a randomised clinical trial designed to evaluate the effect of IL-6 inhibition on myocardial injury in patients with STEMI.

Table 1 Baseline characteristics

Age (years)	58.7 ± 8.9
Male gender	32 (80.0)
Body mass index (kg/m2)	27.6 ± 4.2
Cardiovascular risk factors	
Current smoker / former smoker	19 (47.5) /9 (22.5)
Hypertension	13 (32.5)
Diabetes mellitus	5 (12.5)

Data are given as number (percent) or mean ± SD

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Impact of therapeutic hypothermia on infarct size in patients with ST-elevation myocardial infarction: a post-hoc analysis on ischemic time from the COOL AMI EU Pilot Trial

D Aradi[1]; D Erlinge[2]; AN Neskovic[3]; B Sredniawa[4]; T Keeble[5]; M Holzer[6]; M Dae[7]; M Noc[8]
[1]Balatonfured State Cardiology Hospital, Interventional Cardiology, Balatonfured, Hungary; *[2]Lund University, Lund, Sweden*; *[3]Clinical Hospital Center Zemun, Belgrade, Serbia*; *[4]Silesian Center for Heart Diseases (SCHD), Zabrze, Poland*; *[5]Mid Essex Hospital NHS Trust, Chelmsford, United Kingdom*; *[6]Medical University of Vienna, Vienna, Austria*; *[7]University of California San Francisco, San Francisco, United States of America*; *[8]University Medical Centre of Ljubljana, Ljubljana, Slovenia*

On behalf of: COOL AMI EU Pilot Trial investigators.
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Background: The COOL AMI EU Pilot trial was a multicenter, prospective, randomized, controlled pilot trial to assess the feasibility of using intravascular therapeutic hypothermia (TH) as an adjunctive therapy to primary PCI (PPCI) in patients with anterior ST-elevation myocardial infarction (STEMI). As a secondary endpoint, we reported a non-significant, 7.1% absolute and 30% relative reduction in infarct size in the TH group. However, hypothermia patients had a longer ischemic time (IT) than controls due to non-cooling related delays from symptom onset to randomization. Since IT is an established predictor of infarct size, we aimed to further evaluate its potential impact on trial
Results: Methods: Fifty conscious patients with anterior STEMI and symptom duration < 6 hours were recruited and randomized to PPCI + TH or PPCI alone. TH was induced using an intravascular temperature management system and rapid infusion of 1L of cold saline, with a target temperature of 32 degrees Celsius. Infarct size (IS, of %LV) was measured by cardiac magnetic resonance (cMR) at 4 to 6 days post-PCI. Adjusted medians for infarct size for TH and control patients were obtained from quantile regression models with ischemic time as a covariate, and compared using the Wald test.
Results: From the 50 randomized patients, 22 in the TH and 23 in the control group completed cMR follow up. At reperfusion, mean intravascular temperature in the TH group was 33.6 +/- 1 degrees Celsius. TH patients had a significantly longer IT (mean 262 ± 79 vs 200 ± 65 minutes, P = 0.01) due to a potential chanceful longer delay from symptom onset to randomization ($p < 0.01$) . After adjustment for this imbalance, we observed a significant, 37% relative risk reduction in infarct size with an absolute decrease of 9.9% in the TH group as compared to control PPCI patients ($p < 0.05$).
Conclusions: In the COOL AMI EU Pilot Trial, following adjustment for ischemic time, therapeutic hypothermia was associated with a 37% reduction in infarct size in anterior STEMI. These results hold promise for improved clinical outcomes in patients with STEMI treated with hypothermia, and warrant a large-scale trial powered for clinical efficacy, where the risk of chanceful between-group differences are minimized.

P497

Heart failure in elderly patients after acute ST-elevation myocardial infarction

U Kostomaj[1]; A Kenk[1]; A Andreja Sinkovic[2]; V Kanic[2]; F Naji[2]
[1]University of Maribor, Medical faculty, Maribor, Slovenia; *[2]University Medical Centre Maribor, Maribor, Slovenia*

Background: The incidence of acute ST-elevation myocardial infarction (STEMI) is constantly increasing in younger than in older people, in particular in younger men. The mortality in STEMI patients is influenced by many risk factors, including time delay to treatment, the use of primary percutaneous coronary intervention (PPCI), acute heart failure, assesed by Killip class and advanced age. Predictors of mortality in elderly patients are less well known.
Purpose: To evaluate 30-day and 6-month mortality, as well as predictors of 30-day and 6-month mortality in STEMI patients older than 65 years of age.
Methods. We retrospectively included 286 STEMI patients (67.1% men, mean age 64.8 ± 11.7, age span 35 - 89 years), admitted to University clinical centre Maribor in 2016. Reperfusion strategy was primary percutaneous coronary intervention (PPCI). We evaluated demographic, clinical and mortality data of STEMI patients and compared them between older (over 65 years of age) and younger (younger than 65 years) STEMI patients, as well as independent predictors of 30-day and 6-month mortality of STEMI patients older than 65 years of age.
Results: 49% (140/286) of our STEMI patients were older than 65 years and in comparison to younger ones (< 65 years) they were significantly less likely men (54.3% vs 79.5%, $p < 0.001$), with significantly increased incidence of arterial hypertension (71.4% vs 42.5%, $p < 0.001$), prior diabetes (28.6% vs 14.4%, $p < 0.05$), increased incidence of admission bundle branch block (25.7% vs 9.6%, $p < 0.05$), in-hospital Killip classes II-IV (37.9% vs 23.9%, $p < 0.05$), multivessel coronary artery disease (31.4% vs 20.5%, $p < 0.05$) and increased 30-day (18.6% vs 8.9%, $p < 0.05$) and 6-month mortality (23.6% vs 9.6%, $p < 0.05$). There were nonsignificant differences between younger and older than 65 years in time to PPCI, the use of PPCI, anterior STEMI, TIMI flow III after PPCI and in in-hospital complications such as arrhythmias, in-stent thrombosis, reinfarctions, bleedings. However, cardiogenic shock during in-hospital treatment was most significant independent predictor of 30-day (OR 88.636, 95%CI 10.532 to 745.950, $p < 0.001$), as well as of 6-month mortality (OR 25, 95% CI 7.620 to 82.025, $p < 0.001$) of STEMI patients older than 65 years.
Conclusions: Acute heart failure - in particular cardiogenic shock - is a significant and independent predictor of short and log-term mortality in STEMI patients older than 65 years of age.

Valvular Heart Disease - Pathophysiology and Mechanisms

P498

Right ventricular function in patients with symptomatic aortic stenosis candidate for trans-catheter aortic valve implantation (TAVI): long term results of a single center experience

M Mara Gavazzoni[1]; E Vizzardi[1]; E Sciatti[1]; A Castiello[1]; I Bonadei[1]; R Raddino[1]; C Fiorina[1]; M Adamo[1]; S Curello[1]; M Metra[1]
[1]Civil Hospital of Brescia, Department of Medical and Surgical Specialties, Radiological Sciences and Public Health University, , Brescia, Italy

Background: Lack of knowledge does still exist about role of right ventricular function and right ventricle-arterial coupling as prognostic parameters in patients with symptomatic aortic stenosis candidate for TAVI.
Purpose To evaluate prognostic significance of right ventricular free wall deformation imaging and right ventricular arterial-coupling in a cohort of patients with heart failure due to severe aortic stenosis candidate for TAVI.
Methods: The study is a retrospective analysis of 56 patients with aortic stenosis admitted to our department with heart failure and candidate for TAVI (mean age: 81,6 ± 6,3 years) ; follow up period was 8,5 ± 0,4 years. Left ventricular ejection fraction was preserved in most patients (median value: 51% ± 14%) . Imaging of the right ventricle was performed by echocardiography; RV function was defined on the basis of tricuspid annular plane systolic excursion (TAPSE) and its normalization for pulmonary artery systolic pressure (PASP); right ventricular free wall longitudinal strain (RVFWLS%) and its normalization for PASP; fractional area changement (FAC%), peak systolic myocardial velocity by DTI (RVSm). All-cause mortality was the primary endpoint of survival analysis; composite of death and hospitalization for heart failure was the secondary end-point.
Results: Patients in our cohort were homogeneous regard to their demographic characteristics, aortic valve degree and type of degeneration (severe degenerative aortic stenosis), type of intervention (all patients had femoral access), so these parameters were not related to long-term incidence of events. Our patients had left ventricular hypertrophy and mean ejection fraction of 51% ± 14%. After a mean follow up of 8,5 ± 0,4 years, using Cox regression analysis we found that right ventricle free wall longitudinal strain was independently associated with all-cause mortality (HR: 1,5, 95% CI: ,1,1-2,1, P= 0,011); RVFWLS (-%) (HR 7.542, 95% CI 1.325-42.921, P = 0.023), PASP (HR 1.421, 95% CI 1.045-1.932, P= 0.025), TAPSE/PASP (HR 4.977, 95%CI 5.425-21,99, P = 0.044), RVFWLS/PASP (HR 2,333, 95% CI 3,96777-12,999, P = 0.046) were independently associated with composite end-point.
Conclusions: Deformation imaging of right ventricle free wall and correction of contractility parameters for PASP provide better risk stratification at long-term follow up than other echocardiographic parameters in patients with heart failure due to severe aortic stenosis.

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Transcatheter aortic valve replacement (TAVR) leads to an increase in the subendocardial viability index assessed by pulse wave analysis

C Claudia Mueller[1]; G Goliasch[1]; S Schachinger[1]; S Kastl[1]; G Delle-Karth[2]; J Kastner[1]; M Gyongyosi[1]; I Lang[1]; M Gottsauner-Wolf[1]; N Pavo[1]
[1]Medical University of Vienna, Department Internal Medicine II, Division of Cardiology, Vienna, Austria; *[2]Hietzing Hospital, Department of Medicine IV, Vienna, Austria*

Background: Pulse wave analysis (PWA) is a useful tool for non-invasive assessment of central cardiac measures as subendocardial perfusion (Subendocardial Viability Index, SVI) or contractility (dP/dtmax). The immediate influence of transcatheter aortic valve replacement (TAVR) on these indices has not been investigated yet.
Methods: We prospectively enrolled 40 patients presenting with severe aortic stenosis receiving TAVR. Central pressure curves were derived from radial and

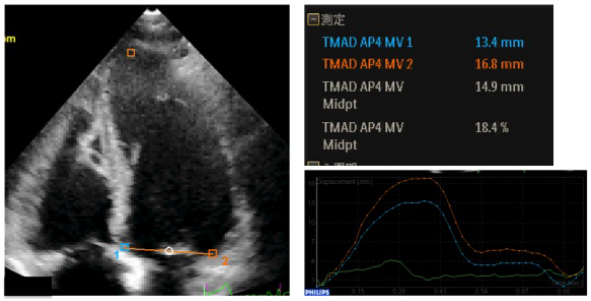
carotid sites using PWA up to 2 days before and 7 days after TAVR. Parameters were compared between peripheral measurement sites. Changes in SVI, dP/dtmax and in indices of vascular stiffness were assessed. Additionally, association of these variables with clinical outcome was evaluated during a 12-month follow-up.
Results: Central waveform parameters were comparable between measurement sites. SVI, but not dP/dtmax, augmentation Index (AIx) or augmentation pressure height (AGPH) correlated significantly with disease severity reflected by peak transvalvular velocity and mean transvalvular pressure gradient over the aortic valve (Vmax, ?Pm) [r=-0.372,p = 0.029 for Vmax and r=-0.371,p = 0.021 for ?Pm]. Vmax decreased from 4.5m/s (IQR:4.1-5.0) to 2.2m/s (IQR:1.9-2.7), (p < 0.001). This resulted in a significant increase in SVI [135.3%(IQR:115.5-150.8) vs. 140.3%(IQR:123.0-172.5),p = 0.039] and dP/dtmax [666mmHg(IQR:489-891) vs. 927mmHg(IQR:693-1092),p < 0.001], and a reduction in AIx [154.8%(IQR:138.3-171.0) vs. 133.5%(IQR:128.3-151.8),p < 0.001] and AGPH [34.1%(IQR:26.8-39.0) vs. 25.0%(IQR 21.8-33.7),p = 0.002], confirming the beneficial effects of replacing the stenotic valve. No association of these parameters could be revealed with outcome.
Conclusions: PWA is suitable for assessing coronary microcirculation and contractility mirrored by SVI and maxdP/dt in the setting of aortic stenosis. PWA parameters attributed to vascular properties should be interpreted with caution.

P500

Speckle-tracking echocardiographic mitral annular displacement can detect latent left ventricular longitudinal systolic dysfunction in patients with chronic aortic regurgitation

T Hozumi[1]; T Nishi[1]; K Terada[1]; K Takemoto[1]; S Ota[1]; M Kashiwagi[1]; K Shimamura[1]; A Kuroi[1]; T Kameyama[1]; Y Matsuo[1]; Y Ino[1]; H Kitabata[1]; T Kubo[1]; A Tanaka[1]; T Akasaka[1]
[1]Wakayama Medical University, Cardiology, Wakayama, Japan

Background: Chronic aortic regurgitation (AR) with reduced ejection fraction (EF) is one of important etiology in patients with heart failure. Previous reports using global longitudinal strain (GLS) analysis have shown left ventricular (LV) longitudinal systolic function decrease prior to reduction in EF in patients with chronic AR. Application of tissue-tracking echocardiography provides quick and easy assessment of mitral annulus displacement (TMAD) which may be used for detection of LV longitudinal systolic dysfunction alternative to GLS.
Purpose: To examine whether TMAD can be used for the detection of LV longitudinal systolic dysfunction in patients with moderate-severe chronic AR with preserved EF.
Methods: The study population consisted of 41 patients with moderate-severe AR and preserved EF (EF>50%, EF: 59±5 %, age: 61±20 years) who underwent tissue-tracking echocardiography (Philips, iE30 or EPIQ, QLAB). %TMAD from apical 4-chamber view was automatically assessed in all the study patients. GLS from apical 4-chamber, 2-chamber, and long-axis views was successfully measured in 36 of 41 patients. The final study population of the 36 patients successfully analyzed by both %TMAD and GLS was divided into two groups; 22 patients with preserved LV longitudinal systolic function (|GLS|>20%; Group-A) and 14 with more decreased LV longitudinal systolic function (|GLS| < 20%; Group-B).
Results: %TMAD was significantly lower in Group-B compared with Group-A (10.2±1.8 vs 14.5±2.1%, p < 0.01). According to ROC curve analysis, a cut-off value of %TMAD < 11.6 had a sensitivity of 100%, specificity of 77% for the presence of decreased LV longitudinal dysfunction (area under the curve: 0.94).
Conclusions: The present results showed that TMAD was useful in the assessment of LV systolic dysfunction in patients with moderate-severe AR and preserved EF. Noninvasive assessment of TMAD may be used for the detection of latent systolic dysfunction in patients with chronic AR and preserved EF.



Assessment of TMAD

P501

Left ventricular compliance and filling early after TAVI in severe aortic stenosis with marked cardiac hypertrophy

TG Thomas Gero Von Lueder[1]; P Hoffmann[2]; R Bjornerheim[1]; M Wennemo[3]; P Majak[4]; A Opdahl[2]; A Al-Ani[2]
[1]Oslo University Hospital, Department of Cardiology, Oslo, Norway; [2]Oslo University Hospital, Department of Cardiology, Division of Cardiovascular and Pulmonary Disease, Oslo, Norway, Oslo, Norway; [3]Oslo University Hospital, Department of Cardiothoracic Anesthesia, Oslo, Norway; [4]Oslo University Hospital, Department of Cardiothoracic Surgery, Oslo, Norway

Background: Left ventricular (LV) hypertrophy in aortic stenosis (AS) is associated with impaired LV relaxation, compliance and filling. While transcatheter aortic valve implantation (TAVI) unloads the LV, the effects of TAVI on these maladaptive changes is unknown.
Purpose: We studied whether TAVI would confer early improvement in LV structure, stiffness, filling pattern and relaxation.
Methods: LV dimensions, doppler velocities, and diastolic wall strain (DWS), an index of LV compliance by echocardiography in 22 patients in sinus rhythm were compared before, at day 2 after and at 3 months after TAVI using a self-expanding system.
Results: see table: Patients exhibited LV hypertrophy, low DWS and severe diastolic functional abnormalities. Three months after TAVI, E/e', an index of LV filling pressures was lower and DWS increased consistent with improved LV compliance; while no other changes in LV structure or function were observed after TAVI. LV mass index (R = 0.54), E velocity and DWS (R=-0.67; both P < 0.05) a baseline correlated with mean pressure gradient at 3 months.
Conclusions: This data in subjects with AS and a high degree of LV hypertrophy shows that cardiac unloading by TAVI improves LV filling pressures and compliance early on but does not alter other measures of LV structure, filling and relaxation. Preexisting LV hypertrophy and stiffness may be important determinants of LV diastolic function early after TAVI.

Tab. 1.Demographics and echocardiography

Variable	Baseline	Day 2 post TAVI	3 months post TAVI
Age	80±2	na	na
Body Mass Index, BMI (kg/m2)	25±1	na	na
NYHA functional class	2.8±0.6	na	na
Mean transvalvular gradient (mmHg)	58±2	7±1***	8±1***
Septal thickness (mm)	13.2±0.4	13.4±0.7	12.6±0.6
LV enddiastolic diameter (mm)	45±1	46±2	45±2
LV mass index (g/m2)	122±7	139±13	117±10
Diastolic wall strain	0.14±0.02	0.18±0.01*	0.22±0.02*
E (m/s)	0.96±0.07	1.10±0.09	0.97±0.07
E/A	1.3±0.2	1.6±0.5	1.3±0.2
E deceleration time (ms)	221±15	202±19	229±20
e´ (cm/s)	4.1±0.3	4.1±0.4	3.9±0.2
E/e´	20.0±2.3	20.8±3.0*	18.7±2.3*
Tei index	0.50±0.03	0.59±0.05	0.56±0.03

na, not applicable; *P?0.05, ***P?0.0001 vs Baseline; ANOVA

P502

The coagulation state of patients with infective endocarditis

M Mariia Sorokina[1]; NM Povalyaev[1]; AA Andreev[1]; AS Pisaryuk[2]; JUL Karaulova[2]; EO Kotova[2]; AN Balandina[3]; DM Polokhov[3]; MA Panteleev[3]; IA Merai[4]; AS Milto[4]
[1]M.V. Lomonosov Moscow State University, Basic Medicine, Moscow, Russian Federation; [2]Peoples Friendship University of Russia (PFUR), Moscow, Russian Federation; [3]Dmitry Rogachev National Research Center of Pediatric Hematology, Oncology and Immunology, Laboratory of cellular hemostasis and thrombosis, Moscow, Russian Federation; [4]V.V. Vinogradov City Clinical Hospital, Moscow, Russian Federation

Background: The activity of the hemostasis system seems to be highly relevant in terms of susceptibility to progression, various complications (heart failure, embolism) and treatment of IE. The incidence of heart failure reaches 50-78% and embolic events occur in 34-56% of patients diagnosed with IE. Both of these complications are independent risk factors for mortality. The laboratory

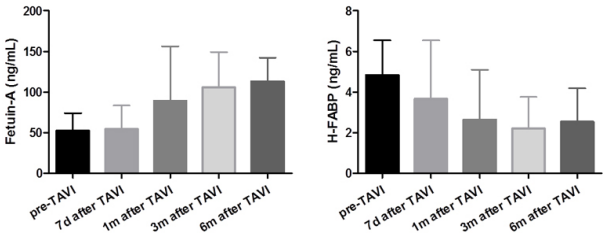
hemostasis assays are supposed to "highlight" patients shifted to hypercoagulation to prevent embolism, as a result, help clinicians to change treatment strategy in time.
Purpose: The aim of this study was to reflect the coagulation state of patients with IE via hemostasis tests in comparison with healthy individuals.
Methods: We conducted an observational study in 15 consecutive patients diagnosed with IE (patients) and in 53 healthy individuals (control group). Blood samples were collected 3-5 hours after the onset of the diagnosis. Platelet functional activity was estimated by flow cytometry, coagulation was assessed using integral assay of thrombodynamics. Mann-Whitney U-test was used for statistical analysis of the data.
Results: Platelet count in patients: median value 175*10^9/l vs 245*10^9/l in controls didn't differ significantly. Practically all platelet functions were profoundly impaired in patients diagnosed with IE according to the test of functional activity. In patients there was a significant decrease in mepacrine uptake in dense granules before activation: median value 70 vs 100 ($p < 0.001$) in healthy individuals. After inductor addition uptake was higher in patients: median 34 vs 24 ($p < 0.001$). CD62p (P-selectin) in patients with IE was significantly lower after activation: median value 82 vs 99 ($p < 0.05$). CD61 (GPIIb-IIIa) binding PAC1 antibody (possible only after platelet activation when CD61 changes its configuration) was significantly higher in endocarditis group before activation: median value 4 vs 3 ($p < 0.05$) and significantly lower after inductor addition: 51 vs 99 ($p < 0.001$) in controls. CD42b (GPIb) was significantly higher only after activation in patients: median value 69,0 vs 57,5 ($p < 0.05$). The percentage of procoagulant platelets (by detecting annexin V) was higher both before: median value 1,53 vs 0,01 ($p < 0.001$) respectively and after activation: median 13,20 vs 0,18 ($p < 0.001$) in IE patients. The granularity of platelets (SSC) before activation was significantly lower in patient: median value 72,0 vs 99,6 ($p < 0.001$). However, platelet size (FSS) in patients was similar to controls. Initial clot growth rate (Vi) in thrombodynamics was increased for patients compared to healthy individuals values: median value was 59,3 μm/min in patients with IE vs 29,0 μm/min in healthy donors ($p < 0.05$). All other parameters of thrombodynamics didn't differ.
Conclusion: Platelets functional activity in IE patients was mostly increased before activation and decreased after. Plasma coagulation reveal hypercoagulation in patients with IE via thrombodymanics.

Valvular Heart Disease - Epidemiology, Prognosis, Outcome

P503
Analysis of novel cardiovascular biomarkers in patients with severe aortic stenosis undergoing TAVI

M Mirna[1]; M Lichtenauer[1]; B Wernly[1]; V Paar[1]; C Jung[2]; UC Hoppe[1]; A Lauten[3]; PC Schulze[4]; D Kretzschmar[4]
[1]Paracelsus Private Medical University, Internal Medicine II, Cardiology, Salzburg, Austria; *[2]Medical Faculty, University Duesseldorf, Division of Cardiology, Pulmonology, and Vascular Medicine, Duesseldorf, Germany*; *[3]Charite University Hospital, Cardiology, Berlin, Germany*; *[4]University Hospital of Jena, Clinic of Internal Medicine I, Jena, Germany*

Background: Novel biomarkers have recently been investigated for their use in the risk stratification of patients with heart failure and acute coronary syndrome and they show promising results in predicting patient outcome. Since transcatheter aortic valve implantation (TAVI) is associated with myocardial injury, we sought to examine wether the procedure is followed by an increase in the plasma levels of GDF-15, H-FABP, Fetuin-A, Galectin-3 and suPAR. We believe that these biomarkers might help to improve periprocedural risk stratification of patients undergoing TAVI in the future.
Methods: We collected blood samples of 79 patients with high-grade aortic valve stenosis undergoing transcatheter aortic valve implantation (TAVI) before and after the intervention (at 7 days, 1 month, 3 months and 6 months post TAVI) and analyzed the plasma concentrations of GDF-15, H-FABP, Fetuin-A, Galectin-3 and suPAR.
Results: Compared to the baseline plasma levels, there was a statistically significant increase in the median concentrations of Fetuin-A (median 53.19 ng/ml, IQR 37.38-77.11 to median 113.2 ng/ml, IQR 85.39-142.6 post TAVI, $p < 0.001$) and sUPAR (median 2758 pg/ml, IQR 2121-3665 to median 3291, IQR 2373-4177 post TAVI, $p < 0.001$). H-FABP showed a statistically significant decrease after TAVI (median 4.9 ng/ml, IQR 2.4-6.61 to median 2.21, IQR 0.76-3.8 post TAVI, $p < 0.001$). Galectin-3 and GDF-15 evidenced no significant change in serum concentration after TAVI.
Conclusion: Transcatheter aortic valve implantation was associated with a significant increase in the plasma levels of Fetuin-A and suPAR and a significant decrease in the concentration of H-FABP. In fact, it has recently been shown that the plasma levels of H-FABP and suPAR are elevated in conditions with ongoing myocardial damage and that they are associated with an increased risk for adverse events in patients with various cardiac diseases. Plasma levels of Fetuin-A have been found to be inversely associated with adverse events in coronary artery disease. The significant decrease in the concentration of H-FABP and the significant increase in the serum concentration of Fetuin-A in our cohort could be associated with a hemodynamic improvement after valve replacement. We therefore hypothesize that these novel biomarkers could add prognostic information for the individual patient and serve to improve periprocedural risk stratification of patients undergoing TAVI in the future.



P504
Echocardiography factors associated with development of late significant tricuspid regurgitation after successful left-sided valve surgery

H Ben Ayed[1]; I Zairi[1]; K Mzoughi[1]; M Jabeur[1]; W Saieb[1]; S Kraiem[1]
[1]Habib Thameur Hospital, CARDIOLOGY DEPARTEMENT, Tunis, Tunisia

Background: Persistent significant tricuspid regurgitation (TR) after successful left-sided valve surgery is frequently reported.
The aim of this study was to determine the clinical and echocardiographic factors which could impact on the development of late significant TR after successful left-sided valve surgery.
Methods: We undertook a retrospective comparative study between 1995 and 2013, including 64 patients divided in two groups, all has undergone surgery for one or double left-valve diseases with minimal TR requiring no act on it.
These patients developed during their follow-up mild to severe tricuspid insufficiency. The study group (n= 32) who developed moderate to severe TR requiring correction of valve defect were compared to a control group (n= 32) paired by the same epidemiological caracteristics but having kept a minimal and stable TR.
Results: The mean age was 48.5 ± 8.5 years with a female predominance Sex-Ratio = 0.28;
In univariate analysis, we retained as predictive preoperative factors of TR evolution, the female gender ($p = 0.002$), atrial fibrillation (AF) ($p = 0.007$), the expansion of the left atrium (LA) ($p = 0.0001$) or the Right Ventricle (RV) ($p = 0.04$) and the pulmonary arterial hypertension ($p = 0.04$). In Postoperative, in addition to precedent factors we retained the left ventricular ejection fraction ($p = 0.0001$), the tricuspid annular dilatation ($p = 0.0001$), the decrease of the TAPSE ($p = 0.0001$) and the increase of the VR Tei-index ($p = 0.0001$).
However, in multivariate analysis, we retained only 3 factors: a female gender, an AF and a LA expansion
Our study was concordant with the most published papers and meta-analysis about this subject.
Conclusion: The indication for more aggressive interventions for low-grade TR in the left valve surgery may be considered for female patients, dilated LA and AF.

P505
Impact of valve type in morbidity and mortality of a population with endocarditis

AC Ana Catarina Gomes[1]; I Cruz[1]; AI Marques[1]; S Alegria[1]; AR Pereira[1]; D Sebaiti[1]; I Rangel[1]; I Joao[1]; H Pereira[1]
[1]Hospital Garcia de Orta, Cardiology, Almada, Portugal

Background: Infective endocarditis still represents a major cause of morbimortality. The population with prosthetic valve is at increased risk of serious complications.
Methods: We analyzed the endocarditis population in our hospital in the last 10 years. The clinical and imaging data were collected as well as the complication rates and mortality data.
Purpose: To compare the clinical features and adverse outcomes of patients with native versus prosthetic endocarditis.
Results: 148 patients, 75% males, 61.5 ± 15.9 years. 51.4% with hypertension (HTN), 18.9% with diabetes mellitus (DM). The aetiology of valvular heart disease: 2 patients with previous IE (infective endocarditis), 9 with degenerative disease, 1 with congenital heart disease, 1 with rheumatic heart disease. Comorbidities:

heart failure (HF) in 27% (6.8% with HF device), pulmonary disease (PD) in 14%, chronic renal disease (CRD) in 14.9% (3.4% on haemodialysis (HD)), chronic hepatic disease (CHD) in 22.3%, HIV seropositive in 13.5%, cancer in 9.5%, 98.6% on immunosuppression (medical cause or drug-related).
76.4% with single valve endocarditis, 14.9% with double valve endocarditis. 56.8% with aortic valve disease, 39.2% with mitral valve disease and 13.5% with right valve heart disease. Native valve disease in 72.3%.
Signs at presentation: fever in 67.1%, murmur in 53.3%, anemia in 39.5%.
Echocardiographic findings: vegetation in 80.4%, abcess in 13.5%, pseudoaneurism in 4.7%, valve obstruction in 6.1%, aneurysm in 3.4%, fistula in 4.1%. Regurgitation was observed in 54.1%.
The populations were similar in terms of gender (p = 0.29), HTN (p = 0.1), DM (p = 0.16), PD (p = 0.80), CRD (p = 0.62), haemodyalisis (p = 0.32), cancer (p = 0.59), HIV infection (p = 0.06), IV drug use (p = 0.10), fever (p = 0.84) and murmur (p = 0.77) at presentation. The microrganisms were also similar between the two groups, except for Staphylococcus epidermidis infection (1.9% vs 9.8%, p = 0.05).
Although, patients with native valve disease had less HF (21.5% vs 41.5%, p = 0.02), haemorrhagic stroke (5.0% vs 44.4%, p = 0.02), aortic (49.5% vs 75.6%, p = 0.005) and right-sided valve diseases (17.8% vs 2.4%, p = 0.01), abcess (8.3% vs 30.8%, p = 0.002) and pseudoaneurism (2.1 vs 12.8%, p = 0.02).
They had more CHD (28.2% vs 7.3%, p = 0.007), vegetations (92.8 vs 74.4%, p = 0.008), regurgitation (67.7% vs 38.5%, p = 0.002) and local destructive lesions (27.1 vs 10.3%, p = 0.04).
No differences were found in survival between patients with native versus prosthetic valve endocarditis (log rank 2.5, p = 0.194).
Conclusion: Patients with native valve disease had more vegetations, local destructive lesions and regurgitation. Although, they had less HF, hemorrhagic stroke, abscess and pseudoaneurysm. Overall, the survival was similar between the two groups.

P506
Predictors of in-hospital mortality in Infective Endocarditis

AC Ana Catarina Gomes[1]; I Cruz[1]; AI Marques[1]; S Alegria[1]; AR Pereira[1]; D Sebaiti[1]; I Rangel[1]; I Joao[1]; H Pereira[1]
[1]*Hospital Garcia de Orta, Cardiology, Almada, Portugal*

Background: Infective endocarditis (IE) still represents a major cause of morbimortality in patients with valvular heart disease. The main causes of mortality are a non-controlled infection, refractory heart failure and embolic complications.
Methods: We analyzed the endocarditis population in our hospital in the last 10 years. The clinical and imaging data were collected as well as the complication rates and mortality data.
Purpose: To determine the independent predictors of hospital mortality in IE patients.
Results: 148 patients, 75% males, 61.5 ± 15.9 years. 51.4% with hypertension (HTN), 18.9% with diabetes mellitus. Aetiology of valvular heart disease: 2 patients with previous IE (infective endocarditis), 9 with degenerative disease, 1 with congenital heart disease, 1 with rheumatic heart disease. Comorbidities: heart failure (HF) in 27% (6.8% with HF device), pulmonary disease (PD) in 14%, chronic renal disease (CRD) in 14.9% (3.4% on haemodialysis (HD)), chronic hepatic disease (CHD) in 22.3%, HIV seropositive in 13.5%, cancer in 9.5%, 98.6% on immunosuppression (medical cause or drug-related).
Microorganisms identified in blood cultures: S. Aureus 23.7%, S. Epidermidis in 3.9%, Streptococcus spp in 28.3%, Enterococcus 11.8%, Gram-negative agents 3.9%, Candida spp 2.0%, others in 6.7% and no identified agent in 19.7%.
Signs at presentation: fever in 67.1%, murmur in 53.3% and anemia in 39.5%.
56.8% with aortic valve disease, 39.2% with mitral valve disease and 13.5% with right valve heart disease. Native valve disease in 72.3% and prosthetic valve disease in the remaining (6.6% with prosthetic valve less than 1 year).
Echocardiographic lesions: vegetation in 80.4%, abcess in 13.5%, pseudoaneurysm in 4.7%, valve obstruction in 6.1%, aneurysm in 3.4% and fistula in 4.1%.
The in-hospital mortality was associated with previous HF (r = 0.24, p = 0.004), HF complications (r = 0.29, p <0.001), septic shock (r = 0.428, p <0.001), S. Aureus IE (r = 0.22, p = 0.008) and abscess (r = 0.20, p = 0.018). The logistic regression showed abcess (OR 3.9, p = 0.048) and prosthetic valve implantation less than 1 year (OR 4.6, p = 0.032), as independent predictors of in-hospital mortality.
Conclusion: The main associations with in-hospital mortality were previous HF diagnosis, "de novo" HF symptoms related to IE, abscess, septic shock and S. Aureus infection. Although, after multivariate analysis, only abscess and recent prosthetic valve implantation remained as independent predictors.

P507
Significance of a new simple echocardiographic parameter for mitral regurgitation severity

A Daimon[1]; M Asakura[1]; A Goda[1]; M Sugahara[1]; K Masai[1]; T Oshita[1]; Y Ohta[1]; T Masuyama[1]
[1]*Hyogo College of Medicine, Cardiovascular Division, Nishinomiya, Japan*

Background: Generally, the severity of mitral regurgitation (MR) is evaluated with proximal isovelocity surface area (PISA) or volumetric methods. However, these methods are time consuming and there are some anatomical difficulties and limitations for the quantification of MR severity and integrated approaches using echocardiography are recommended. Recently, left ventricular early inflow-outflow index (LVEIO index), which is calculated by dividing the mitral E-wave velocity by the LV outflow velocity time integral has been proposed as a new index for evaluation of MR severity. However, its usefulness remained unclear to differentiate the severity in various etiology of MR.
Purpose: The aim of this study was to evaluate the usefulness and determine ideal threshold of LVEIO index to diagnose severe MR in different backgrounds, and we investigated whether LVEIO index can be the prognostic factor among patients with MR.
Methods and Results: We reviewed 76721 transthoracic echocardiographic reports performed at our institution from January 4, 2008 to May 15, 2015. MR severities were evaluated according to the guideline of the American Society of Echocardiography and the European Association of Cardiovascular Imaging. Cases with moderate or severe aortic valve regurgitation, any mitral stenosis, prior mitral valve surgery, congenital heart diseases, LV assist device, or any arrhythmias were excluded. Also cases with inadequate or missing LV inflow or outflow Doppler recordings were excluded. Finally we evaluated 18692 cases and classified them as 17960 of no, trivial, or mild MR (Grade 0/1), 600 of moderate MR (Grade 2), 82 of moderate to severe MR (Grade 3) and 50 of severe MR (Grade 4). The average LVEIO index of Grade 0/1, Grade 2, Grade 3 and Grade 4 were 3.6 ± 1.4, 6.0 ± 2.5, 7.4 ± 3.1 and 9.5 ± 2.8, respectively. For diagnosis of moderate to severe or severe MR, area under the curve for LVEIO was 0.93 by receiver operating characteristic analysis. The optimal threshold of LVEIO was 5.4 to distinguish moderate to severe or severe MR from non-severe MR (sensitivity 84%, specificity 91%). There were no differences in the prognostic value of LVEIO index between the cases with reduced LV ejection fraction (<50%) and preserved LV ejection fraction (= 50%), which area under the curves were 0.94 and 0.92, respectively. We checked up the etiology of MR in grade 2-4, and found that secondary MR had greater average of LVEIO than primary MR (primary MR 5.8, secondary MR 6.9, p <0.0001). In the group of LVEIO index = 5.4, the risk ratio of heart failure hospitalization was 2.7 times high compared with the group of LVEIO index < 5.4 (p = 0.009, Hazard ratio 1.75, 95%CI 1.18 to 2.58).
Conclusion: LVEIO is a simple and useful method to diagnose severe MR by using adequate thresholds regardless of LVEF and can be the predictor for heart failure hospitalization in patients with MR.

Valvular Heart Disease - Treatment

P508
The importance of heart failure with reduced ejection fraction in a cohort with infective endocarditis: a single-centre experience

CP Primus[1]; J Bragg[2]; KS Rathod[1]; K Wong[1]; R Uppal[1]; S Bhattacharyya[1]; LC Davies[1]; S Woldman[1]; MD Thomas[1]
[1]*Barts Heart Centre, London, United Kingdom*; [2]*University College London Hospitals, London, United Kingdom*

On behalf of: Barts Heart Centre Infective Endocarditis Multi-Disciplinary Team

Introduction: The 2015 ESC Guidelines on Infective Endocarditis (IE) acknowledge the importance of congestive cardiac failure (CCF) as an independent predictor of morbidity and mortality in this challenging disease. Left heart valve lesions are well known to cause CCF in IE. However, there is no published literature investigating the importance of heart failure with reduced ejection fraction (HFrEF) on outcomes in this population.
Purpose: We sought to establish the incidence of HFrEF in our IE cohort. As a cardiothoracic centre, we further sought to understand the impact of left ventricular systolic dysfunction (LVSD) on medical vs surgical management of IE and ultimately inpatient mortality.
Methods: Medical records of all patients referred to the Endocarditis Team (MDT) were reviewed (October 2015 to date). Each case was reviewed for MDT consensus of diagnosis by modified Duke's Criteria, medical vs surgical management and mortality. Echocardiographic findings were reviewed for EF in the study immediately prior to MDT decision.
Results: IE was confirmed or probable in 289 patients (male = 195) aged 56.5 years (range 16-89). Native valves were culprit in 205 patients, prosthetic in 84

patients, with concomitant device IE in 24 patients. LVEF was normal/hyperdynamic (EF>55%, range 55-81%) in 206 patients (71.3%), with LVSD (EF < 45%, range 9-45%) in 55 (19.0%) patients.
Cardiac surgery was mandated in 139 (48%) patients and device extraction in 15 (5%). The primary indication for surgery was CCF with refractory pulmonary oedema in 59 (42.4%) patients: 37 due to valvular insufficiency; 15 with decompensated LVSD; 7 in cardiogenic shock. Other important surgical indications were: a haemodynamically significant valve lesion (n = 50, 36.0%); intracardiac abscess (n = 28, 20.1%); uncontrolled infection despite appropriate antibiotics (n = 26, 18.7%).
Overall inpatient mortality was 49/289 (16.9%), of whom 19 had advanced non-cardiac medical comorbidities that precluded surgical intervention. Of the 13 surgical deaths, 6 underwent surgery for CCF. Importantly however, LVSD had no bearing on overall, nor surgical, mortality by hazard ratio (HR). There was however a trend towards increased mortality in medically managed IE with LVSD [HR 1.83 (95% CI 0.99-3.38) p = 0.053].
Discussion: Moderate to severe LVSD was seen in 19% of our large IE cohort. To our knowledge, this has not been previously reported. CCF was the primary indication for surgical intervention in 42.4% of our patients, as per published series, and is well established as an independent predictor of in-hospital and 1-year mortality. Critically however, the importance of HFrEF has not been widely discussed. Our data suggest that HFrEF does not increase mortality in those requiring surgery for IE. Further work is required to understand whether the trend in medically managed patients is a facet of HFrEF or whether aggressive HF management is required to allow early surgery in this high-risk group.

P509

Relationship among gradient and systolic function: prognosis impact after TAVR

P Pablo Meras Colunga[1]; FJ Irazusta Cordoba[1]; VA Rial Baston[1]; D Gemma[1]; R Mori Junco[1]; AM Iniesta Manjavacas[1]; O Gonzalez Fernandez[1]; A Rivas Perez[1]; A Velez Salas[1]; T Lopez Fernandez[1]; R Moreno[1]; JL Lopez Sendon[1]
[1]University Hospital La Paz, Cardiology, Madrid, Spain

Introduction: Among patients (p.) undergoing transcatheter aortic valve replacement (TAVR), some studies suggest that the presence of low gradient may associate a worse prognosis, with even more impact than the presence of ventricular dysfunction.

Table 1.

Groups	LVEF >40% Gradient >40 mmHg	LVEF >40% Gradient <40 mmHg	LVEF <40% Gradient >40 mmHg	LVEF <40% Gradient <40 mmHg
N	101	75	22	11
Age (years)	81.6 (±7.5)	81.3 (±6.2)	79.3 (±8.4)	78.4 (±9.4)
Female sex	56.4	53.3	31.8	45.5
Hypertension Diabetes Dyslipemia Chronic kidney disease / dyalisis	85.1 41.6 61.4 36 4	88 44 62.7 36.5 5.4	86.4 63.6 57.1 63.6 9.1	81.8 54.5 45.5 54.5 0
Coronary artery disease Complete revascularization	41.6 27.7	56 33.3	68.2 13.6	45.5 27.3
EuroScore II STS	3.9 ±3.3 4.4 ±3	4.4 ±3.1 4.7 ±2.6	9.9 ±7.7 5.4 ±2.1	7.8 ±4.3 6.6 ±4.1
Hospital stay (days)	13.1 ±12	15.8 ±19	13.6 ±10	17.1 ±22
Pacemaker implant Minor / major vascular complication Bleeding Heart failure	14.9 10.9 / 5 11.9 3	18.7 13.3/ 6.7 14.7 9.3	13,6 4.5 / 0 9.1 4.5	9.1 36.4 / 0 9.1 0
1-year mortality	15.8	20	18.2	0

Table 1. Baseline characteristics and main complications. Data are expressed as percentages or as mean (+/- standard deviation).

Methods: We made a retrospective analysis of 209 consecutive p. undergoing TAVR at our center, divided into 4 groups according to ventricular dysfunction (LVEF < 40%) and low mean gradients (< 40 mmHg) as measured by echocardiography.

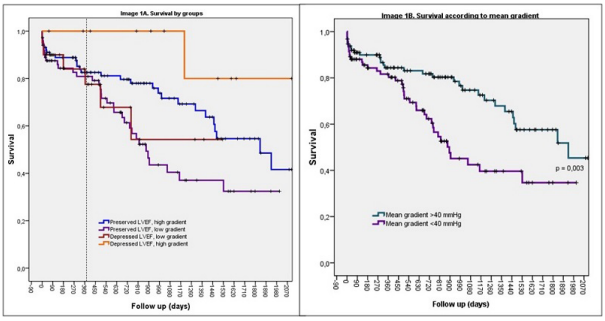


Image 1. Kaplan-Meier survival.

We analysed baseline characteristics and complications of each group, as well as survival rates with Kaplan-Meier curves.
Results: Mean age was 80,1 years, 52.2% were female, with a mean EuroScore II of 4.9% and STS of 4.8% and a mean follow up of almost two years (23.8 ± 20.3 months). Baseline characteristics and main complications are detailed in table 1.
Regarding Kaplan-Meier survival analysis (image 1), p. with low aortic gradient had a significantly higher mortality rate (p = 0.003 compared with the groups with high gradient). Importantly, this occurred both for those with preserved and depressed ejection fraction. These differences were increased after the first year of follow up.
In our series, p. with ventricular dysfunction and high aortic gradient had a good survival rate, being this finding limited by a low number of individuals in that group.
Conclusions: Our results support the presence of a worse prognosis - with higher mortality rates at follow up- in p. with aortic stenosis and low aortic gradient undergoing TAVR, and this is independent of the presence or absence of ventricular dysfunction.

P510

Do the patients with coronary artery disease have the same benefits from transcatheter aortic valve implantation?

PM Paulo Maia Araujo[1]; A Nunes[1]; S Torres[1]; M Braga[1]; R Pinto[1]; J Rodrigues[1]; RA Rodrigues[1]; PB Almeida[1]; MB Campelo[1]; JC Silva[1]; MJ Maciel[1]
[1]Sao Joao Hospital, Cardiology, Porto, Portugal

Introduction: Transcatheter aortic valve implantation (TAVI) is an effective treatment for symptomatic severe aortic stenosis, considered at high surgical risk. Coronary artery disease (CAD) is a frequent comorbidity in these patients (pts) and can influence the results of this procedure.
Purpose: To evaluate if the beneficial effects of TAVI on morbi/mortality and on the symptoms improvement are comparable in patients with or without CAD.
Methods: We retrospectively evaluated pts submitted to TAVI in our hospital between October 2014 and December 2016. All pts had symptomatic severe aortic stenosis prior to the procedure and the decision for referral for TAVI was made by a multidisciplinary Heart Team. CAD was defined as the presence of obstructive lesions (any stenosis = 70% or left main [LM] stenosis = 50%).
Results: During this period, 89 pts were submitted to TAVI, with a mean age of 80.2 ± 7.1 years, of whom 51.7% (n = 46) were female. Forty two pts (47.2%) had CAD: one vessel in 19.1%; 2 vessels in 4.5%; 3 vessels in 5.6%; involvement of LM in 33%. Of this group, 47.6% had been previously submitted to PCI and 35.7% to CABG. Additionally, in fifteen pts (35.7% of CAD group) periprocedural PCI was performed.
Baseline characteristics weren't significantly different between pts with/wihout CAD regarding to age (81.1 vs 79.5 years; p = 0.69), sex (45.2% vs 57.4% female; p = 0.25), left ventricular ejection fraction (55.0% vs 50.7%; p = 0.66), NYHA class = 2 (97.6% vs 100%; p = 0.29) or presence of angina (26.2% vs 14.9%; p = 0.19). As expected, EuroScore II was higher in CAD pts (7.8% vs 3.8%; p < 0.01).
Incidence of intra/postprocedural complications was similar between CAD pts vs no CAD: 64.3% vs 68.1% (p= 0.71). However, mean stay was higher in CAD pts (15.3 vs 12.4 days; p= 0.01). Only one patient had in-hospital mortality (no CAD).
During a mean time of follow-up of 386 ± 93 days after discharge, CAD pts had similar rates of all-causes mortality (9.8% vs 4.3%, p = 0.32), but cardiovascular mortality was tendentially higher (7.3% vs 0%), although not reaching statistical significance (p = 0.06).
CAD group had higher rates of hospitalizations: 39.0% vs 19.6% (p = 0.05).
At one year after discharge, in the CAD group, TAVI resulted in a significant reduction of angina (pre-TAVI: 26.2% vs post-TAVI 5.7%; p < 0.01) and of NYHA class = 2 (pre-TAVI: 97.6% vs post-TAVI 37.1%; p < 0.01). The proportion of pts reporting an overall improvement on functional capacity after the procedure was high, with similar rates between pts with or without CAD: 85.7% vs 76.7% (p = 0.32).

Conclusion: In this population, the presence of CAD was associated with higher morbidity and a tendency to higher cardiovascular mortality after TAVI. However, this procedure successfully improved symptoms and functional capacity in CAD group, similarly to the other pts. Therefore, TAVI has important clinical benefits even in pts with CAD.

P511

Anticoagulant strategy for prosthetic valve in patients with endocarditis does not influence anemia, preexistent heart failure and mortality

MM Monica Mariana Baluta[1]; E Panaitescu[2]; MM Vintila[3]
[1]*Carol Davila University of Medicine-St Pantelimon Clinical Emergency Hospital-Cardiology Department, bucharest, Romania*; [2]*Carol Davila University of Medicine and Pharmacy , Medical Informatics and Biostatistics, Marketing, Medical Technology , Bucharest, Romania*; [3]*St. Pantelimon Emergency Hospital, Cardiology, Bucharest, Romania*

Introduction: The type of anticoagulant therapy (ACT) used in patients with prosthetic valve endocarditis (PVE) is individualized by the endocarditis team.
Purpose: To determine the safety of anticoagulant therapy in PVE patients with anemia and prior heart failure.
Method: We analyzed 56 patients who fulfilled the modified Duke's criteria of PVE (early 29, late 27) out of which 86% with mechanical and 14% with biologic valves. At admission patients presents with anemia (Hemoglobin less than 10 g/dl) and describe various degree of dyspnea with or without congestion. PVE approach was intended to be initially conservative with surgical rescue if the patient condition requires that. We analyzed the type of ACT, clinical and paraclinical variable from patients follow up notes.
Results: Of these 56 patients, 71% were on oral anticoagulant therapy (OACT), 14% on low molecular weight heparin (LMWH), 9% were OACT-naïve during hospitalization. Aspirin was associated with OACT in 36% patients and with LMWH in 14%. The mean age of 36 men and 20 women included in this study was 54.64 ± 11.34 years (range 28-74 years) at admission. Survivors (90.4%) received antibiotics during 33.55 ± 12.8 days and 71% responds well to antibiotic therapy only. Antibiotic responders had initial Hb 9.76 ± 1.4 g/dl and deceased ones de 8.58 ± 1.38 g/dl, p = 0.07. Anticoagulant therapy was stopped in 1 case of hemorrhagic stroke and 1 episode of severe digestive bleeding. Patients that received transfusions had a higher mortality (p = 0.008). The ACT type was not related to mortality p= 0.52, neither Aspirin if associated p = 1.0 (Fisher's Exact Test). However in studied patients mortality was influenced by anemia per se at admission (p = 0.001) and further major bleeding (p = 0.007) irrespective of the ACT status. PVE type, baseline ejection fraction (EF), NYHA class or anemia, were not statistically related to hemodynamic instability. Study limitation: the sample size was small.
Conclusions: Anticoagulant therapy associated or not with aspirin was safe in patients with prosthetic valve endocarditis. Irrespective of the anticoagulant strategy type, there was no significant difference in the incidence of post admission hemorrhagic stroke and major bleeding.
Anemia degree and transfusions significantly alter the patient prognosis in term of increased mortality without a relationship with baseline EF, hemodynamic stability or NYHA class.
Anemia remains not only a marker of infection but also a strong predictor of adverse outcome without being influenced by the anticoagulant strategy.

P512

Congestive heart failure in patients with post rheumatic valvulopathies: occurrence and management in a tertiairy subsaharan centre

J C Jacques Cabral Tantchou[1]; TTJC Tantchou Tchoumi[1]; JCA Jean Claude[1]; MM Mve Mvondo[1]; GB Gianfranco[1]
[1]*St. Elizabeth Catholic General Hospital, Cardiac centre, Kumbo, Cameroon*

On behalf of: -
Funding Acknowledgements: -

The aim of the study was to investigate the occurrence, the management and challenges faced in patients with congestive heart failure in St. Elizabeth catholic general hospital Shisong, cardiac centre.
Material and Methods: Between November 2002 and November 2008, a population of 581 patients were diagnosed with congestive heart failure according to the modified Framingham criteria for the diagnosis of heart failure. Complementary investigations used to confirm and establish the aetiology of the disease were the chest X ray, electrocardiography, bi-dimensional doppler echocardiography.
Results: Congestive heart failure was diagnosed in 287 females and 294 males, aged between 9 and 76 years old (40,5 ± 15 years old). Post rheumatic valvulopathies (14,6%) and congenital heart diseases (1,9%) are the first aetiologic factor of congestive heart failure in the young, meanwhile cardiomyopathies (8,3%) in elderly followed by hypertensive cardiomyopathy (4,4%). Congestive heart failure was also seen in adults with congenital heart diseases in 0,01%. In patients with post rheumatic valvulopathies, congestive heart failure is due to left ventricular systolic dysfunction. The mean duration of hospital stay for the compensation treatment was nine days. Financial limitation is causing the exacerbation of the disease and premature death.
Conclusion: Congestive heart failure is mainly due to post rheumatic valvulopathies in young patients in our centre. National program for fight against rheumatic fever and complications are of great urgency in our country. The compensation treatment of congestive heart failure is challenging in our milieu, characterized by poor compliance and financial limitation.

P513

Transcatheter aortic valve implantation: a real-life experience

M Marta Braga[1]; P Araujo[1]; A Nunes[1]; S Torres[1]; R Pinto[1]; J Rodrigues[1]; RA Rodrigues[1]; PB Almeida[1]; M Vasconcelos[1]; D Magalhaes[1]; JC Silva[1]; MJ Maciel[1]
[1]*Sao Joao Hospital, Porto, Portugal*

Background: Transcatheter aortic valve implantation (TAVI) is a therapeutic solution for patients with severe symptomatic aortic stenosis who are not candidate for conventional surgery. Despite its growth, TAVI is an invasive procedure in evolving and requires further refinement to reduce complications. The aim of this study was to describe the baseline characteristics and the short-outcomes in a cohort of patients referenced for TAVI procedure.
Methods: We retrospectively analysed data of a cohort of patients submitted a TAVI in a single centre, from October 2014 to December 2016. Data were collected from the electronic clinical process and registered in a uniform base.
Results: Of a total of 89 patients, 51.7% were female. Mean age of patients was 80.2 ± 7.1 years. The prevalence of hypertension was 82.0% and of diabetes was 34.8%. Almost half of patients had obstructive coronary artery disease and 19.1% had history of cardiac surgery. Cerebral vascular disease was present in 22.5% and peripheral artery disease was diagnosed in 21.3% of the cohort. More than half of patients met criteria of chronic kidney disease. The prevalence of chronic obstructive pulmonary disease was 11.2%. Mean euroscore II was 5.7 ± 0.5. Significant aortic calcification was present in 52.8%. Previous EKG showed first or Mobitz I second degree atrialventricular block in 74.2% of the patients and 12.3% had complete right or left branch block. Corevalve Evolute was the prothesis chosen for most patients and femoral artery was the main vascular access for the procedure. Regarding the in-hospital outcomes, 44.9% of the patients had a haemorrhagic complication peri-procedure with need of blood transfusion. Vascular complications were found in 12.4% of the patients. About 19.1% of the patients had rhythmic abnormalities requiring definite pacemaker implantation. Although 13.5% of the patients presented acute kidney failure, only 2.2% needed dialyses. Acute stroke was diagnosed in 4.5% of the patients. Moderated to severe paravalvular regurgitation was found in 2.2% of the patients. Only 1 patient died in-hospital stay.
Conclusions: Although TAVI can improve long-term outcomes of selected patients, this procedure had risks. Most TAVI complications occurred in periprocedural period and more studies are needed to understand their rate in real-world. Anticipating complications, as well as their prompt detection and management, is crucial to limiting the potential consequences of these adverse events.

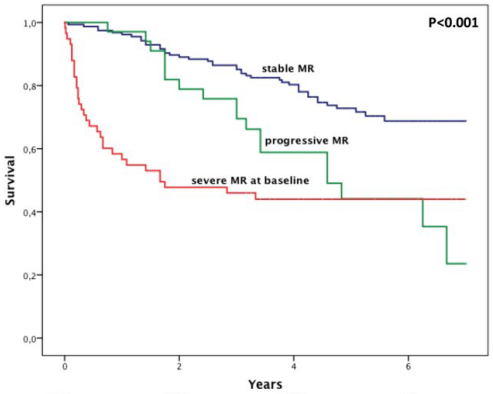
P514

Evolution of Functional Mitral Regurgitation

P E Philipp Emanuel Bartko[1]; N Pavo[1]; A Perez-Serradilla[1]; H Arfsten[1]; R Wurm[1]; I Lang[1]; G Strunk[1]; J Dal-Bianco[2]; R Levine[2]; M Huelsmann[1]; G Goliasch[1]
[1]*Medical University of Vienna, Department of Internal Medicine II, Division of Cardiology, Vienna, Austria*; [2]*Massachusetts General Hospital, Institute for Heart, Vascular and Stroke Care, Boston, United States of America*

Aims:Functional mitral regurgitation (FMR) drives adverse remodeling towards late heart failure stages. Little is known about the evolution of FMR under guideline-directed therapy and its relation to cardiac remodeling and outcome. We aimed to assess incidence, impact and predictors of progressive functional mitral regurgitation in patients under guideline-directed therapy.
Methods and Results: Of 249 patients with chronic heart failure and reduced ejection fraction receiving guideline-directed therapy 81% remained stable whereas 19% had progressive FMR. Those patients were more symptomatic(P < 0.001), had higher neurohumoral activation(various neurohumoral pathways in heart failure, all P < 0.05), larger left atria(P = 0.004) and more tricuspid regurgitation(P = 0.02). During a median follow up of 61 months(IQR50-72), 61patients died. Progression of FMR conveyed an increased risk of mortality - univariately(HR 2.33; 95%CI 1.34-4.08; P = 0.003), that persisted after multivariate adjustment using a bootstrap-selected confounder model(adj.HR 2.48; 95%CI 1.40-4.39; P = 0.002). Conclusions:Every fifth patient with chronic heart failure suffers from FMR progression. This entity is associated with a more than two-fold increased risk of death even after careful multivariable

adjustment. Symptomatic status, left atrial size, tricuspid regurgitation and neurohumoral pathways help to identify patients at risk for progressive FMR in an early disease process and open the possibility for closer follow-up and timely intervention.



Stable MR	157	138	108	34
Progressive MR	34	27	16	6
Severe MR at baseline	58	27	19	9

Kaplan Meier Estimates of Mortality

Myocardial Disease - Clinical

P515

Viral genome changes and the impact of viral genome

D Dalibor Mlejnek[1]; JK Krejci[1]; EO Ozabalova[1]; PH Hude[1]; VZ Zampachova[2]; IS Svobodova[2]; TF Freiberger[3]; RS Stepanova[3]; LS Spinarova[1]
[1]St. Anne's University Hospital, First Department of Internal Medicine - Cardioangiology, Brno, Czech Republic; *[2]St. Anne's University Hospital, First Department of Pathological Anatomy, Brno, Czech Republic*; *[3]Masaryk University, Brno, Czech Republic*

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Introduction: Viral infections are considered the most frequent cause of myocarditis and dilated cardiomyopathy (DCM).
Material and Methods: We investigated the changes in viral presence and the impact of viral genome persistence in myocardium on echocardiographic parameters, functional status and some laboratory parameters in a 6-month follow-up. Fifty-four patients with a recent onset DCM, left ventricular ejection fraction < 40% and biopsy-proven myocarditis (<14 mononuclear leukocytes/mm2 and/or >7 T-lymphocytes/mm2) were enrolled. Polymerase chain reaction was performed to detect pathogens in myocardium. Patients were divided according to the administered therapy: standard heart failure medication (46 patients) and immunosuppressive therapy (8 patients).
Results: In the standard heart failure medication group viral clearance was observed in 13 patients and viral persistence in 24 patients in the follow-up period. Comparing both groups, there was no statistically significant difference - LVEF improvement of 12.0 ± 11.4% vs. 18.3 ± 12.6%, decrease in NYHA class of 0.7 ± 0.7 vs. 1.0 ± 0.7, decline in NT-proBNP of 1335 ± 1933ng/l vs. 1942 ± 3242ng/l and decrease in infiltrating leukocytes of 11.1 ± 15.8 vs. 6.7 ± 23.0 cells/mm2 and T-lymphocytes of 5.8 ± 15.1 vs. 1.8 ± 10.9 cells/mm2 (all p = n.s.). A decrease in PCR positive patients from 37 to 29 was observed. The number of PVB19 positive PCR findings decreased from 5 to 4 in patients with immunosuppressive therapy.
Conclusions: A decrease in the number of positive PCR findings in control EMB was observed. Viral genome persistence was not associated with worse outcome in short-term follow-up.

P516

Iron deficiency relates to neurohormonal activation in acute myocarditis

P Pawel Franczuk[1]; K Kulej-Lyko[1]; M Drozd[1]; M Tkaczyszyn[1]; N Sidorowicz[2]; I Flinta[3]; P Gac[4]; W Banasiak[2]; P Ponikowski[1]; EA Jankowska[1]
[1]Wroclaw Medical University, Department of Heart Diseases, Wroclaw, Poland; *[2]Military Hospital, Cardiology Department, Centre for Heart Diseases, Wroclaw, Poland*; *[3]Wroclaw Medical University, Department of Physiology, Wroclaw, Poland*; *[4]Military Hospital, Department of Radiology and Diagnostic Imaging, Wroclaw, Poland*

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INTRODUCTION: Acute myocarditis (MCD) can progress to post-myocarditis non-ischaemic cardiomyopathy (CM). Immune response is considered the major pathomechanism of progressive myocarditis. Optimal iron status is essential for the functioning of immune cells, cardiomyocytes and cardiofibroblasts. Therefore, there are premises to consider iron metabolism as a significant modulator of complex pathophysiology of MCD.
Purpose: We investigated iron status in MCD and related it to the clinical characteristics of examined patients.
Methods: We prospectively recruited consecutive patients hospitalized for MCD in a tertiary referral cardiology center in 2015-2017. According to the European Society of Cardiology position statement, all subjects had comprehensive laboratory tests, transthoracic echocardiography, cardiac magnetic resonance, and coronary angiography or coronary computed tomography angiography. Iron deficiency (ID) was defined as serum ferritin < 100 μg/l or ferritin 100-299 μg/l with transferrin saturation (TSAT) < 20%.
Results: Study group comprised of 27 patients with confirmed MCD [age: 29 (25-34) years, men: 96%, left ventricular ejection fraction (LVEF): 58 ± 7%, and left ventricular global longitudinal strain (GLS): −18% ± 2%]. First measured C-reactive protein (CRP) was 55 ± 51 mg/l, N-terminal pro-B type natriuretic peptide (NT-proBNP) - 429 (184-1130) pg/ml, high sensitivity cardiac troponin I (hs-cTnI) - 5,8 (2,2-11,7) μg/l. ID was present in 8 patients (30%), serum ferritin was 305 ± 213 μg/l, transferrin saturation - 22 ± 9%, mean soluble transferrin receptor (sTfR) - 1,2 ± 0,3 mg/l. Ferritin < 100 μg/l was present in 4% patients, ferritin 100-299 μg/l - 59%, TSAT < 20% - 48%, mean reticulocyte hemoglobin content (CHR) < 28 pg - 19%. Only 1 patient during hospitalization developed anaemia (defined as hemoglobin < 12 g/dl in women and < 13 g/dl in men). Between patients with ID and without ID there were no differences in LVEF (56 ± 8 vs. 58 ± 7%), first measured CRP 42,5 ± 30,1 vs. 59,7 ± 57,3 mg/l) and first measured hs-cTnI - [7,9 (3,5-10,3) vs. 8,3 (4,0-17,3)] μg/l. However, patients with ID had higher NT-proBNP on admission than subjects without ID [983 (278-1734) pg/ml vs. 479 (141-542) pg/ml; p = 0,04]. Patients with TSAT < 20% had higher peak NT-proBNP [1130 (371-1504) pg/ml vs. 395 (261-542) pg/ml; p = 0,02]. All patients survived hospitalization and no subject needed left ventricular assist device (LVAD).
Conclusions: ID is present in 30% patients hospitalized for MCD and relates to indices of neurohormonal activation. Follow-up of these patients is needed to compare long-term outcomes (i.a. the development of CM) according to the presence of ID during hospitalization.

P517

Role of myocardial fibrosis in hypertrophic cardiomyopathy: A systematic review and updated meta-analysis of risk markers for sudden death

MI Marcelo Imbroinise Bittencourt[1]; SA Cader[1]; DV Araujo[1]; ALF Salles[1]; FN Albuquerque[1]; PPM Spineti[1]; DC Albuquerque[1]; R Mourilhe-Rocha[1]
[1]State University of Rio de Janeiro, Cardiology, Rio de Janeiro, Brazil

Background: Hypertrophic cardiomyopathy (HCM) is associated with sudden death (SD). Myocardial fibrosis is reportedly correlated with SD in these patients.
Purpose We performed a systematic review with meta-analysis, updating the risk markers (RMs) in HCM emphasizing myocardial fibrosis.
Methods: We reviewed HCM studies that addressed severe arrhythmic outcomes (SD, aborted SD, documented sustained ventricular tachycardia, or appropriate shock in patients with ICD) and the certain RMs: SD family history, severe ventricular hypertrophy, unexplained syncope, non-sustained ventricular tachycardia (NSVT) on 24-hour Holter monitoring, abnormal blood pressure response to exercise (ABPRE), and left ventricular outflow tract obstruction (LVOTO) in the MEDLINE, LILACS, and SciELO databases. We used relative risks (RRs) as an effect measure and random models for the analysis.
Results: Twenty-one studies were selected (14,901 patients aged 45 ± 16 years; men, 62.8%). Myocardial fibrosis was the major RM correlated with severe arrhythmic outcomes (RR, 3.43; 95% CI, 1.95-6.03). The other RMs, except for LVOTO, were also predictors: SD family history (RR, 1.75; 95% CI, 1.39-2.20), severe ventricular hypertrophy (RR, 1.86; 95% CI, 1.26-2.74), unexplained syncope (RR, 2.27; 95% CI, 1.69-3.07), NSVT (RR, 2.79; 95% CI, 2.29-3.41), and ABPRE (RR, 1.53; 95% CI, 1.12-2.08).
Conclusions: We confirmed the association of myocardial fibrosis and other RMs with severe arrhythmic outcomes in HCM and emphasize the need for new prediction models in managing these patients.

P518

BNP in patients with hypertrophic cardiomyopathy: results of a national registry

E Elisabete Bernardes[1]; A Lebreiro[2]; A Sousa[1]; S Leite[3]; C Sousa[2]; A Belo[4]; BY Hypertrophic Cardiomyopathy Registry Investigators[4]
[1]University of Porto, Faculty of Medicine, Porto, Portugal; *[2]Sao Joao Hospital, Cardiology, Porto, Portugal*; *[3]Hospital Guimaraes, Cardiology, Guimaraes, Portugal*; *[4]Centro Nacional de Coleção de Dados, Coimbra, Portugal*

Introduction: In hypertrophic cardiomyopathy (HCM), plasma levels of B-type natriuretic peptide (BNP) have been associated with different parameters of left ventricle remodeling and clinical outcomes. A major issue is to understand if the occasional measurement of BNP in HCM is more dependent of the morpho-functional disease parameters (due to ongoing slow progressive disease mechanisms) or are mostly related with the acute condition of the patient (such as transient higher intraventricular pressure) at the time of blood collection.
Objective: In this study, we sought to determine if BNP measured in an occasional blood sample maintains any correlation with clinical parameters and if the associations are affected by the body mass index (BMI) in HCM patients.
Methods: We analyzed data from the National Registry of adults with HCM. All the included patients have BNP measurements, and the highest concentration of BNP was the value considered for the associations with clinical variables.
Results: Among 247 HCM patients, 57% males, 94% had asymmetrical LV hypertrophy, 38% intraventricular gradient, 16% moderate-severe mitral insufficiency, 68% symptoms at first consultation and 24% BMI >30. BNP correlated with age at diagnosis ($r = 0,300$; $p = 0,000$), left atrium diameter ($r = 0,292$; $p = 0,000$) and volume ($r = 0,353$, $P = 0,003$), septum ($r = 0,172$; $p = 0,008$) and posterior wall thickness ($r = 0,177$; $p = 0,007$) and the number of hypertrophied segments ($r = 0,303$; $p = 0,009$). BNP was negatively correlated with body surface area ($r=-0,273$; $p = 0,000$) but not with BMI. BNP also didn't correlate with intraventricular gradient.
Conclusion: Our results reinforce the usefulness of BNP measurement as a marker of LV remodeling in HCM, particularly the parameters related to LV hypertrophy and left atrium dilatation. BMI seems to not significantly affect these associations.

P519

The impact of hypertension overlapping on hypertrophic cardiomyopathy

TCP Gil[1]; MB Castier[1]; AFP Gondar[1]; ALF Sales[1]; RM Rocha[1]
[1]State University of Rio de Janeiro (UERJ), FCM- Pedro Ernesto University Hospital , Rio de Janeiro, Brazil

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Background: The differential diagnosis between hypertensive heart disease and hypertrophic cardiomyopathy (HCM) in general is not dificult. But many patients with HCM have systemic arterial hypertension associated. Assessing the magnitude of this association is fundamental to prognosis.
Objective: Compare HCM patients with and without systemic arterial hypertension associated.
Methods: In a sectional study, 45 HCM patients were consecutively recruited from Pedro Ernesto University Hospital / State University of Rio de Janeiro (22 males, mean age 45 + 14 years). 14 of these had systemic arterial hypertension. The diagnosis of HCM was confirmed by magnetic resonance imaging. The echocardiographic transthoracic studies were performed (iE-33 Matrix, Philips), using QLAB software. The main parameters related to the differential diagnosis between these diseases were evaluated. Two-dimensional echocardiography assessed left ventricular outflow tract obstruction, diastolic function and myocardial deformation through the global longitudinal strain (GLS). Left atrial volume and left ventricular mass were analyzed by three-dimensional echocardiography. The statistical software package R (version 3.2.4) was used to compare the averages (t test).
Results: No significant difference was observed between the groups concerning gender, age and body surface area. The mean systolic and diastolic pressures were higher in the group of hypertensive patients ($p < 0.05$). No differences were observed between the groups in relation to left ventricular outflow obstruction, diastolic function, left ventricular mass and left atrial volume. GLS had lower mean values in hypertensive group ($p = 0.03$).
Conclusion: Although the mean blood pressures were higher in the group of hypertensive patients, no significant difference was observed between the groups in relation to ventricular mass, left atrial volume and diastolic function, parameters directly influenced by arterial hypertension. The mean lower GLS in hypertensive patients reflects a worse systolic function and may represent a factor of poor prognosis. Prospective studies are needed for a better evaluation.

P520

Predictors of ACEI/ ARB therapy in patients with hypertrophic cardiomyopathy: results of a national registry

E Elisabete Bernardes[1]; A Lebreiro[2]; C Sousa[2]; S Leite[3]; A Sousa[1]; A Belo[4]; BY Hypertrophic Cardiomyopathy Registry Investigators[4]
[1]University of Porto, Faculty of Medicine, Porto, Portugal; *[2]Sao Joao Hospital, Cardiology, Porto, Portugal*; *[3]Hospital Guimaraes, Cardiology, Guimaraes, Portugal*; *[4]Centro Nacional de Coleção de Dados, Coimbra, Portugal*

Introduction: Angiotensin-converting enzyme inhibitors (ACEI) and angiotensin II receptor blockers (ARB) are not considered disease-modifying drugs in hypertrophic cardiomyopathy (HCM) and their use is usually dependent on other clinical indications. Few data exist about the use of ACEI/ARB in HC in the real world, particularly in patients with intraventricular obstruction.
Objective: In this study, we sought to determine the frequency of ACEI / ARB therapy in patients with HCM and the predictors for their use.
Methods: We analyzed data of patients included in a large National Registry of adults with HCM and evaluated the associations of ACEI/ARB therapy with different clinical and echocardiographic variables.
Results: Among 1021 patients with HC, 397 (39%) were medicated with ACEI and/or ARB. Of these, the majority had hypertension (85%) and asymmetric left ventricular (LV) hypertrophy (86%), 38% had an intraventricular dynamic obstruction and 10% had LV systolic dysfunction. Symptoms of heart failure at first visit were present in 67% of those under ACEI/ARB and concomitant coronary heart disease was present in 9.2%. In multivariate analysis, the use of ACEI / ARB was associated with the presence of hypertension ($b= 4,44$; $P = 0,00$) and LV systolic dysfunction ($b = 1.86$; $p = 0.04$), and negatively related with intraventricular gradient ($b=-0,95$; $p = 0,02$) and abnormal blood pressure response in treadmill test ($b=-1,09$; $p = 0,04$).
Conclusion: Even in the absence of specific recommendations, ACEI / ARB are frequently used in patients with HCM, including in the presence of an intraventricular gradient, suggesting good tolerability. The main factors favoring their use in clinical practice are the coexistence of hypertension and LV systolic dysfunction.

P521

Beneficial effects of immunoadsorption in dilated cardiomyopathy patients revealed by meta-analysis

M Noutsias[1]; M Ali[1]; M Teren[1]; M Matiakis[1]; S Sakellaropoulos[1]; AG Rigopoulos[1]
[1]University Clinic Halle (Saale), Mid-German Heart Center, Department of Internal Medicine III (KIM-III), Division of Cardiology, Halle, Germany

Introduction: Humoral anticardiac autoimmunity is involved in the pathogenesis of dilated cardiomyopathy (DCM). Several anticardiac autoantibodies have been identified in DCM patients. Immunoadsorption (IA), aiming at elimination of autoantibodies, may be a promising immunomodulatory regimen in DCM.
Methods: Using standardized literature search modes, n = 100 publications referring to IA treatment in DCM patients were retrieved. Out of these, n = 18 publications prospective investigations with >8 DCM patients met the inclusion criteria of the meta-analysis, encompassing n = 528 DCM patients and n = 145 control patients.
Results: The demographic and clinical data of the n = 528 patients of the 18 included publications were as follows at baseline before IA: age: 51.5+3.1 years; men: n = 431 (81.6%); history of DCM: 51.4+20.8 months; LVEF: 25.6+4.6%; LVEDD: 69.8+3.2 mm. Histological analyses of endomyocardial biopsies (EMB) were available in n = 6 investigations / n = 84 patients, and were entirely negative for active myocarditis. In one study, IA was accompanied by a significant decrement of immunohistologically quantified intramyocardial infiltrates and HLA expression in DCM patients. Virological analyses of EMB were available in n = 6 publications / n = 292 patients, and viral genomes as detected by PCR were reported in n = 60 (20.5%) of these patients. After five courses of IA, the immunoglobulin levels decreased significantly from 10.7+0.8 to 1.1+0.5 g/l ($p < 0.0001$). Follow up analyses were carried out at a median of 4.5 months (interquartile range: 3-6 months). LVEF rose to 32.0+6.3% ($p = 0.0015$), and LVEDD decreased to 63.9+1.2 mm ($p = 0.0011$). NYHA functional class decreased from 2.9+0.4 to 1.9+0.2 ($p < 0.0001$). A significant decrease of indices of oxidative stress after IA was determined in DCM patients in one of the included studies. A substantial relative reduction of the 5-year mortality by 41% was reported in one prospective trial in IA treated DCM-patients compared to controls.
Conclusions: This meta-analysis on n = 528 DCM patients under IA, which reduces significantly immunoglobulin levels, summarizes several beneficial clinical effects: Significant improvement of LVEF, of NYHA functional class, and decrement of LVEDD. Further, reduction of intramyocardial inflammation and of oxidative stress, as well as reduction of mortality were published in some investigations. These results may be prone to general error sources underlying meta-analyses (e.g. publication and selection bias). A multi-center, randomized IA trial is warranted to foster the

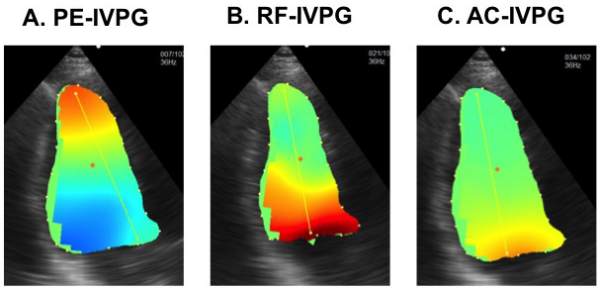
evidence on the clinical and prognostic benefits of IA in DCM, and to furthermore elucidate the profiles of "responders" versus "non-responders".

P522

Noninvasive assessment of intra-ventricular pressure gradients estimated by vector flow mapping in patients with dilated cardiomyopathy

T Hozumi[1]; Y Nozawa[1]; T Nishi[1]; K Takemoto[1]; S Ota[1]; M Kashiwagi[1]; K Shimamura[1]; A Kuroi[1]; T Kameyama[1]; Y Matsuo[1]; Y Ino[1]; H Kitabata[1]; T Kubo[1]; A Tanaka[1]; T Akasaka[1]
[1]*Wakayama Medical University, Cardiology, Wakayama, Japan*

Background: Previous studies have reported that there are intraventricular pressure gradients (IVPG) between left ventricular (LV) base and apex during diastole and between LV apex and outflow tract during systole using invasive catheter method and noninvasive color M-mode echocardiography. However, IVPG has not been widely measured in the clinical practice because it requires invasive process or non-commercially available software. Recent introduction of vector flow mapping (VFM) using combination of color Doppler and tissue Doppler echocardiography provides noninvasive assessment of IVPG which may be used as additional index for LV function in patients with dilated cardiomyopathy (DCM).
Purpose: To examine characteristics in IVPG assessed by VFM in patients with DCM compared with healthy subjects with preserved EF.
Methods: The study population consists of 45 subjects; 27 subjects with DCM (Group-D, EF: 32 ± 8%), 18 healthy subjects with preserved EF (Group-C, EF: 63 ± 3%). Patients with segmental wall motion abnormalities, significant valvular diseases, and arrhythmia were not included in this study population. Apical long-axis views were recorded by color Doppler echocardiography(Prosound F 75 and a10, Hitachi, Japan. Peak IVPG between apex and LV outflow tract during pre-ejection period (PE-IVPG, figure A), peak IVPG between mitral annulus and apex during rapid filling period (RF-IVPG, figure B), and atrial contraction period (AC-IVPG, figure C) were assessed using commercially available VFM analysis software (DAS-RS1, Hitachi).



IVPG measurement by VFM

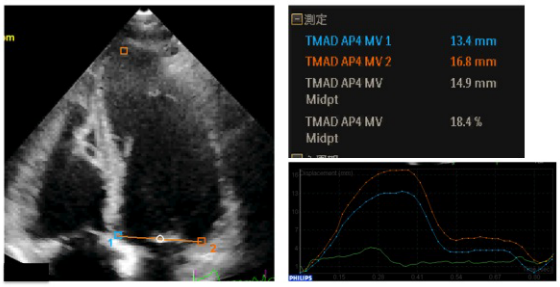
Results: 1) PE-IVPG in Group-D was significantly lower than that in Group-C (0.95 ± 0.56 vs 1.34 ± 0.48 mmHg, $p < 0.05$).
2) RF-IVPG in Group-D was significantly lower compared with that in Group-C (0.65 ± 0.37 vs 2.33 ± 1.11 mmHg, $p < 0.01$).
3) AC-IVPG in Group-D was significantly lower compared with that in Group-C (0.62 ± 0.43 vs 0.89 ± 0.30 mmHg, $p < 0.05$).
Conclusions: VFM analysis showed that IVPG during pre-ejection, rapid filling, and atrial contraction period were lower in patients with DCM compared with healthy subjects with preserved EF. The present results suggest that noninvasive IVPG estimated by VFM can be used as additional index for LV function in patients with DCM.

P523

Noninvasive assessment of left ventricular longitudinal systolic dysfunction in patients with dilated cardiomyopathy by speckle-tracking echocardiographic mitral annular displacement

T Hozumi[1]; K Terada[1]; T Nishi[1]; K Takemoto[1]; S Ota[1]; M Kashiwagi[1]; K Shimamura[1]; A Kuroi[1]; T Kameyama[1]; Y Matsuo[1]; Y Ino[1]; H Kitabata[1]; T Kubo[1]; A Tanaka[1]; T Akasaka[1]
[1]*Wakayama Medical University, Cardiology, Wakayama, Japan*

Background: Severely decreased left ventricular (LV) global longitudinal strain (GLS) obtained from 3 apical echocardiographic views has been reported to be a prognostic index in patients with reduced LV ejection fraction (EF) including dilated cardiomyopathy (DCM). Mitral annular displacement by speckle-tracking echocardiography (TMAD) from single 4-chamber view provides quick assessment of LV longitudinal systolic dysfunction in patients with preserved EF. However, it remains whether this simple index can be used as an alternative index to GLS in patients with DCM.
Purpose: To evaluate whether TMAD from single view can be used for the assessment of LV longitudinal systolic dysfunction alternative to GLS in patients with DCM.
Methods: The study population consists of 39 patients with DCM (Group-D, age: 60 ± 12 years, EF: 31 ± 5%) and 22 patients without cardiac diseases (Group-C, age: 64 ± 13 years, EF: 62 ± 3%) in whom GLS was successfully assessed from apical 4-chamber, 2-chamber, and long-axis view (EPIQ, Philips Medical systems). TMAD was quickly assessed as the base-to-apex displacement of mid-point mitral annular line in 4-chamber view by setting ROI in septal and lateral mitral annuls and apex with QLAB software (Philips Medical systems). The percentage of TMAD to LV length from the mid-point of mitral annuls to the apex at end-diastole (% TMAD) was automatically calculated.
Results: Both GLS and %TMAD in Group-D was significantly smaller than those in Group-C (|GLS|: 11.1 ± 2.7 vs 21.3 ± 2.3%, $p < 0.001$, %TMAD: 7.2 ± 2.6 vs 15.2 ± 3.3 %, $p < 0.001$). Group-D was divided into two groups; 16 patients with |GLS| < 10.0% (Group-Da) and 23 patients with |GLS|>10.0% (Group-Db). %TMAD was significantly lower in Group-Da compared with Group-Db (5.1 ± 1.1 vs 8.8 ± 2.2, $p < 0.001$). A cut-off value of %TMAD < 6.4 had a sensitivity of 94% and specificity of 91% for the presence of severely decreased LV longitudinal systolic function.
Conclusions: TMAD rapidly estimated by speckle-tracking echocardiography was useful for the assessment of severely decreased LV longitudinal systolic function in patients with DCM. TMAD can be used as the prognostic index alternative to GLS in patients with DCM.



P524

The prevalence and prognostic significance of right ventricular involvement evaluated by cardiac magnetic resonance in nonischemic dilated cardiomyopathy

AR Ana Rita Pereira[1]; AR Almeida[1]; I Cruz[1]; A Marques[1]; S Alegria[1]; AC Gomes[1]; D Sebaiti[1]; A Briosa[1]; LR Lopes[2]; M Ramalho[3]; H Pereira[1]
[1]*Hospital Garcia de Orta, Cardiology, Almada, Portugal*; [2]*Barts Health NHS Trust, Cardiology, London, United Kingdom*; [3]*Hospital Garcia de Orta, Radiology, Almada, Portugal*

Introduction: Cardiac magnetic resonance (CMR) is the gold-standard technique for the assessment of ventricular structure and function. Left ventricular (LV) volumes and ejection fraction (LVEF), as well as, late enhancement gadolinium (LGE) are strong predictors of outcome in nonischemic dilated cardiomyopathy (DCM). Nevertheless, there are limited data regarding the prognostic significance of right ventricular involvement in this patients (pts).
Purpose: To evaluate the prevalence and prognostic value of the right ventricular (RV) involvement in pts with DCM.
Methods: Retrospective unicenter study that included the pts followed for DCM with LVEF < 40% at the time of diagnosis and submitted to CMR to complete the diagnostic evaluation. The DCM diagnosis was established by the presence of LV dilation in the absence of uncontrolled arterial hypertension, hypertrophic or restrictive cardiomyopathy, significant valvular or coronary disease. The primary endpoint (PE) was a composite endpoint of all-cause mortality, ventricular arrhythmias (VA) with hemodynamic instability and unplanned heart failure (HF) admission. Secondary endpoint (SE) was LVEF recovery (= 50%).
Results: Forty-nine pts were included: 30 (61,2%) male; mean age 54 ± 12 years. At the time of diagnosis, 30 (61,2%) pts were in NYHA functional class = III with a median NT-proBNP value of 2451 pg/mL [interquartile range (IQR) 2233 pg/mL]. Initial LVEF, measured by transthoracic echocardiogram, was 25 ± 8%. The mean values of RV parameters obtained by CMR were: RV end-diastolic volume (RVEDV) 89 ± 34 ml/m^2, RV end-systolic volume (RVESV) 55 ± 36 ml/m^2 and RV ejection fraction (RVEF) 41 ± 18%. Twelve (22,2%) pts had RV dilation, 21 (38,9%) RV systolic

dysfunction (RVSD) and 2 (3,7%) LGE in the RV free wall. At a median follow-up (FU) of 26 months (IQR 51 months), there were 22 primary events: 5 deaths, 3 AV with hemodynamic instability and 14 unplanned HF admissions. Seventeen (34,7%) pts recovered LVEF. A significantly higher number of PE events were observed in pts with RVSD [4 pts (19%) with preserved RVEF vs 14 pts (50%) with depressed RVEF, p = 0,04]. As expected, pts who have experienced primary adverse events had a significantly lower mean of RVEF (34 ± 17% vs 45 ± 18%, p = 0,04). However, no significant difference was found between RVEF and time until PE occurrence (log rank 0,17; p = 0,68). We did not also found a significant correlation between RVEF and LVEF (p = 0,69), as well as, an association between primary adverse events and RVEDV (p = 0, 17), RVESV (p = 0,13) and LGE in the RV free wall (p = 0,99). No RV structural and functional parameters were associated with SE occurrence.
Conclusions: In this study, RVSD was associated with medium to long term adverse events in pts with DCM. These results support a potential role of CMR assessment of RV function in the evaluation and risk stratification of DCM pts but not as a predictor of LVEF recovery.

P525
Influence of atrial fibrillation on clinical status and parameters of hemodynamics in dilated cardiomyopathy patients

MF Salikhova[1]; TA Abdullaev[1]; I A Igor Tsoy[1]; YR Akhmatov[1]
[1]Specialized Cardiology Center of the Republic of Uzbekistan, heart failure , Tashkent, Uzbekistan

The aim: Evaluation of parameters of hemodynamics in dilated cardiomyopathy (DCM) pts complicated by atrial fibrillation (AF).
Material and Methods: The study includes 35 DCM pts (27 male and 8 female) with the newly discovered AF which diagnosed during initial application to clinic. Depending on the rhythm there were formed: gr I with 16 pts (average age of 44,8 ± 2,4 years) who were treated by pharmacological (amiodarone) cardioversion with restoration of sinus rhythm (SR) with optimal background therapy of chronic heart failure. Second gr was formed by 19 pts (average age of 53,2 ± 1,8 years) whose rhythm had not restored. Evaluation of EKG and EchoCG parameters was done. Median of observation comprised 22,5 months. Average functional class of HF in 1st gr comprised 3,1 ± 0,22 and in 2nd gr– 2,9 ± 0,58 (?>0.05).
Results: Analysis of clinic status of pts revealed improvement of indices comparing to control period. Thus, average functional class of HF at 1st gr decreased up to 2,5 ± 0,11 and 2,5 ± 0,13 in 2nd gr (both ? <0,05), whereas results of 6-minute walking test (6MWT) increased on 47,8% in 1st gr and 33,4% in 2nd gr. (both ? <0,05). After SR recovering in 1st gr we observed an increase of systolic arterial pressure on 12,6 mm Hg (? <0,05), whereas 2nd gr had this parameter unchanged. As for heart rate 1st gr had positive dynamics; lowering of heart rate on 18,5 bpm (p <0,05), 2nd gr– on 5,3 bpm (p>0,05). Analysing EKG-indices there were revealed an extension of interval QTc on 13,7% at pts after SR recovering (? <0,05) with unchanged parameters of QRS duration in both grs. SR recovering at 1st gr was accompanied by decrease of volume of left atrial on 7,3%, EDV LV - on 6,8%, ESV LV – on 18,5% (all ?>0.05) with respective increase of LVEF on 9,4% (p <0,05). 2nd gr did not show significant dynamics of EchoKG-parameters (??? ?>0,05). Analysis of EchoKG-parameters of right heart departments in 1st gr revealed regression of volume of right ventricle on 6,5% (?>0,05), whereas these parameters of 2nd g remained on the same level.
Conclusion: For DCMP pts complicated by atrial fibrillation - during long-time observation the recovering of sinus rhythm contributes to improvement of general clinic status of such category of pts that shows not only as regress of heart failure appearance but also as positive dynamics from EchoKG-parameters.

P526
Dilatative cardiomyopathy and atrial fibrillation

O Ovidiu Tica[1]; OA Tica[2]
[1]University of Medicine of Oradea, Morphological Department, Oradea, Romania; *[2]University of Medicine of Oradea, Cardiology Department, Oradea, Romania*

Introduction: Atrial fibrillation(AF) is a common arrhythmia in patients with dilated cardiomyopathy(DCM). AF presence in patients with DCM influences the long term evolution
Aim: To assess and to quantify if AF is a predictive factor for DCM patients and how it influence the prognosis and mortality of these patients.
Method: We conducted a retrospective study among adult patients, who had a clinical diagnosis of DCM and AF. We included 253 patients admitted consecutively in our clinic between January 2013 and December 2014 diagnosed with dilated cardiomyopathy and atrial fibrillation divided according to etiology in non-ischemic and ischemic. Blood test, clinical examination, ECG, and echocardiography was performed. Patients were followed for 2.3 years. They were divided into 2 groups according to the DCM etiology: non-ischemic and ischemic.
Results: In our study AF was identified in the non-ischemic DCM group in 10.67% as paroxystic AF, in 11.46% as persistent AF, 13.04% as long standing persistent and in 12.25% as permanent AF. In the ischemic DCM group, 7.51% of patients have paroxystic AF, 9.48% have persistent AF; 11.06 % have long standing persistent, 10.27% have permanent AF. NYHA class >3, left ventricular ejection fraction < 35%, presence of mitral regurgitation greater than grade 2, QRS duration = 110ms, LV end-diastolic diameter >63mm were ominous signs, and patients with al lest one of these this factors have a poor prognosis. Overall mortality, was influenced by the presence of AF(p = 0.002).
Conclusions: AF turned out to be a condition that can contribute to lower quality of life and heart failure worsening, influencing the patients prognosis and mortality.

P527
Rationale and design for the Peripartum Cardiomyopathy in Nigeria (PEACE) registry, and results for cardiac function in pregnancy sub-study

KM Karaye[1]; IY Mohammed[1]; H Sa'idu[2]; NA Ishaq[3]; SA Balarabe[4]; J Tukur[1]; TA Adedeji[5]; ON Makinde[6]; RA Adebayo[7]
[1]Bayero University/Aminu Kano Teaching Hospital, Kano, Nigeria; *[2]Bayero University, Medicine, Kano, Nigeria*; *[3]Aminu Kano Teaching Hospital, Medicine, Kano, Nigeria*; *[4]Mohammed Abdullahi Wase Specialist Hospital, Medicine, Kano, Nigeria*; *[5]Obafemi Awolowo University Teaching Hospital, Chemical Pathology, Ile Ife, Nigeria*; *[6]Obafemi Awolowo University Teaching Hospital, Obstetrics and Gynaecology, Ile Ife, Nigeria*; *[7]Obafemi Awolowo University Teaching Hospital, Ile Ife, Nigeria*

On behalf of: Peripartum Cardiomyopathy in Nigeria (PEACE) Registry
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Background: Nigeria probably has the highest burden of Peripartum Cardiomyopathy (PPCM) in the world. However, much of the epidemiology of the disease is yet to be described in a comprehensive national study. In addition, the relationship between selenium deficiency and PPCM seems to be relevant in the Sahel regions of Africa, and if proven, could potentially lead to a cure of the disease. Finally, the data on cardiac function in pregnancy in Nigeria is limited, and its relationship with selenium deficiency has not yet been described.
Purpose: To primarily describe the burden, ventricular remodelling and survival of PPCM in Nigeria. In the sub-studies, we aimed to describe the relationship between selenium deficiency, oxidative stress and PPCM, the impact of sodium selenite supplementation on left ventricular reverse remodelling, change in New York Heart Association functional class and survival in PPCM, and the prevalence of selenium deficiency and its relationship with cardiac function in apparently healthy pregnant women.
Methods: The main Registry and the first sub-study are prospective longitudinal studies, while the second sub-study is an open-label randomised trial. 20 study centres across Nigeria have been recruiting PPCM subjects for the main registry; from June to December 2017 in most centres, but till 31st March 2018 for the late-starters, while the sub-studies are going on in 4 centres in 2 cities. PPCM subjects will be followed up for at least 1 year. Serum selenium and glutathione peroxidise (GPO) is being assayed at recruitment for consecutive PPCM patients with left ventricular ejection fraction <45% at 6 months postpartum. 200 subjects with selenium deficiency are being randomised into treatment (Selenium Selenite 200μg tablets daily for 3 months) and control arms. In the second sub-study, 120 apparently healthy pregnant women have been recruited at 28-38 weeks of gestation and are being reviewed at 6-8 weeks postpartum, and their serum selenium and GPO levels were measured at recruitment.
Results: A total of 131 apparently healthy pregnant women with a mean age of 29.6 ± 5.3 years, and 270 PPCM patients with a mean age of 28.3 ± 7.2 years have thus far been recruited (censored on 10th January 2018). The sub-study on apparently healthy pregnant women will be completed in March 2018 and the results could be presented at the HFA Congress in May 2018.
Conclusion: This is the largest systematic evaluation of PPCM in Nigeria, and it is hoped that the information will assist in developing locally applicable treatment guidelines and policies for the disease. (ClinicalTrials.gov Identifier: NCT03081949)

P528
Characterization of a population with Left Ventricle Non Compaction - a Multicentric Study

J Joao Pedro De Sousa Bispo[1]; H Antunes[2]; N Marques[1]; N Craveiro[3]; L Reis[4]; R Guerreiro[5]; R Santos[6]; O Azevedo[7]
[1]Faro Hospital, Cardiology, Faro, Portugal; *[2]Hospital Sao Teotonio, Viseu, Portugal*; *[3]Hospital of Santarem, Cardiology, Santarem, Portugal*; *[4]University Hospitals of Coimbra, Cardiology, Coimbra, Portugal*; *[5]Hospital Espirito Santo de Evora, Evora, Portugal*; *[6]Hospital Centre do Tamega e Sousa, Penafiel, Portugal*; *[7]Alto Ave Hospital Center, Guimaraes, Portugal*

On behalf of: Grupo Sunshine

Introduction: Left Ventricle Non-Compaction (LVNC) is a cardiomyopathy in which the left ventricular walls are non-compacted with deep trabeculations. It has an

estimated prevalence of 0,014 a 1,3%. Patients can present from asymptomatic to advanced heart failure (HF), arrhythmias, and systemic embolism (SE).
Objective: To characterize a population of patients with LVNC
Methods: A data base of LVNC patients that were followed as outpatients in 12 public hospitals between January of 2007 and December of 2017 was created. We conducted a retrospective and descriptive analysis of the baseline characteristics, form of presentation, diagnostic methods and genetic testing **Results: Results:** 120 patients were included in the study, 70 (58,3%) were male, average age of 46,79 ± 18,1 years, 114 (95%) caucasians. Family history of LVNC was present in 21 (17,5%) cases. Most common form of presentation was asymptomatic in 42 (35%) cases, HF in 39 (32,5%) - with 11 (9,2%) patients in NYHA III or IV - and arrhythmia in 17 (14,2%). The diagnosis was made by echocardiogram (TTE) in 70 (58,3%) patients and by magnetic resonance imaging (MRI) in 50 (41,7%). The most frequently present TTE diagnostic criteria were the Jenni criteria, present in 85 patients (70,8%). 61 (50,8%) patients also had significant valve disease, most frequently in the mitral valve (in 57 cases) and tricuspid (in 39 cases). Average ejection fraction was 47,9 ± 15,7%. On MRI 18 (70,8%) patients had late gadolinium enhancement. On the 12 lead ECG, 106 (88,3%) patients were in sinus rhythm, 11 (9,2%) in atrial fibrillation, and 2 (1,7%) in atrial flutter. 15 (12,5%) had left bundle branch block, and 4 (3,3%) had right bundle brunch block. 24h Holter monitoring was performed in 101 (84,2%) patients, and 3 (2,5%) patients had periods with 2nd degree AV block, 3 (2,5%) had periods of 3rd degree AV block, 21 (17,5%) had periods of supraventricular tachycardia, 23 (19,2%) periods of ventricular tachycardia, but only 1 (0,8%) of these casas was sustained. Genetic study was performed in 43 (35,8%) patients, and mutations were found in the MYH7 gene in 3 (2,5%) patients, in the MYBPC3 in 6 (5,0%) and the TNNT2 in 1 (0,8%). Follow-up was 3,54 ± 2,67 years, and during that time a total of 6 (5,0%) patients died (3 for advanced HF, 1 for sudden death, 3 with non-cardiovascular causes), 9 (7,5%) had stroke, and 1 (0,8%) had MI. 55 (45,8%) had HF (16 more patients than at presentation).
Conclusion: LVNC remains a poorly understood cardiomyopathy, without specific treatment. In our population, the most frequent complications were HF, arrhythmias and SE events. In our study, we also had a relatively high prevalence of significant valve disease, mostly mitral. The genetic etiology of LVNC remains understudied. Several genes have been implicated. In our population, the number of mutated genes was relatively low, which may mean that there may be other affected genes that have yet to be identified.

P529

Myocardial infarction (necrosis) as a typical manifestation of noncompact cardiomyopathy

O V Olga Blagova[1]; NV Varionchik[1]; EV Pavlenko[1]; AV Nedostup[1]; EA Kogan[1]; VP Sedov[1]; NV Gagarina[1]; EA Mershina[2]; VE Sinitsyn[2]
[1]I.M.Sechenov I Moscow State Medical University, Moscow, Russian Federation; *[2]Roszdrav Medical Rehabilitation Center, Moscow, Russian Federation*

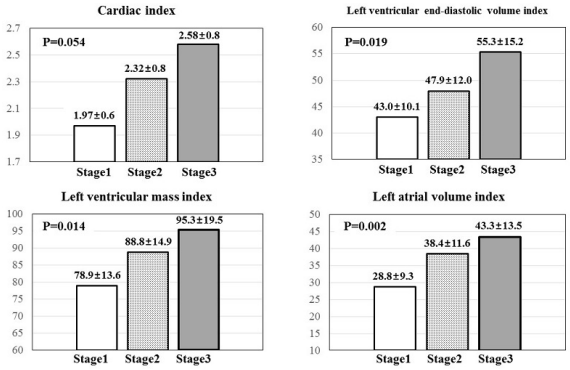
Purpose: To study the incidence of acute myocardial infarction (MI) in patients with noncompact myocardium (NCM) and its possible specific mechanisms, influence on the prognosis and means of prevention.
Methods: We observed 85 adult patients with NCM. The study included 10 patients (7 men, mean age 46.3 ± 15.8 years) who developed acute MI. The diagnosis of NCM is established according to the current visual criteria (using Eco-CG, MRI in 5 patients and cardiac CT in 7 patients). Mean follow-up was 10,5 [1,75; 32,25] months. In all patients were performed the anti-heart antibodies and virus genome investigation and coronary visualization (7 coronary angiography, 7 CT). Additionally were performed the troponin measurement (n = 7), morphological study of the myocardium (n = 6), myocardial scintigraphy with 99mTc (n = 6) and DNA diagnosis.
Results: In 4 of the 10 patients MI was the first manifestation of the NCM. The clinical picture of MI was presented typical angina with dyspnea (50%), isolated asthma (10%) and ventricular arrhythmias (sustained ventricular tachycardia, fibrillation, sudden death, 40%). Stable angina was observed in only 2 patients (with intact coronary arteries). In two patients with MI in the debut of the disease was detected pathogenic mutation in the gene MyBPC3. They were identified four mechanisms of MI, which can be combined. 1. Thromboembolism in the coronary arteries from the left chambers of the heart (verified at autopsy in one patient and can be assumed in 5 patients). 2. Accession of myocarditis with the development of vasculitis, focal necrosis in ischemic myocardium (6 patients, morphologically verified myocarditis in 2 patients, viral genome in the blood or myocardium in 3 patients). 3. Severe coronary atherosclerosis (2 patients). 4 The sharp deterioration of blood flow of a non-compact layer in the presence of low cardiac output (more than half of the patients). Risk factors for MI were intracardiac thrombosis, low ejection fraction, atrial fibrillation, the combination of NCM with hypertrophic cardiomyopathy (in two patients).
Conclusions: Myocardial infarction (necrosis) is a typical manifestation of NCM (in 11.8%). The MI with intact coronary arteries requires the exclusion of NCM. The main mechanisms of MI in NCM are thromboembolism, myocarditis, disturbances of microcirculation under the NCM, and coronary atherosclerosis. MI is a life-threatening complication of NCM leading to a severe worsening of the initial heart failure and ventricular arrhythmias. Mortality among patients with MI was 20%. As a means for MI prevention must considered the appointment of anticoagulant therapy at least in patients with atrial fibrillation and systolic dysfunction, as well as the timely diagnosis and treatment of myocarditis.

P530

Liver cirrhosis related changes in cardiac function and structure, beyond diastolic dysfunction.

MN Mi-Na Kim[1]; TH Kim[1]; YS Seo[1]; SM Park[1]; SH Um[1]; WJ Shim[1]
[1]Korea university anam hospital, Seoul, Korea Republic of

Background: Patients with liver cirrhosis (LC) could develop a progressive impairment of cardiac function and change of cardiovascular structure in their disease course. These changes are related with worsen clinical manifestation and poorer prognosis. But cirrhotic cardiomyopathy might be difficult to determine due to the complex and muddled diagnostic criteria. The aim of this study was to evaluate cardiac structural and functional changes according to disease severity in patients with LC.
Methods: 74 patients (F/M = 17/57, 54.9 ± 10.2yrs) who was newly diagnosed LC were included. In each patient, the model for end-stage liver disease (MELD)



score was calculated for assessment of severity of LC and the stage of LC was evaluated by the presence of varix or ascites (Stage1: compensated patients without varix and ascites, Stage2: Compensated patients with varix and without ascites, Stage3: Decompensated patients with ascites). Cardiac structure and function were assessed by trans-thoracic echocardiography.
Results: Among 74 patients, stage 3 was present in 39 patients (6%) and 22 patients (14.9%) were belonged to stage 2. The mean age and presences of diabetes, hypertension and coronary artery disease were not different between the groups. The MELD score was gradually increased, according to raising the stage of LC. (Stage1: 11.3 ± 6.2, Stage2: 13.9 ± 7.3 and Stage3: 16.3 ± 6.3, P = 0.05)
Cardiac index (CI) had a trend to be progressively increased from Stage1 to Stage3 (1.97 ± 0.6, 2.32 ± 0.8 and 2.58 ± 0.8, P = 0.054). Left ventricular (LV) volume and mass index were increased from Stage1 to Stage3. Left atrial volume index was also increased (Figure). But LV ejection fraction, global longitudinal strain (GLS) and diastolic functional parameters, including E of E prime, were not different between the groups. In the evaluation of relations between MELD score and cardiac functional and structural parameters, GLS as well as CI was independently related with MELD score by multivariate analysis. (OR = 2.24, P = 0.03 and OR = 3.73, P <0.001, respectively).
Conclusion: In advanced stage of cirrhotic patients, the cardiac output was increased and LV was larger and thicker. The hepatic function was independently associated with cardiac output and LV myocardial mechanics. To evaluate diastolic dysfunction might be limited in these high cardiac output stated LC patients. From these, a subtle change of ventricular tissue mechanics would be one of precursors of cirrhotic cardiomyopathy. A new definition of cirrhotic cardiomyopathy might be needed.

Pulmonary Circulation, Pulmonary Embolism, Right Heart Failure - Clinical

P531

The product of TRPG and Pulmonary artery diameter/Aortic diameter is a useful screening parameter for detecting pulmonary hypertension in systemic sclerosis patients

Y Yoshiyuki Orihara[1]; M Asakura[1]; A Eguchi[1]; T Ando[1]; Y Okuhara[1]; M Ishihara[1]; T Masuyama[1]
[1]*Hyogo College of Medicine, Cardiovascular Division, Nishinomiya, Japan*

Background: Systemic sclerosis (SSc) is a connective tissue disease characterized by inflammation and fibrosis of the skin and certain internal organs, and vascular injury due to autoimmunity. Compared with SSc patients without pulmonary arterial hypertension (PAH), poor survival rate in SSc patients with PAH was revealed. Accurate assessment of PAH is important for the management of patients with SSc. However, tricuspid regurgitate jet pressure gradient (TRPG), an echocardiographic parameter commonly used for estimating PAH, does not always reflect accurate invasive pressures in all patients. Several reports showed that a ratio of diameter of pulmonary artery to ascending aorta (rPA) calculated by computed tomography (CT) were correlated with severity of pulmonary hypertension. Neither TRPG nor rPA does not reach a satisfactory level to assess the degree of PAH in SSc patients. We hypothesized that the product of TRPG and rPA (pTRPA) would be a novel parameter to estimate the severity of PH accurately in SSc patients.
Purpose: the purpose of this study was to determine whether pTRPA was a useful parameter for detecting PH in SSc patients.
Methods: Thirty six SSc patients who visited our hospital and presented tricuspid regurgitation jet velocity = 2.5 m/s were enrolled in this study. All patients performed echocardiography, chest CT and right heart catherization. PAH was defined as mean pulmonary arterial pressure (mPAP) = 25mmHg and mean pulmonary arterial wedge pressure (mPAWP) = 15mmHg. We measured both a widest pulmonary artery diameter and an adjacent ascending aorta diameter at the same level of the bifurcation of the main pulmonary artery using CT images.
Results: Mean age was 64.2 years old and 29 patients were female. Echocardiography showed mean TRPG was 35.1 mmHg and average left ventricular ejection fraction were 71.0%. Average mPAP and mPAWP were 24.7 mmHg and 10.1 mmHg, respectively. Average pulmonary artery diameter and ascending aorta diameter were 31.6mm and 30.1mm, respectively. Mean rPA were 1.06 and mean pTRPA were 37.9. Mean PAP was well correlated with TRPG ($r = 0.734$, $p < 0.001$), rPA ($r = 0.584$, $p < 0.001$), pTRPA ($r = 0.848$, $p < 0.001$), respectively. Among three parameters, the highest area under the curve by receiver operating characteristic (ROC) analysis to predict mPAP = 25mmHg was found for pTRPA with area of 0.917. In addition, ROC in pTRPA showed sensitivity was 0.933 and best cutoff value was 33.1. When SSc patients in this cohort is divided into two groups according to this best cutoff value, positive predictive value was 0.74 and negative predictive value was 0.93.
Conclusion: The product of TRPG and pulmonary artery diameter/Aortic diameter may be a potential, useful, and nonivasive parameter for detecting the severity of PH in patients with SSc.

P532

Pulmonary Vascular Distensibility In Pulmonary Hypertension Due To Left Heart Disease

C Christian Gerges[1]; M Gerges[1]; IM Lang[1]
[1]*Medical University of Vienna, Department of Internal Medicine II, Division of Cardiology, Vienna, Austria*

Background: The diameter of healthy pulmonary vessels increases by 2% per mmHg of transmural pressure. A model of the pulmonary circulation incorporating the coefficient of distensiblity (a, percentage change in diameter per mmHg increase in distending pressure) can be used to describe this behavior. In patients with pulmonary vascular disease a is reduced to 0.25%/mmHg. We sought to describe loss vascular distensibility in patients with pulmonary hypertension (PH) due to left heart disease (LHD).
Methods: Distensibility a was estimated in 119 patients using following formula:
mPAP = [(1 + a*PAWP)5 + 5a*PVR*CO] 1/5 - 1] / a
(mPAP = mean pulmonary artery pressure; PAWP = pulmonary arterial wedge pressure; PVR = pulmonary vascular resistance; CO = cardiac output)
Distensible properties in combined pre- and post-capillary PH (Cpc-PH, n = 30) were compared with isolated post-capillary PH (Ipc-PH; n = 30) and patients with idiopathic pulmonary arterial hypertension (iPAH, n = 29). Subjects with normal pulmonary hemodynamics (n = 30) served as controls.
Results: Distensibility a was lowest in iPAH, intermediate in PH-LHD and preserved in controls (0.23 ± 0.12%/mmHg vs. 0.63 ± 0.23%/mmHg vs. 2.3 ± 1.2%/mmHg, $p < 0.001$). Despite higher mPAWP in Ipc-PH (31.2 ± 7.2mmHg) than in Cpc-PH (25.4 ± 4.9mmHg, $p = 0.001$), distensibility a was lower in Cpc-PH (0.53 ± 0.21%/mmHg) than in Ipc-PH (0.74 ± 0.20%/mmHg, $p < 0.0001$). Distensibility a was significantly correlated with DPG ($r=-0.64$; $p < 0.001$) and PVR ($r=-0.74$; $p < 0.001$) in patients with PH-LHD.
Conclusion: Distensibility of pulmonary vessels is impaired in PH-LHD, and worst in iPAH. Despite similar or even higher mPAWP in Ipc-PH, pulmonary vessels are less distensible in Cpc-PH, presumably because of pulmonary vascular remodeling.

P533

Insulin resistance in pulmonary hypertension

N Naderi[1]; S Taghavi[1]; A Amin[1]; Z Ghaemmaghami[1]; M Nouri[1]; M M Ansari-Ramandi[1]; A Zavarei[1]
[1]*Rajaie Cardiovascular Medical and Research Center,Iran University of Medical Sciences, Tehran, Iran (Islamic Republic of)*

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Introduction: The relationship of glucose intolerance and insulin resistance (IR) with pulmonary hypertension (PH) has been suggested . In present study we measured insulin level in patients with pulmonary hypertension without history of diabetes mellitus(DM) or glucose intolerance.
Methods: Fifty-nine patients with Pulmonary hypertension in accordance with updated clinical classification of pulmonary hypertension were enrolled.Demographic ,functional ,laboratory and hemodynamic data were obtained. The homeostasis model assessment of insulin resistance (HOMA-IR) was used to assess IR.
Results: Regarding the PH classification 47.5% of them had class I of PH, 28.8% class II,5.1% class III,16.9% class IV and 1.7 % class V . With respect to the Iranian cut point of HOMA-IR 27% of patients had IR. IR was more common in patients with pre-capillary PH than post capillary ones. There was no difference between IR and insulin sensitive (IS) group regarding NYHA class, 6MWT, laboratory tests and hemodynamic data.
Conclusion: IR seems to be a common finding in PH. However, further studies are needed to clarify the role of IR in pathogenesis and progression of PH in particular in patients with pre capillary pulmonary hypertension.

Table 1

Variables	Insulin Resistance N = 16	Insulin Sensitive N = 43	P value
Sex (female), number(%)	9(57)	23(53)	NS
Age year , mean (SD)	46.2(19.9)	45.8(16.5)	NS
Body mass index, Kg/m ^{2}, mean (SD)	24.3(5.8)	23.8(4.6)	NS
Pulmonary hypertension hemodynamic type			0.02
Pre capillary	15	27	
Post capillary	1	16	
NYHA Class			NS
I	0	1(2.3)	
II	8(50)	18(42)	
III	8(50)	21(49)	
IV	0	3(7)	
6MWT,meter,median(IQR)	375(300-403)	330(280-390)	NS
Cardiac index ,mean (SD)	2.6(0.6)	2.3(0.6)	NS
Right atrial pressure ,median(IQR)	8.5(7-13)	11(8-16)	NS
Mean pulmonary artery pressure,median(IQR)	33(27-51)	40(27-49)	NS

Comparison demographic ,clinical and hemodynamic findings in insulin sensitive and resistance pulmonary hypertension patients

P534

Evaluation of breathlessness during daily living activities in patients with pulmonary arterial hypertension

RENGIN Demir[1]; RAZIYE Atar[1]; UMIT S Yasar[1]; SERDAR Kucukoglu[1]
[1]*Istanbul University Cardiology Institute, Department of Cardiology, Istanbul, Turkey*

Pulmonary arterial hypertension (PAH) is a clinical condition characterized by the presence of pre-capillary PH and pulmonary vascular resistance >3 Wood units, in the absence of other causes of pre-capillary PH such as PH due to lung diseases, chronic thromboembolic PH, or other rare diseases. Patients with PAH has symptoms of exertional dyspnea, fatique and their quality of life is reduced. The aim of this study was to evaluate breathlessness during daily living activities in patients with pulmonary arterial hypertension. Sixty one patients were included in the study (mean age 46.5, 17 men/44 women). Thirtytwo patients were in WHO Functional Class II, 29 were in WHO Functional Class III. Exercise capacity, activities of daily living, fatique and quality of life were assessed. The 6-minute walk test (6MWT) was used to evaluate exercise capacity. The London Chest Activity of Daily Living (LCADL) scale was used to measure the impact of breathlessness on activities of daily living. LCADL is divided in 4 domains: self-care (4 items), domestic (6 items) physical activity (2 items) and leisure (3 items). Each item is scored from 0 to 5 points. The total scores range from 0 to 75 with higher scores corresponding to greater limitation in activity of daily living. Fatique was assessed with the Fatique Severity Scale (FSS). Quality of life was assessed by the Nottingham Health Profile (NHP). LCADL scale total score was 25.6. Mean 6MWT distance was 427.2 m. LCADL scale total score showed positive correlation with age (r= 0.26, p = 0.004), functional class (r= 0.45, p = 0.0002), fatique (r= 0.55 p= < 0.0001) NHP total score (r= 0.61 p= < 0.0001) and negative correlation with 6MWT distance (r= -0.39, p = 0.002). Breathlessness during daily living activities in patients with PAH is correlated with fatique severity, exercise capacity and the severity of PAH and is also correlated with decrease in quality of life.

Hypertension - Other

P535

Obesity types affect development of major cardiovascular risks :Data from Korean National Health Insurance Service

EJ Cho[1]; SH Park[2]; HY Lee[3]; JH Shin[4]; HK Jeon[1]
[1]*Catholic University of Korea, Cardiology division, Seoul, Korea Republic of*; [2]*Yonsei University , Cardiology, Seoul, Korea Republic of*; [3]*Seoul National University, Cardiology, Seoul, Korea Republic of*; [4]*Hanyang University, cardiology, Seoul, Korea Republic of*

Background: Population based study demonstrated that obesity (defined as increased body mass index, BMI) is important predictor for developing hypertension and diabetes mellitus (DM), which have been well known major cardiovascular (CV) risk factors. Increased waist circumference (WC) representative of central obesity is focused as main factor for developing CV disease and its major risks.
Purpose: This study was to evaluate obesity as a predictor for new onset of hypertension and DM within 1-year in previously normotensives or normoglycemic subjects.
Methods: The Korean National Health Insurance Service - National Sample Cohort (NHIS-NSC) established data about BMI and WC with medical, social and familial histories in 2009 and have been followed up for 1 years. Among total 349,257 subjects with age more than 20 year-old, 95,124 (normotensive group: 75.2% of population were 25-55 year-old, 54121(56.9%) male) of normotensives for evaluate new hypertension and 120,501 (normoglycemic group: 83.6% of population were 25-65 year-old, 67,183 (55.8%) male) normoglycemic subjects for evaluate new DM were analyzed.
Results: During 1-year follow-up period, 3,773 (3.97%) new hypertension in normotensive group and 1,594 (1.32%) new DM in normoglycemic group were developed. Binary logistic regression analysis revealed that BMI was the predictor (Exp(B) = 1.18, Sig < 0.001) for new onset hypertension with age (Exp(B) = 1.31, Sig < 0.001), sex (Exp(B) = 0.664, Sig < 0.001), dyslipidemia and family history of hypertension. For new onset DM, WC (Exp(B) = 1.04, Sig < 0.001), age (Exp(B) = 1.26, Sig < 0.001), sex Exp(B) = 0.664, Sig < 0.001) and family history of DM (Exp(B) = 1.76, Sig < 0.001) were the independent predictors.
Conclusion: Increase of BMI is independent predictor for new onset hypertension and increase of WC is independent predictor for new onset DM within 1-year. Obesity type might affects development of different major CV risks and hence, obesity itself is the important risk factor for CV disease.

P536

Relationship of cardiac magnetic resonance-derived myocardial fibrosis and molecular biomarkers of fibrosis with cardiac geometry and strain in hypertensive heart disease

G Gernot Pichler[1]; F Martinez Garcia[2]; E Solaz[2]; O Calaforra[1]; A Ruiz[1]; B Lopez[3]; J Diez[3]; M San Andres Marco[4]; A Maceira Gonzalez[5]; J Redon[6]
[1]*Research Foundation Hospital of Valencia (INCLIVA), Cardiometabolic and Renal Risk, Valencia, Spain*; [2]*University Hospital Clinic of Valencia, Valencia, Spain*; [3]*Center for Applied Medical Research, Pamplona, Spain*; [4]*Fundación CETIR Centre Medic, Valencia, Spain*; [5]*ERESA Medical Center, Cardiac Imaging Unit, Valencia, Spain*; [6]*University of Valencia, Department of Medicine, Valencia, Spain*

Background: Hypertension is an etiologic factor for heart failure by inducing left ventricular hypertrophy (LVH). Myocardial fibrosis is a relevant component of LVH due to the impact in ventricular dysfunction. Novel cardiac magnetic resonance (CMR) imaging techniques have shown potential in quantification of diffuse cardiac fibrosis, with T1 mapping, and estimating preclinical cardiac dysfunction, with strain analysis.
Purpose: The aim was to investigate the relationship of CMR-assessed fibrosis and molecular biomarkers of fibrosis with cardiac geometry and strain in hypertensives with LVH.
Methods: CMR was performed on a 3T scanner in hypertensive individuals with positive ECG-derived criteria for LVH and free of cardiomyopathy other than LVH. Extracellular volume fraction (ECV) and the partition coefficient as measures of cardiac fibrosis were assessed using the T1 mapping technique shMOLLI. Longitudinal, circumferential and radial strain were assessed using CMR-feature tracking. Molecular biomarkers of collagen synthesis (PICP and PIIINP) and collagen degradation (CITP and MMP-1) were measured in blood using commercial kits. Pearson's correlation and multiple linear regression analysis controlling for gender, age, height, weight, heart rate and 24-h systolic BP were performed in order to assess the relationship between available variables.
Results: 36 hypertensives (83% males, mean age 50.6 ± 4.3) underwent CMR imaging, and T1 mapping was performed in 29 (79% males, mean age 50.1 ± 4.3) participants. Correlation models showed a significant relationship of ECV and the partition coefficient with left atrial (LA) diameter, LV mass, LV posterior wall thickness, LV end-diastolic volume and longitudinal strain. In fully adjusted regression models, ECV was associated with LA diameter (ß = 0.75, p = 0.005, R2 = 0.47) and longitudinal strain (ß = 0.43, p = 0.030, R2 = 0.38) (figure 1); the partition coefficient was associated with LV posterior wall thickness (ß = 0.53, p = 0.046, R2 = 0.49). Regarding molecular biomarkers of fibrosis, longitudinal strain was associated with CITP (ß = 0.46, p = 0.025, R2 = 0.25), and circumferential strain was inversely associated with MMP-1 (ß=-0.38, p = 0.047, R2 = 0.32) in fully adjusted regression models. No significant association between molecular biomarkers of fibrosis and CMR-derived cardiac geometry or fibrosis was observed.
Conclusions: CMR-assessed fibrosis showed significant associations with cardiac geometry and myocardial strain: A greater extension of cardiac fibrosis was related to an increase in cardiac dimensions (LV posterior wall thickness, LA diameter) and a reduction (i.e., "less negative" values) in longitudinal strain. Molecular biomarkers of collagen degradation were associated with myocardial strain but not with the extension of CMR-derived cardiac fibrosis.
Figure 1: Regression line, scatter plot and correlation coefficient for the association between ECV and longitudinal strain.

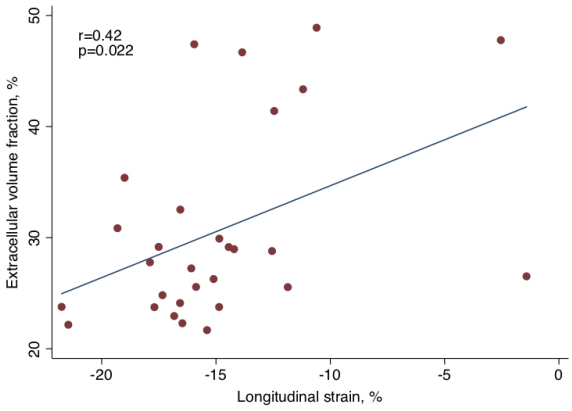

Figure 1

P537

Arterial hypertension in heart transplanted recipients

M Simonenko[1]; P Fedotov[2]; Y Sazonova[3]; M Sitnikova[2]; M Karpenko[4]
[1]Almazov National Medical Research Centre, Cardiopulmonary Exercise Test, Saint-Petersburg, Russian Federation; *[2]Almazov National Medical Research Centre, Heart Failure Department, Saint-Petersburg, Russian Federation*; *[3]Almazov National Medical Research Centre, Thoracic Surgery and Transplantation Laboratory, Saint-Petersburg, Russian Federation*; *[4]Almazov National Medical Research Centre, Chairman of Scientific Clinical Council, Deputy Director for Science and Medical Work, Saint-Petersburg, Russian Federation*

Background: Post-transplantation arterial hypertension (AH) is a major cardiovascular problem and is present in 50-90% of patients after heart transplantation (HTx). Multiple factors are involved in generating AH after HTx; these include immunosuppression, increased sensitivity of beta-adrenergic receptors due to donor heart denervation, worsening of endothelial function and drug nephrotoxicity.
Purpose: to estimate the frequency of AH following HTx and define factors which may impact on its development.
Methods: From 2010 to 2017 we performed 96 HTx (mean age - 46,5 ± 13,9 yrs; m - 70), 38,5% (n = 37) of them coped with AH prior HTx. In fact, 83% (n = 30) of recipients with AH were smoking before HTx and had ischemic heart disease (IHD) (p <0,001). After HTx all patients were treated with triple-drug therapy (steroids, calcineurin inhibitors, mycophenolate mofetil/everolimus) and induction (basiliximab - 79% (n = 76), thymoglobulin - 21% (n = 20)). Post-HTx hypertension was defined as the need to use drugs for its control. We estimated post-transplant outcomes.
Results: During early-term follow-up (less than 1 month) 8 patients died in ICU. In fact, only 15% (n = 13 from 88) of recipients (mean age - 32 ± 15 yrs) had normal blood pressure (BP) through the whole posttransplant follow-up (30,4 ± 23,9 months). During 6 months after HTx 56% (n = 49) of patients required antihypertensive drugs, 2 drugs were prescribed 18 of them and 3 drugs - 2 of them. During this period the most often used single class of drugs were angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARB) (46%, n = 32), followed by calcium channel blockers (CCBs) (37%, n = 26) and beta-blockers (10%, n = 7). From 6 months to 1 yr after HTx AH was diagnosed in 68% of patients: 19 recipients were treated with 2 classes of drugs and 2 of them - with 3 drugs. During 1st yr more patients with AH prior HTx coped with post-transplant AH than those who did not have high BP before it (72% (n = 26) vs. 45% (n = 27), p <0,05). More than 1 yr after HTx AH was present in 81% of patients, 21 recipient followed by 2 classes of drugs and 4 - by 3 drugs or more. Two yrs after HTx the amount of patients with AH increased to 79%, 2 drugs were prescribed 16 of them, 3 drugs or more - 5 recipients. In long-term follow-up the most used drugs were ACE inhibitors or ARB and then CCBs. In addition, male gender (76% (n = 53) vs. 46% (n = 6), p <0,05), smoking prior HTx (70% (n = 49) vs. 15% (n = 2), p <0,001), family history of AH (40% (n = 28) vs. 8% (n = 1), p <0,05) and IHD (54% (n = 38) vs. 15% (n = 2), p <0,05) were associated with post-HTx AH. We found corellations between AH and male gender (r = 0,41; p <0,001), smoking (r = 0,35; p <0,001) and advanced age (r = 0,35; p <0,05).
Conclusion: After HTx most of patients coped with AH. In some patients it can be controlled with a single antihypertensive agent. The most important factors in the development of AH are IHD and the presence of AH prior HTx, male gender and smoking.

P538

Longitudinal systolic strain of left ventricle in association with hypertension and its control in a population

V Guseva[1]; A Ryabikov[2]; E Voronina[1]; Y Palekhina[1]; S Shakhmatov[1]; MV Holmes[3]; M Bobak[4]; S Malyutina[1]
[1]Institute of Internal & Preventive Medicine SB RAS, Novosibirsk, Russian Federation; *[2]Novosibirsk State Medical University, Novosibirsk, Russian Federation*; *[3]University of Oxford, Oxford, United Kingdom*; *[4]University College London, London, United Kingdom*

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BACKGROUND: Ultrasound assessment of systolic myocardial strain allows non-invasive identification of early stages of heart failure with preserved ventricular ejection fraction. There is evidence of a decline of global longitudinal strain of left ventricle (LV) in hypertension (HT) with left ventricular hypertrophy (LVH); however, these findings were reported for clinical samples with overt HT. Data on the relationship between longitudinal strain and blood pressure (BP) and HT in a general population is scarce.
Purpose: We aimed to study a relationship between peak systolic global longitudinal strain (GLS) and strain rate (GSR) of (LV) and HT and BP control in a general population sample aged over 50 years.
DESIGN and METHODS. The cross-sectional study was based on a population cohort (HAPIEE, Novosibirsk). In a random sample (n = 446, aged 58-82) we conducted echocardiography and evaluated GLS and GSR of LV by speckle tracking technique. ANOVA multivariable models were applied for analysis.
Results: The prevalence of HT In studied sample was 78,9%. The mean GLS value was - 18.7% (SD3.79), it was lower in men than in women (- 18.2% vs - 19.2%, p = 0.005). The mean GSR value was - 0.84 s-1 (SD 0.17), and did not differ by sex. The absolute value of GLS in HT was lower than in normotensives: - 18.5% (SD3.73) vs - 19.9% (SD3.42), p = 0.003; this difference was independent of age, sex and LV myocardium mass index (IMM), p = 0.011; but it was attenuated in a multivariate model including BMI. In HT groups, the GLS was the lowest among those "treated ineffectively" (0.043) and significantly lower versus normotensives independently of age, sex and myocardium mass index (p = 0.008). The absolute value of GSR in HT was lower than in normotensives: - 0.83 s-1 (SD 0.17) versus - 0.90 s-1 (SD 0.17), p < 0.001; and persisted in multivariable models. GSR was the lowest among those "treated ineffectively" and significantly lower versus normotensives in multivariable models independently of age, sex, BMI and myocardium mass index (p = 0.017; 0.002).
CONCLUSION: In studied population sample, GLS and GSR of LV were associated with HT; however, the association between GLS and HT was largely explained by BMI. In hypertensives, the lowest GLS and GSR, as well as higher extent of LVH, were found among those treated ineffectively, which might reflect the initial reduction of systolic ventricular function in hypertension with inadequate control of BP.

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Acute heart failure in hypertensive crisis: focus on left ventricular diastolic dysfunction

AR Aida Babaeva[1]; EA Slepukhina[1]; SI Davydov[1]; KS Solodenkova[2]; MA Osadchuk[2]
[1]Volgograd State Medical University, Volgograd, Russian Federation; *[2]I.M. Sechenov First Moscow State Medical University, Moscow, Russian Federation*

Background: Acute left ventricular failure (ALVF) could occur in patients with arterial hypertension (AH) in the setting of hypertensive crisis (HC) even in the absence of systolic dysfunction. In sever HC dramatically elevated BP leading to increased peripheral resistance seems to be a crucial factor in pathogenesis of ALVF. Myocardial remodeling and hypertrophy in AH commonly is associated with diastolic dysfunction (DD), which contributes to a cardiac output reduction.
Aims. The purpose of this clinical study was to assess the frequency of ALVF due to HC in patients who were hospitalized at cardiology department and evaluate the role of LV DD in the AHF manifestation in the patients with hypertensive crisis.
Methods: We analyzed 294 medical cards of pts who were hospitalized at cardiology ward of in-patient clinic due to ALVF (pulmonary edema) during last 10-year period. Among total ALVF cohort we separated and studied the medical cards of 67 pts (27 women and 40 men, mean age 73.28 ± 9.25) with AH and HC. Clinical, laboratory and instrumental data were analyzed in term to reveal the relationship between DD and ALVF. The diagnosis of AHF and its severity was proved on the basis of indicated respiratory rate (RR), clinical and radiologic signs of the pulmonary congestion, and the brain natriuretic peptide (BNP) levels. The presence of DD was confirmed according to the recommendations of the American Society of Echocardiography in conjunction with the European Association for Cardiovascular Imaging (2016).
Results: The commonest cause of ALVF was acute coronary syndrome (ACS), which was diagnosed in 68.38% pts, the second common cause was complicated HC (in 23% pts), arrhythmias accounted for 5.5% cases and other cardiovascular diseases were diagnosed in 4.11% of pts with ALVF. Echocardiography data from 67 pts with ALVF due to HC demonstrated that 23 pts (34.33%) did not have systolic dysfunction. The mean LV ejection fraction in this subgroup accounted for 56.05% ± 2.06%. Along with this there were not significant changes in final diastolic size of LV (mean size 5.25 ± 0.39 sm). In compliance with Doppler echocardiography protocols DD was diagnosed in 18 pts (26.87%) (mean ratio E/e' was 19.45 ± 2.34): the 1st degree of DD was documented in 12 (17.91%) pts, the 2nd degree DD - in 6 (8.96%) pts. There was strong positive correlation between the clinical (RR, pulmonary rules, HR), instrumental (PAP) and laboratory (BNP) data reflecting the severity of pulmonary congestion on the one hand and DD indices on the other hand (r>0.6, p < 0.05).
Conclusion: Sever hypertensive crisis is common cause of ALVF and reason for urgent hospitalization in AH. About one third of pts presented with ALVF due to HC do not have systolic dysfunction. Determined diastolic dysfunction was in 26.87% cases. Revealed relationship between the severity of ALVF and signs of LV DD confirms the important role of LVDD in AHF manifestation.

Obesity

P540

Early beneficial effect of bariatric surgery on subclinical myocardial impairment using global LV longitudinal strain in severely obese patients: contribution of abdominal visceral fat mobilization

ME Piche[1]; M Rodriguez-Flores[2]; K O Connor[1]; P Garceau[3]; A Auclair[1]; J Martin[1]; MA Clavel[1]; P Poirier[1]
[1]*Quebec Heart and Lung Institute, Quebec, Canada*; [2]*National Institute of Medical Sciences and Nutrition Salvador Zubiran, Mexico City, Mexico*; [3]*Montreal Heart Institute, Montreal, Canada*

Background/Introduction: The effect of bariatric surgery on subclinical myocardial function assessed using global left ventricular (LV) longitudinal strain (GLS) in severely obese individuals with normal LV dimensions and function is unclear.
Purpose: We explored the early effect of bariatric surgery on subclinical obesity-related myocardial performance impairment, and its relationship with changes in body fat distribution and cardiometabolic profile following bariatric surgery.
Methods: Thirty-eight severely obese patients (age, 41 ± 11 years; BMI, 48.4 ± 7.4 kg/m2, 40% type 2 diabetes) with preserved LV ejection fraction (<50%) who underwent biliopancreatic diversion with duodenal switch (BPD-DS) bariatric surgery, and 13 age and sex-matched healthy non-obese controls were studied. Blood samples and computed tomography were performed at baseline and 6 months following surgery. Comprehensive standard LV echocardiographic evaluation as well as GLS measurements were obtained preoperatively and 6 months post-bariatric surgery.
Results: Preoperatively, severely obese patients displayed a significant impairment in GLS vs. non-obese controls (-17.3 ± 2.5 vs. -19.7 ± 1.5%, $P < 0.01$). Six months post-bariatric surgery, mean GLS was comparable between obese patients and non-obese controls (-19.2 ± 2.1 vs. -19.7 ± 1.5%, P = NS), and GLS was normalized in 82% of severely obese patients ($P < 0.001$). The mean percentage of weight loss at 6 months was 26.3 ± 5.2%. Change in GLS following bariatric surgery was significantly associated with changes in abdominal visceral fat levels ($r = 0.43$, $P < 0.05$) and hs-CRP levels ($r = 0.45$, $P < 0.01$), whereas no significant association was found with percentage of weight loss and changes in insulin sensitivity, heart rate variability parameters or NT-proBNP levels. Additional subgroup analysis showed that those who experienced improvement in GLS post-bariatric surgery ($n = 31$) showed higher reduction in abdominal visceral fat and hs-CRP levels than those who worsened GLS ($P < 0.05$).
Conclusions: Severely obese patients with preserved LV ejection fraction showed a significant subclinical myocardial impairment as assessed by GLS measurements, which normalized at 6 months following bariatric surgery. This improvement in subclinical myocardial function was related to a greater mobilization of visceral fat depot following bariatric surgery.

P541

Food of Short supply chain impacts metabolism and cardiovascular risk. A survey in Southern Italy

M De Rosa[1]; R Giannotti[1]; AV Pascale[1]; R Finelli[1]; V Visco[1]; M Ilario[2]; M Ciccarelli[1]; G Iaccarino[1]
[1]*University of Salerno, Dept. of Medicine, Surgery and Dentistry, Salerno, Italy*; [2]*Division of Health Innovation, Campania Region Health Department, Naples, Italy*

Background: Dietary habits influence not only body weight but also cardio-metabolic risk factors, including cholesterol, blood pressure (BP), glucose homeostasis, inflammation and visceral adiposity. In the past decades, the development of big retail distribution of food has favored energy-dense and processed foods over than fresh ones, with high fat, sugar and salt content. The so called "Western-style diet" played a key role in the spreading of diet-related chronic diseases such as obesity, type II diabetes, cardiovascular diseases. Recent studies showed that specific foods and overall dietary patterns, rather than single isolated nutrient removal from diet, are more relevant for cardio-metabolic health. Several public health interventions around the word advocate for locally grown fresh foods (Short Supply Chain-SSC- Reg. (EU)1305/13) in order to improve general population dietary habits.
Purpose: To evaluate whether food from SSC can influence metabolic outcomes and cardiovascular risk.
Methods: We carried out body weight and blood pressure measurements and collected blood samples and information on dietary habits of 539 participants in the Salerno Area (Southern Italy) during the World Hypertension Day. All of them answered an 8 items-survey to calculate a dietary score (SSC-DS) that quantifies the tendency to purchase fresh and local foods rather than industrial ones. Blood glucose, insulin, HOMA-IR Index, lipid profile, markers of renal function were assessed as metabolic outcomes, while cardiovascular risk (CVR) was calculated according to the Framingham charts. Following data quality check, data from 365 subjects were analyzed. Pearson correlation and multivariate analysis were performed to explore the relationship between the SSC-DS, metabolic outcomes and cardiovascular risk.
Results: The overall population mean age was 51.95 ± 0.7 and female sex was slightly prevalent (57.8%), while mean body mass index (BMI) was 27.08 ± 0.3. SSC-DS was inversely correlated with blood glucose ($r = -0.148$, $p < 0.01$), insulin ($r = -0.291$, $p < 0.01$), HOMA-IR index ($r = -0.325$, $p < 0.01$) and CVR score ($r = -0.113$, $p < 0.05$). CVR score was correlated also with several other parameters, such as body weight, blood glucose, urea, triglycerides and diastolic blood pressure, not included in Framingham Risk Score calculation. After multivariate analysis which included all these parameters, SSC-DS confirmed its impact on CVR.
Conclusions: : These data support the hypothesis that SSC can improve cardio-metabolic health. If confirmed in larger prospective studies, these results could promote public interventions to improve people's lifestyle.

P542

Molecular genetic markers of endothelial function in obese patients with chronic heart failure

T Tatiana Zaletova[1]; A Bogdanov[1]; S Derbeneva[1]; T Feofanova[1]; I Vorojko[1]
[1]*Research Institute of Nutrition of Russian Academy of Medical Sciences, Moscow, Russian Federation*

Introduction: Nitric oxide (NO) is synthesized in the endothelium by a specific enzyme - NO synthase, which in turn is regulated by a gene of endothelial NOS-3 synthase (NOS3). A DNA sequence of NOS3 gene, in which guanine (G) is replaced by thymine (T) at position 894, is called genetic marker G894T. As a result of this substitution in the amino acid sequence of the protein, glutamate at position 298 is replaced by aspartate (Glu298Asp), which changes protein properties. A sequence in the regulatory DNA region of the NOS3 gene, in which thymine (T) is replaced by cytosine (C) at position 786, is called genetic marker T (-786) C. Possible genotypes are ?/?, ?/?, ?/?. This substitution causes a significant reduction in gene expression and NO synthesis by the endothelium.
Objectives: To study molecular genetic predictors of chronic heart failure development in obese patients with chronic heart failure (CHF).
Methods. Samples of biomaterials (whole blood) were taken from 104 obese patients, of Russian nationality, who lived in Moscow. Consequently all patients were divided into two groups: Group 1 - Grade 3 Obesity (O3) - 50 obese patients without CHF ("CHF –"); Group 2 - Grade 3 Obesity + CHF (O3+CHF) - 54 obese patients with CHF ("CHF +").
Results: No difference was shown in the incidence of T allele between "CHF +" and "CHF -" groups while studying frequency distribution of alleles of NOS3 gene polymorphic marker G894T. In males genotype frequencies in the control group and in the main group show that polymorphic marker G894T of NOS3 gene is not associated with the development of HF in obese male subjects. In female CHF patients, genotype NOS3 T / T ($p = 0.04$) and T allele incidence ($p = 0.04$) were significantly more common. At the same time, relative risk of HF development in patients with the given genotype was 2.73 times higher (RR = 2.27, 95% CI [0.31-12.18]). Distribution analysis of allele frequency and genotypes of polymorphic marker T786C of NOS3 gene did not reveal any differences between sexes in both "CHF +" and "CHF -" groups.
Conclusions: Thus, the study suggests that verifying mutations of NOS3 gene to stratify the risk of CHF development in obese patients is reasonable only in females, with G894T being informative.

P543

The effect of high plasma nesfatin-1 level on metabolic risk factors in hypertensive patients

M Maryna Vizir[1]
[1]*Kharkiv National Medical University, Kharkiv, Ukraine*

Background: Estimation of total cardiovascular risk is based on blood pressure level, risk factors and presence of organ damage. The link between such factors as hypertension, obesity, hypercholesterolemia, insulin resistance exists at the level of pathogenetic mechanisms. Nesfatin-1 was discovered as anorectic peptide secreted by hypothalamus, adipose tissue and other organs. Currently, its possible role in the development of concomitant diseases and the possibility of its use for therapeutic purposes are being studied.
Purpose: To investigate the association between the highest plasma nesfatin-1 levels and metabolic parameters in hypertensive patients.
Methods: 106 patients with essential hypertension were examined. Anthropometric data were obtained. Fasting and postprandial glucose levels were determined by the glucose oxidase method. Insulin (mkIE/ml) and nesfatin-1 (ng/ml) levels were determined by enzyme immunoassay method. Total cholesterol, triglycerides,

high-density lipoprotein cholesterol (HDLc) and low-density lipoprotein cholesterol were measured. The atherogenic coefficient was obtained as non-HDLc/HDLc. Nesfatin-1 levels were divided into quartiles, and these 4 groups (Q1-4) were used for comparing of results using the Mann-Whitney test, ANOVA rank Kruskal-Wallis test, the median test. Spearman's rank correlation coefficient was used for estimation of the relationship between two variables.
Results: The range of nesfatin-1 distribution was from 4.88 to 9.71 ng/ml. Patients of Q4 (= 8.44 ng/ml) were characterized by lower body mass index (p = 0.01), hips circumference (p = 0.002), lower levels of postprandial glucose (p = 0.03), HDLc (p = 0.01) and higher levels of triglyceride (p = 0.02).
Application of Spearman's rank correlation coefficient to Q4 parameters showed negative correlation of nesfatin-1 with weight (r= -0.356, $p < 0.01$), body mass index (r= -0.514, $p < 0.001$), waist circumference (r= -0.451, $p < 0.001$), hips circumference (r= -0.471, $p < 0.001$), levels of fasting glucose (r= -0.289, $p < 0.05$), postprandial glucose (r= -0.468, $p < 0.05$), and positive correlation of nesfatin-1 with atherogenic coefficient (r= 0.288, $p < 0.05$).
Conclusions: Higher nesfatin-1 levels in hypertensive patients were accompanied by lower anthropometric and glycemic parameters and increased atherogenic risk. These data may have important value for early diagnostics and treatment of patients in order to reduce cardiovascular risk.

Diabetes and the Heart

P544
Association between crucial risk factors for heart failure and gut microbiota: Moscow study

DA Daria Kashtanova[1]; ON Tkacheva[2]; AS Popenko[3]; AV Tyakht[3]; EN Doudinskaya[2]; DG Alexeev[3]; YUV Kotovskaya[2]
[1]National Research Center for Preventive Medicine, "Research of Age and Age-associated Conditions" Department, Moscow, Russian Federation; *[2]Russian National Research Medical University, Russian Clinical Research Center for Gerontology, Moscow, Russian Federation*; *[3]Moscow Institute of Physics and Technology, Moscow, Russian Federation*

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Introduction: Diabetes mellitus type 2 (DM), obesity (O) and abdominal obesity (AO), arterial (AH), high fat diet (HFD) are important modifiable risk factors (RF) for heart failure. At the same time recent years have brought interesting insights into the human gut microbiota impact on cardiovascular diseases (CVD). The aim of this study was to evaluate the associations between all these factors including gut microbiota composition in apparently healthy individuals from Moscow.
Materials and Methods: The study included 98 Moscow residents, 66 women and 32 men aged 25 to 76y/o (52 ± 13y/o) carefully selected through exclusion of CVD by

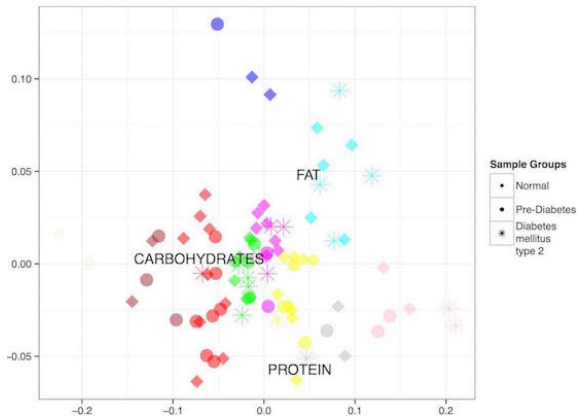


Fig. 1. Diet clusters

means of clinical and laboratory evaluation, ECG, treadmill test, ECHOCG, carotid ultrasound examination. RF were considered as follows: new onset 1st grade AH, O and AO except morbid, new onset DM, HFD. Gut microbiota was studied by 16S rRNA sequencing (V3-V4 regions). Diet - by quantitative assessment. Statistical analysis was performed using the R3.1.0., generalized linear models (FDR, age and sex adjusted) and clustering methods.
Results: 1st grade AH was detected in 37%, O in 25%, AO in 55%, DM in 23%, HFD - in 39%. Low bacterial alpha-diversity was associated with DM (FDR 0,015, k-means clustering). DM as well as O and AO were associated with high abundance of gram-negative opportunistic genera Serratia (FDR 0.003; 0.003; 0.004) and Prevotella (FDR 0.001; < 0.001; < 0.001). Low Oscillospira abundance was strongly correlated with abdominal obesity (FDR < 0.001). This genus is a "central enigmatic component" of the gut microbiome, which reduce inflammation and associated with leanness and high physical activity level. Interestingly, Blautia genus was highly abundant in patients with AH (FDR 0.002) and DM (FDR < 0.001). These bacteria induce low-grade inflammation and convert CO2 into acetate, which is an established lipids precursor. HFD was associated with low representation of Bifidobacterium (FDR 0.008). Samples were clustered by diet (protein, fat, carbohydrate consumption) with Calinski-Harabasz criterion. Cluster with very high consumption of fat contained 50/50% stool samples from donors with DM and normal glucose metabolism (Fig. 1, cian color). There were no differences between these patients in caloric consumption, age, sex and diet features. Although DM in high fat cluster was strongly correlated with Blautia representation (FDR 0.0001).
Conclusions: We concede that gut microbiota composition shifts along with classical risk factors act together to influence metabolic and CVD risk. Also we propose that combination of HFD with high Blautia abundance may lead to DM.

Exercise Testing

P545
Atrial geometrical and functional remodelling in long-term endurance training athletes

A A Molnar[1]; B Lakatos[1]; B Solymossi[1]; Z Tarcza[1]; C Bognar[1]; O Kiss[1]; A Kovacs[1]; B Merkely[1]
[1]Semmelweis University, Heart and Vascular Center, Budapest, Hungary

Purpose: Left atrial (LA) enlargement is common in master athletes. It is suggested that this represents a physiologic adaptation to long-term endurance training and not a consequence of increased left ventricular filling pressures secondary to diastolic dysfunction. The aim of our study was to investigate atrial remodelling and exercise capacity of elite athletes.
Methods: Sixty professional football male players (17.7 ± 3 years) and 20 non-sportive males (18.9 ± 1.9 years) were compared. All subjects underwent ECG, spiroergometry and two-dimensional transthoracic echocardiographic examination (Philips EPIQ7 Ultrasound) with the evaluation of left (LA), right atrial (RA) dimensions and deformation by strain and strain rate. Images were analyzed off-line with a commercially available software (TomTec 2D Cardiac Performance Analysis). LA and RA strains and strain rates were calculated with the reference point set at the onset of the P wave of the surface ECG, which allowed identifying left atrial contraction strain (LASa) and contraction strain rate (LASRa), atrial conduit strain (LASc) and conduit strain rate (LASRc), and finally atrial reserve strain (LASr) and reserve strain rate (LASRr). Maximum oxygen uptake (peak VO2) was defined as the highest value reached at the end of the exercise.
Results: LA and RA volumes were larger in athletes than in controls (52.2 ± 18.2 vs. 43.1 ± 12.4 mL, $p < 0.05$ and 56.5 ± 19.3 vs. 46.0 ± 10.4 mL, $p < 0.05$ respectively). LASa and LASRa during active atrial contraction were decreased in athletes (-8.1 ± 3.1 vs. -10.1 ± 3.5 %, p = 0.01; -0.91 ± 0.4 vs. -1.2 ± 0.4, p = 0.01). Athletes LA volumes trend to correlate with LASa (r = -0.22, p = 0.08) and show a significant correlation with peak VO2 (r= 0.33, $p < 0.01$). Furthermore, there was a significant correlation between peak VO2 and LA ejection fraction, LASc, LASRc, LASr and LASRr (r= -0.27, r= 0.38, r= 0.43, r= 0.32, r= -0.38 respectively, $p < 0.05$).
CONCLUSION: Endurance athletes showed left atrial enlargement and decreased left atrial contraction deformation as a physiologic response to long-term endurance training. Beyond, this adaptation correlates with maximum oxygen uptake reflecting physical capacity in a given athlete. The key challenge in an athlete's screening is the distinction between abnormal and normal which is hindered by the fact of the adaptation to sports activity.

P546
Detection of oscillatory ventilation in different phases of cardiopulmonary exercise testing is associated with the functional capacity of patients with chronic heart failure

N Panagopoulou[1]; L Karatzanos[1]; V Zarvalias[1]; P Ferentinos[2]; C Kapelios[3]; S Dimopoulos[1]; A Ntalianis[4]; E Repasos[4]; S Nanas[1]; A Sideris[5]
[1]Clinical Ergospirometry, Exercise & Rehabilitation Laboratory, NKUA, Athens, Greece; *[2]Carnegie Faculty , School of Sport, Leeds Beckett University, Leeds, United Kingdom*; *[3]Laiko General Hospital of Athens, Cardiology Department, Athens, Greece*; *[4]Department of Therapeutics, School of Medicine, NKUA, Athens, Greece*; *[5]Evaggelismos General Hospital of Athens, 2nd Cardiology Department, Athens, Greece*

Intoduction: Oscillatory ventilation (OV) is an abnormal breathing pattern chronic heart failure (CHF) patients present during exercise phase in cardiopulmonary exercise testing (CPET) and it is highly associated with poor prognosis.
Purpose: To seek possible associations of the OV during exercise and/or recovery phase with the functional capacity of patients with CHF.
Methods: 267 patients (age: 54 ± 13 years) with stable systolic CHF were prospectively enrolled and evaluated with maximum, symptom-limited CPET.

Criteria to determine oscillatory cycles were based on amplitude = 15% of the average resting amplitude, lasting = 60% of total CPET phase duration. These criteria were applied at both the exercise and the recovery phase (3min duration). The following 3 OV groups were identified: a) OV occuring during exercise and recovery phases (E-ROV), b) OV occuring only at exercise phase (EOV) and c) OV occuring only at the recovery phase (ROV). Groups were compared for CPET parameters, LVEF and OV specific characteristics (percentage of duration, average amplitude and average length). Values are expressed as mean ± SD.

Results: A total of 85 E-ROV, 58 EOV and 44 ROV were identified. Significant differences in VO2peak, VEpeak and VO2/t slope were found among the study groups (Table 1). EOV patients displayed broader average OV length at exercise than E-ROV (50 ± 18 sec vs 45 ± 13 sec respectively, p = 0.05). No differences were observed (p>0.05) for percentage of duration (80 ± 12% vs 77 ± 11%) and average amplitude (7.4 ± 4.0 L/min vs 7.6 ± 4.5 L/min).

Conclusions: Among patients with CHF, OV can appear in different phases of CPET. An OV pattern only during the phase of exercise associates with a worse functional capacity and consequently with a potentially higher severity in CHF patients. Broader average oscillatory length, likely reflects higher circulatory delay, could explain, up to some extent, the worse functional capacity in EOV CHF subgroup.

Table 1. Comparison of the three OV groups for CPET parameters and LVEF

	EOV	E-ROV	ROV	p
N	58	85	44	
VO_2peak (ml/kg/min)	15.8±5.8	19.4±8.1*	20.0±8.6*	0.024
VE/VCO_2	35.8±7.9	33.9±7.0	33.6±8.8	0.13
VE peak (L/min)	54.6±16.0	67.2±20.6*	68.0±22.6*	0.001
VO_2/t slope (L/min^2)	0.46±0.28	0.56±0.33	0.61±0.34*	0.037
LVEF (%)	29±9	31±9	29±8	0.35

*: significant differences compared to EOV group (p < 0.05)

P547

Echocardiographic findings in amateur male marathon runners

Z Lewicka-Potocka[1]; A Dabrowska-Kugacka[2]; L Danilowicz-Szymanowicz[2]; R Galaska[1]; M Kubik[2]; AM Kaleta[2]; E Lewicka[2]; G Raczak[2]
[1]Medical University of Gdansk, First Department of Cardiology, Gdansk, Poland; *[2]Medical University of Gdansk, Department of Cardiology and Electrotherapy, Gdansk, Poland*

Background: Regular and moderate physical activity has a number of positive effects on human organism, however the "upper dose" of beneficial endurance exercise has not been determined yet. Long-term endurance training can lead to multiple well-described adaptations in cardiac morphology, called the "athlete's heart". Marathon running has become very popular now, however, very little is known whether any physiological remodeling appears also in amateur marathon runners. The question arises which reference values should be applied in echocardiographic assessment of amateur runners, should ranges for competitive athletes or those for general population be used?

Purpose: We analyzed heart structure of amateur marathon runners by means of echocardiography to verify whether they fulfill the current normative values criteria for adults.

Methods: We included 34 amateur male marathon runners in the mean age of 40 years (24-55). Transthoracic echocardiography included two-dimensional conventional measurements, spectral and tissue Doppler, and flow propagation velocity. The examination was performed two weeks before their attendance in the 2nd PZU Marathon in Gdansk, Poland. We compared echocardiographic results with published reference values for adults, as well as professional athletes.

Results: The comparison was made for general adult population. The mean left atrial area index was 11.2 cm2/m2 and in 22 out of 34 (65%) participants it exceeded the upper normal value for adults. The mean left atrial volume index was 35.2 ml/m2 and in 26 (76%) subjects it was greater than the upper normal value for adults. The mean interventricular septum dimension was 1.12 cm and it exceeded the normal range in 22 men (65%). The mean left ventricular mass was 94.55 g/m2 and it was increased in 10 subjects (29%). The mean proximal right ventricular outflow diameter was 2.99 cm and was beyond the norm in 16 (47%), while the mean basal right ventricular dimension was 3.75 cm and it exceeded the normal range in 5 individuals (15%).

Conclusion(s)

When compared with the reference ranges for general adult controls, amateur male marathon runners fulfilled the general criteria or presented larger dimensions. Left atrial enlargement was the most often finding. Presented results may suggest that physiological remodeling within the heart can appear also in amateur athletes, what should be taken into account when echocardiographic examination is performed in individuals with the marathon attendance history.

P548

Benefits of cardiac rehabilitation in diabetic patients after an acute coronary syndrome

M Marta Braga[1]; A Rocha[1]; H Nascimento[1]; R Pinto[1]; P Araujo[1]; S Torres[1]; A Nunes[1]; V Araujo[1]; F Parada-Pereira[1]; MJ Maciel[1]
[1]Sao Joao Hospital, Porto, Portugal

Introduction and Purpose: Diabetes mellitus is a major risk factor for cardiovascular (CV) disease. It is well known that cardiac rehabilitation program (CRP) improves outcome in patients after acute coronary syndrome (ACS). The aim of this study was to characterize the risk profile of diabetic patients and evaluate the impact of CRP in functional capacity (FC) in these patients comparing to non-diabetic patients.

Methods: We analysed data prospectively collected from patients who completed a CRP after an ACS, from 2008 and 2016. Patients were divided in two groups: Diabetic patients (G1) and non-diabetic patients (G2), according to International Diabetes Foundation criteria. FC was assessed using a standard exercise test (ET), including exercise duration and intensity in metabolic equivalents (METs).

Results: Of 734 patients, 133 patients were diabetic (18.1%). Mean age was 59.9 ± 8.9 years in G1 and 53.2 ± 9.6 years in G2, p < 0.001. In both groups, most patients were male. Only 23.5% of diabetic patients were insulin dependent and initial mean glycated haemoglobin was 7.7 ± 1.4%. Concerning to other CV risk factor, hypertension (53.4% vs 39.1%, p = 0.003), dyslipidaemia (72.2% vs 58.7%, p = 0.011) and obesity (35.4% vs 22.7%) were more frequent in G1, while smoking was more prevalent in G2 (33.1% vs 57.7%, p < 0.001). About 50.0% of patients in G1 had multivessel coronary artery disease, comparing to 24.5% in G2 (p = 0.021) and coronary artery bypass graft occurred more frequently in G1 (15.8% vs 6.3%). Mean left ventricular ejection fraction was similar in both groups (52.6 ± 12.6 vs 52.6 ± 11.4). Regarding baseline FC, ET duration was 7.3 ± 2.1 min in G1 and 8.7 ± 2.4 min in G2 (p < 0.001), and ET intensity was 7.9 ± 2.0 METs in G1 and 9.2 ± 2.3 METs (p < 0.001). In the end of CRP, both patients improved their FC, duration (increase of 18.0% in G1 and 17.3% in G2) and intensity (increase of 16.9% in G1 and 16.0 in G2) without statistically significant difference. Mean glycated haemoglobin of G1 patients after CRP was 6.2 ± 1.0%.

Conclusions: Diabetic patient had higher CV risk profile comparing to non-diabetic and even so they had lower participation in CRP. In spite of showing worse ET results at the beginning and at the end of CRP, they had improved their FC in a similar form as the non-diabetic patients. This study highlights the need to identify and correct the barriers to CRP recruitment of this higher risk group of patients.

P549

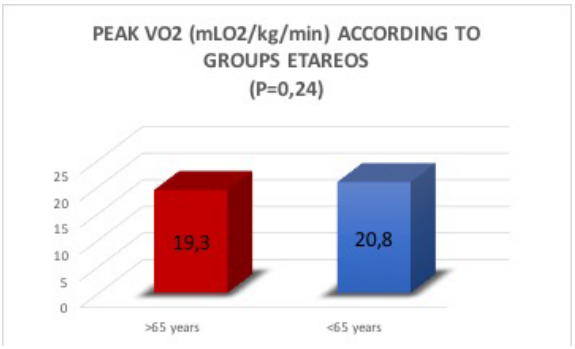
Cardiorespiratory efficiency to the exercise in elderly patients with ischemic cardiopathy

N G Uribe Heredia[1]; R Arroyo Espliguero[2]; LG Piccone Saponara[3]; H Alvaro Fernandez[1]; LG Gil Fraguas[1]; E Vallejo Sacristan[1]; E Novo Garcia[2]; B Tarancon Zubimendi[2]; B Garcia Magallon[2]; C Toran Martinez[2]; ME Jimenez Martinez[2]; JL Garcia Gonzalez[2]; MA San Martin Gomez[2]; M Viana Llamas[2]; JL Balaguer Recena[2]
[1]University Hospital of Guadalajara, Cardiac Rehabilitation Unit, Guadalajara, Spain; *[2]Guadalajara University General Hospital, Cardiology Department, Guadalajara, Spain*; *[3]Hospital General de Ciudad Real, Nefrology, Ciudad Real, Spain*

Introduction: The prevalence of coronary disease increases with age, with the cardiovascular cause being the main cause of death in people over 65 years old, up to 80% of cases according to some series.

PARAMETERS	>65 years	<65 years	P
METS	7,9 + 1,6	8,3 + 2,5	0,47
BP sistolic at maximum load (mmHg)	171,8 + 15,2	162,4 + 17,7	0,03
RER at maximum load	1,1 + 0,1	1,09 + 0,09	0,73
Peak VO_2 (mLO_2/kg/min)	19,3 + 4,2	20,8 + 6,7	0,24
Predicted percentage VO2	79,3 + 20,9	77,9 + 19,7	0,79
O_2 pulse trajectory (mL/beat)	11,6 + 2,6	14,2 + 3,8	0,001
Predicted percentage PO2 (%)	82,7 + 15,3	79,6 + 17,1	0,45
Volumen Tidal at maximum load (L/min)	1,67 + 0,5	1,96 + 0,6	0,04
$P_{ET}CO_2$ at maximum load (mmHg)	30,9 + 3,6	33,4 + 4,1	0,01
Ventilation minute (L/min)	59,8 + 17,4	67,1 + 20,4	0,12
Porcentaje predicho VE (%)	99,3 + 25,1	79,9 + 26,2	0,01
VE/VCO2 slope	33,4 + 4,3	32,1 + 6,6	0,3

Methods: Cross-sectional study. 91 patients subjected to cardiopulmonary exercise testing, with a diagnosis of ischemic heart disease who underwent cardiac catheterization and coronary revascularization for an acute coronary syndrome, between 2-3 months before the test. The patients were divided into two groups (group 1:>65 years, group 2: <65 years). We evaluated demographic variables, percutaneous angioplasty, anthropometric, echocardiographic, CVRF and comorbidities. SPSS 20. Qualitative variables were evaluated with X2. The quantitative variables are expressed as means+/-SD, being evaluated with the Student's T test. Statistical significance p <0.05.
Results: 91 patients; 21.7% (20 pctes) were >65 years old, the mean age was 56.9 ± 9.5 years, 9.8% women (9 pts). Among the baseline characteristics of both groups, we found that those >65 years had lower BMI (p = 0.04), without finding differences in other CVRF, comorbidities and echocardiographic characteristics. The parameters of oxygen consumption, in absolute value and adjusted per kilogram of weight are detailed in table 1.
Conclusions: : In our study, patients older than 65 years showed an aerobic capacity with cardiopulmonary response within normality, similar to younger patients, although with higher blood pressure at rest and at maximum load and slight tendency to hyperventilation, without showing greater alteration of the ventilation/perfusion relationship.



P550
Preliminary results in physical recovery after laparoscopic vs. open liver resection

S Stephanie Kampf[1]; C Schwarz[1]; M Sponder[2]; J Bergler-Klein[2]; C Sandurkov[3]; K Kaczirek[1]
[1]Medical University of Vienna, Department of Surgery, Vienna, Austria; *[2]Medical University of Vienna, AKH - Vienna, Cardiology Clinic, Vienna, Austria*; *[3]Medical University of Vienna, Division of Anatomy, Vienna, Austria*

Background: Minimally invasive laparoscopic surgery has proven to be equivalent in colorectal and gastric surgery. The role in liver surgery still remains controversial. This study was designed to investigate the impact of laparoscopic liver resection compared to open surgery on short- and long-term postoperative fitness and inflammatory response.
Methods: 40 Patients undergoing liver resection will be included into a laparoscopic (group 1) or open surgery group (group 2). Post-operative recovery is measured by bicycle stress testing at month 1 and 6 and compared to the preoperative performance. Standardized performance (%) for bicycle stress testing was calculated based on age, sex, height and weight. Postoperative recovery was compared between groups as mean change of performance (%).
Results: 15 patients completed the 1st month control, 9 patients the full trial. 3 of 9 patients had laparoscopic and 6 of 9 patients had open surgery. Mean arterial blood pressure was 104 ± 14 mmHg in group 1 vs. 111 ± 9 mmHg in group 2 (p = 0.51). Mean heart rate preoperative was 77 ± 12 bpm in group 1, respectively 75 ± 15 bpm in group 2 (p = 0.76). 1 month postop mean heart rate was 79 ± 19 bpm in group 1, respectively 73 ± 16 bpm in group 2 (p = 0.51).
Mean preoperative performance was 78 ± 19 % in group 1 and 80 ± 16 % in group 2 (p = 0.82). Baseline performance for both groups therefore was below average due to multimorbidity and age. One month postoperatively the relative performance changes to baseline were -3.8% in group 1 vs. -6.4% in group 2 and -7.7% in group 1 vs. -8.9% in group 2 at 6 months. Postoperative mean CRP was 3.6 vs 5.2 in group 2, postop AST (378 vs. 396U/L), ALT (335 vs. 332U/L), bilirubin (0.55 vs. 0.88mg/dL), prothrombin time (65 vs. 58%) showed no statistical difference.
Conclusion: So far, recovery after laparoscopic vs. open surgery did not show any statistical significant **Results:** However, a tendency regarding faster recovery recovery could be observed after after laparoscopic surgery, but due to the small sample size no definite conclusion can be drawn yet.

Autoimmune/Chronic Inflammatory Disorders and Heart Disease

P551
Atrial Arrhythmias and Sarcoidosis: Prevalence and clinical implications

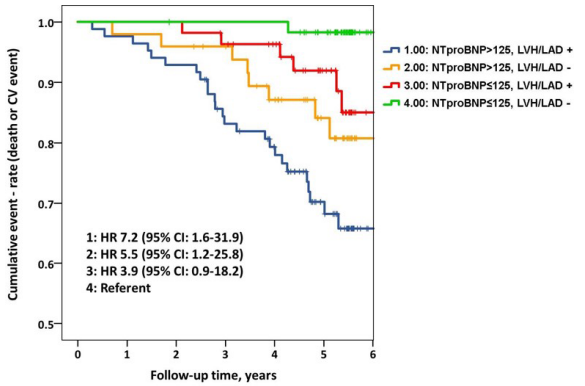
E Elias Gialafos[1]; S Katsanos[2]; L Kolilekas[3]; E Tsougos[4]; E Manali[2]; G Stratakos[1]; N Koulouris[1]; S Papiris[2]; G Filippatos[2]
[1]University of Athens, Athens, Greece; *[2]Attikon University Hospital, Athens, Greece*; *[3]Sotiria Regional Chest Diseases Hospital, 7th Department of Pulmunology, Chest Disease Hospital "Sotiria", Athens, Greece*; *[4]Errikos Dunant Hospital, 2nd Cardiac Department, Athens, Greece*

Introduction: Cardiac sarcoidosis is a major cause of morbidity and mortality in affected individuals. Ventricular arrhythmias are one of the main causes of sudden death in cardiac sarcoidosis .However, the incidence of atrial arrhythmias (AA) in sarcoidosis is not well known. Aim of this study was the assessment of the prevalence as well as the predictors of atrial arrhythmias in a large population of patients with sarcoidosis.
Methods: We included 328 patients with biopsy proven sarcoidosis (121 males, 52.78 ± 12.46 yo) who underwent a full cardiac examination included cardiac magnetic resonance (CMR) for workup of suspected cardiac sarcoid involvement. ECG, Holter monitoring or implantable cardioverter defibrillator interrogations were used to document AA. Echocardiographic data, lung function tests, demographics, and extracardiac involvement were recorded, and univariate and logistic regressions were performed to compare characteristics of patients with and without documented AA.
Results: The prevalence of AA was 30.3% with atrial fibrillation being the most common type of arrhythmias with 12,7%. Age (p = 0.002, CI:1.014-1.060), diffusing capacity for carbon monoxide (p:0.026, CI:0.968-0.998) and cardiac involvement (p = 0.0001, CI: 0.121-0.377) were independent predictors of AA on multivariate analysis. Feeling of palpitation, arterial hypertension, dyslipidemia, increased left atrial diameter, valvular dysfunction, diastolic dysfunction, total lung capacity and left anterior hemiblock on ECG were predictors of AA on univariate analysis.
Conclusion: In a large cohort of sarcoidosis patients, this study found a prevalence of AA of about 30%. AA in patients with is associated with cardiac involvent and the feeling of palpitation.

P552
Presence of echocardiographic criteria for heart failure with preserved ejection fraction multiplies the risk for death and cardiovascular events in patients with rheumatic diseases

M Breunig[1]; C Morbach[1]; S Kleinert[2]; H-P Tony[3]; CE Angermann[4]; S Stoerk[1]
[1]University Hospital of Würzburg, Comprehensive Heart Failure Center and Dept. of Medicine I, Würzburg, Germany; *[2]University Hospital of Würzburg, Dept. of Rheumatology/Clinical Immunology and Rheumatology and Nephrology Erlangen, Erlangen, Würzburg, Germany*; *[3]University Hospital of Würzburg, Dept. of Rheumatology/ Clinical Immunology, Würzburg, Germany*; *[4]University of Würzburg, Comprehensive Heart Failure Center, Würzburg, Germany*

Background: Patients with rheumatic diseases (RD) have an increased risk for cardiovascular (CV) disease and heart failure (HF). Clinical assessment of HF signs & symptoms in RD is often limited by functional impairment. We investigated the prognostic value of echocardiographic and neurohormonal criteria for HF with preserved ejection fraction (HFpEF) in patients with RD.
Methods: This prospective, single-center study included consecutive RD outpatients considered at increased risk for CV events according to ESC score (= 3%), pathological ECG, or elevated NTproBNP (<200 pg/mL) as published by this group*.



Clinical assessment and transthoracic echocardiography according to ESC criteria was performed. Presence of HFpEF was assumed positive, if patients had NTproBNP >125 pg/mL, and either left ventricular hypertrophy (LVH; averaged septal-posterior wall thickness >11 mm) or left atrial dilation (LAD; LA Diameter >43 mm), regardless of presence of dyspnea. Kaplan-Meier plots were generated, and hazard ratios (HR) with 95% confidence intervals were computed using Cox regression with adjustment for age.

Results: Out of 764 patients (mean age 51 yrs, 70% female) 46% had rheumatoid arthritis (RA), 34% systemic autoimmune diseases (SAI; connective tissue disease or vasculitis), and 20% spondylo-arthritis (SpA); 248 of these patients (mean age 61 ± 13 yrs, 62% female, RA 46%; SAI 32%; SpA 22%) had valid echocardiographic data (4 patients with LV ejection fraction < 50% were excluded; follow-up data was missing in 3 cases). After a median follow-up time of 5.4 yrs, 20.6% of patients (group 1-4: n= 19/5/8/1 respectively) had died or suffered a CV event (myocardial infarction 4.1%; stroke 1.8%; decompensated HF 1.8%; resuscitation 0.9%).

In univariable analysis NTproBNP >125 pg/ml (HR 3.6; 1.9-6.8, p = 0.0001), LAD or LVH (HR 2.3; 1.1-4.5, p = 0.02), and age per 5 years (HR 1.4, 1.2-1.6, p < 0.0001) were significant predictors for an increased risk for death or CV event.

Compared to the referent group consisting of patients with no signs of LVH or LAD in the presence of normal NTproBNP (group 4; n = 59, 23.8%), patients with echocardiographic criteria for HFpEF (group 1; n = 84, 33.9%) had a 7-fold increased risk for death or CV event: HR 7.2 (1.6-31.9; figure). The event risk for both patients with elevated NTproBNP but absent LVH or LAD (group 2; n = 49, 19.8%) as patients with normal NTproBNP but presence of LVH or LAD (group 3; n = 56, 22.6%) was also 5- to 6-fold increased: HR 5.5 (1.2-25.8) and 5.5 (0.9-18.2), respectively.

Conclusions: In patients with RD with an increased baseline CV risk, echocardiographic criteria suggestive of HFpEF are highly relevant indicators of worse outcome (7-fold increased risk for death or CVE), in particular in conjunction with an elevated NTproBNP value, irrespective of clinical presentation.

* Breunig M et al. Simple screening tools predict death and cardiovascular events in patients with rheumatic disease. Scand J Rheumatol 2017

P553

Use of standard cardio-vascular risk estimation scales may not be enough in patients with rheumatoid arthritis

E Troitskaya[1]; S Velmakin[1]; S Villevalde[1]; Z Kobalava[1]
[1]*Peoples'Friendship University of Russia (RUDN University), Moscow, Russian Federation*

Objective: Rheumatoid arthritis (RA) is associated with increased cardiovascular (CV) risk. Besides monitoring of the disease activity, identification of high CV risk patients is of great importance.

The aim of the study was to assess the abilities of 3 risk models (SCORE, QRisk 2 and 10-year ASCVD) in detecting high CV risk RA patients.

Materials and methods: 56 patients with RA (ACR/EULAR 2010) without known CV disease were examined (84% females, age 58.4 ± 14.1 (M ± SD) years, BMI 26.1 ± 5.4 kg/m2, smokers 9%, arterial hypertension (AH) 64%, dyslipidemia 57%, diabetes 7%). Median duration of RA was 7 years (IQR 2-14). Seropositive RA was diagnosed in 73% of patients. Median hsCRP was 7.8 mg/dl (IQR 2;21.4), rheumatoid factor (RF) - 61.2 IU/ml (IQR 18.5;179.2), mean DAS-28(CRP) - 3,7 ± 1,2. All patients received disease-modifying antirheumatic drugs. SCORE, QRisk2 and 2013 ACC/AHA 10-year ASCVD risk and EULAR recommended modified versions were calculated. Patients with SCORE = 5%, QRisk2 = 20% and ASCVD risk = 7.5% were classified as having high CV risk. Carotid intima-media thickness (CIMT) = 0,9 mm and/or carotid plaques detected by ultrasonography were used as the gold standard test for high CV risk. p < 0.05 was considered significant.

Results: The median SCORE, QRisk2 and ASCVD were 2.2% (IQR 0.6;4.9), 10.2% (3.4;19.2) and 4.9% (1.5;12.8) respectively. The proportion of high-risk patients was as follows: 14 (25%), 13 (23%), 24 (43%) for SCORE, QRisk2 and ASCVD. Mean CIMT was 0.76 ± 0.24 mm. US criteria for subclinical atherosclerosis (US+) were found in 27 (48%) pts. Discriminating capacities for the indexes were as follows: AUC 0.723 (CI 95% 0.626-0.821) for SCORE, AUC 0.705 (CI 95% 0.606-0.804) for QRisk2 and AUC 0.837 (CI 95% 0.757-0.917) for ASCVD. The percentages of high-risk patients in US+ group were as follows: 13 (48%), 12 (44%) and 21 (78%), respectively, (p < 0.05 compared to ASCVD). After multiplying by 1.5 (EULAR 2016) mASCVD reclassified 2 (7.4%) and mSCORE - 4 (14.8%) pts from moderate to high risk. Use of lower cut-off values for risk indices (SCORE = 1%, QRisk2 = 10% and ASCVD = 5%) resulted in better detection of US+ pts (100%, 85% and 85% respectively).

Conclusions: The 2013 ACC/AHA 10-year ASCVD risk estimator is better than the SCORE and QRisk2 indices for the detection of high CV risk RA patients. Adjustment of the threshold may be a better modification of risk scales than use of the EULAR multiplier factor.

P554

High prevalence of left ventricular systolic dysfunction assessed by speckle tracking in asymptomatic patients with diabetes mellitus type 1

C Chris Kapelios[1]; S Liatis[1]; M Bonou[1]; A Tentolouris[1]; I Eleftheriadou[1]; P Mantzouratou[1]; E Papachristoforou[1]; K Barmpagianni[1]; D Tsiliggiris[1]; J Barbetseas[1]
[1]*Laiko University General Hospital, Athens, Greece*

Background: Diabetes mellitus type 1 (DM1) primarily affects young, otherwise healthy, individuals. Cardiomyopathy presenting in these patients is usually the direct result of hyperglycemia and its effects. Thus, this subset of patients is of special clinical interest. Pre-symptomatic diagnosis of myocardial injury could enable prompt and potentially more effective implementation of therapeutic measures. However, the data that are available to date on the specific topic are limited.

Methods: We investigated the association between global longitudinal strain (GLS), an established index of subclinical left ventricular systolic dysfunction (SLVSD), assessed by 2-D speckle tracking and a) patient history, b) demographic and clinical baseline characteristics, c) autonomic nervous system function, measured using the battery of the 4 standardized tests proposed by Ewing, d) arterial stiffness, assessed by calculating pulse wave velocity between the carotid and common femoral arteries, e) prevalence and severity of diabetic nephropathy and f) prevalence and severity of diabetic retinopathy in patients with DM1 and no history of cardiovascular disease.

Results: We prospectively enrolled seventy-three asymptomatic patients with DM1. Thirteen (17.8%) were men, while mean age, disease duration and glycated hemoglobin were 36.8 ± 12.9 years, 19.9 ± 10.3 years and 7.2 ± 1.2%, respectively. SLVSD, defined as a value of GLS> -19.6%, was prevalent in 32/73 (43.8%) patients. GLS was significantly associated with body mass index (BMI, Pearson co-efficient, r = 0.387, P = 0.001) and glycated hemoglobin levels (r = 0.296, P = 0.015). Logistic regression analysis demonstrated a significant association between presence of SLVSD and ??? (OR: 1.232; 95% CI:1.074-1.414, P = 0.003) and glycated hemoglobin (HR: 1.699; 95%CI: 1.034-2.791, P = 0.034).

Conclusion: Our results indicate that apart from chronic hyperglycemia a dysmetabolic component, expressed by a higher BMI, may be implicated in the pathogenesis of premature myocardial injury, which leads to diabetic cardiomyopathy, in patients with DM1.

Cardiovascular Nursing - Other

P555

Effects of tailored telemonitoring on functional status and quality of life in patients with heart failure

J Josiane Boyne[1]; A Gingele[2]; B Ramaekers[3]; HP Brunner La Rocca[2]; GJ De Weerd[4]; J Kragten[5]; V Van Empel[2]; HJM Vrijhoef[2]; APM Gorgels[2]; G Cleuren[2]; C Knackstedt[2]
[1]*University Hospital Maastricht, Maastricht, Netherlands*; [2]*Maastricht University Medical Center, Maastricht, Netherlands*; [3]*Maastricht University Medical Center, Department of Clinical Epidemiology and Medical Technology Assessment (KEMTA), Maastricht, Netherlands*; [4]*Zuyderland Medical Center, Cardiology, Sittard, Netherlands*; [5]*Zuyderland Medical Center, Cardiology, Heerlen, Netherlands*

Aims: Functional status and quality of life (QoL) are important in patients with heart failure (HF). Little is known about the effect of telemonitoring (TM) on functional status and QoL in HF patients.

Methods/Results: 382 HF-patients (NYHA class 2-4) were included in a randomized controlled trial to compare tailored TM to usual care. At baseline (T0) and after 12 month (T12), patients' functional status was determined by Metabolic equivalent scores (METS) and Borg rating of perceived exertion scale (Borg). QoL was measured with the EuroQol five dimensions questionnaire (EQ-5D) and EQ-5D visual analogue scale (VAS). By analyzing electronic patient files, clinical data about mortality was obtained. TM was significantly related with an increase in METS after one year (Regression coefficient 0.318; p = 0.01). Telemonitoring did not have an effect on changes in Borg, EQ-5D and VAS after one year.
We found that EQ-5D (Hazard ratio (HR) 0.19, 95% Confidence interval (CI) 0.07-0.54), EQ-5D VAS (HR 0.98, 95%CI 0.96-0.99), Borg (HR 1.21, 95%CI 1.11-1.31) and METS at T0 (HR 0.73, 95%CI 0.58-0.93) were significantly associated with survival at T12.
In both groups, an increase of METS (T12-T0) was correlated with improved Utility (p <0.05) and a decrease of Borg (T12-T0) (p <0.05).
Conclusions: TM increased functional status of patients with HF, whereas no effect on QoL could be found. EQ-5D, Borg and METS can be used to predict survival in HF patients.

Mean scores of VAS, Utility, METS and Bo

Group	Score T0 (SD)	Score T12 (SD)	Δ T12-T0	Coefficient Intervention Group	p-value
	VAS	VAS			
Control (C) (n = 173)	57.82 (18.45)	63.18 (17.55)	5.36		
Intervention (I) (n = 179)	63.31 (16.84)	66.03 (15.34)	2.72	-0.081	0.95
	Utility	Utility			
C (n = 173)	0.61 (0.30)	0.63 (0.30)	0.02		
I (n = 179)	0.64 (0.30)	0.65 (0.28)	0.01	0.005	0.83
	METS	METS			
C (n = 173)	4.10 (1.79)	3.91 (1.70)	-0.19		
I (n = 179)	4.35 (1.82)	4.36 (1.86)	0.01	0.318	0.01
	Borg	Borg			
C (n = 173)	10.76 (3.76)	10.81 (3.74)	0.05		
I (n = 179)	10.25 (3.71)	10.18 (3.62)	-0.07	-0.368	0.22

Borg = Borg rating of perceived exertion scale; METS = Metabolic equivalent scores; n = numbers; P < 0,05 was considered statistical significant; SD = Standard deviation; Utility = calculated with EQ-5D scores; VAS = visual analogue scale.

P556

Communication difficulties in the care pathway of patients admitted to hospital with acute decompensated heart failure

M Walshe[1]; C Keane[1]; M Ledwidge[1]; J Gallagher[1]; R O'hanlon[1]; K Mc Donald[1]
[1]St Vincent's University Hospital, Heart Failure Unit, Dublin, Ireland

On behalf of: The Heart Failure Unit, St Vincent's Hospital
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Communication difficulties in the care pathway of patients admitted to hospital with acute decompensated heart failure.
Effective management of any chronic illness requires effective communication between all involved in delivering and receiving care. Central to this is effective inter-personnel communication and access to medical records. Heart failure (HF) care in particular demands good communication given the complexity of the illness and the tendency towards poly pharmacy.
Method: In an ongoing study defining the care pathways of patients admitted with ADHF (Acute decompensated HF) (de novo presentations, DN; and known HF patients, KHF) we assessed specific features of communication along the care pathway: availability of HF records on Emergency Department (ED) presentation and clinically stable natriuretic peptide (NP) level and weight record for KHF patients. Confirmation of self-care education of DN patients was also assessed, as was education of DN relative or carer, including frequency of sessions for both. In addition, availability of medication lists on presentation, and confirmation of discharge information communications to GP and community pharmacist for all patients, were examined.
Population: Eighty eight patients admitted to hospital with ADHF: 52.2% (46) DN, 47.7% (42) KHF, mean age 76 years, with a mean of 5 comorbidities.
Results: Of 88 patients followed 21 bypassed the ED. Of the 67 who attended the ED 43.2 % (28) were KHF. HF records were available for 39.2% (11); NP during clinical stability was available for 28.5% (8) KHF, no NP on record for DN. Weight records were available for 21.4% (6) of known patients. Medication lists were available in ED for 38.8% (26) of all patients; Eighty-eight % (37) of the DN patients received education; of these 29.7% (11) received 1 session and 70.27% (26) received 1-3 sessions. Thirty-five% (15) relatives or carers received education with 46.6% (7) receiving 1 session and 53.3% (8) receiving 1-3 sessions. No prescriptions were faxed to community pharmacists, and 73.75% (59) patients discharged had letters sent to GP.
Conclusion: This data highlights the communication difficulties present at various points in the care pathway of patients admitted to hospital with ADHF. Improved data access and inter-individual communication is necessary system-wide, to optimise management of HF patients.

P557

Palliative care in cardiac transplant: heart team perception

V L Vera Lucia Pessoa[1]; LC Souza[1]; DL Salles[1]; MGV Sobral[1]; VRF Cestari[1]; RS Florencio[1]; WM Barroso[1]; TMM Moreira[2]; JCS Santiago[3]; AACC Lima[2]
[1]HOSPITAL DE MESSEJANA DR CARLOS ALBERTO STUDART GOMES, Fortaleza, Brazil; [2]State of Ceara University, Nursing Graduation, FORTALEZA, Brazil; [3]Federal University of Ceara, FORTALEZA, Brazil

Introduction: The cardiac transplantation is the main alternative to refractory cardiac insufficiency; however, the patients need to have caring in many ways and, still, have a survival time of ten years. Thus, it is inevitable to consider the probability of death and suffering among these people, appearing the need of a caring directed to comfort, which is a scenario to palliative care. Method: It is an exploratory study with a qualitative approach, in which it was sought to know the perception of professionals who work in the cardiac transplantation area of palliative caring in their field of work. Ten professionals from the heart team were interviewed guided by a semi-structured interview, in which there were two doctors, one nutritionist, one psychologist, one social worker and five nurses. The interviews were recorded and, after transcription, organized and analyzed with the IRAMUTEQ software.
Results: The discursive corpus was presented in a dendrogram with the following analytical classes: Unsafety and uncertainty in indicating palliative care; Feelings and expectations related to palliation. The professionals' perception of palliative care is restricted to keep the comfort to the patient, but there is no clarity about how to conduct this care. There is a clear difficulty in establishing criteria to guide cardiac transplanted patients to palliative caring, it is punctuated aspects like clinical features, age, and comorbidities but there is no parameters definition. The professionals also related that an important obstacle in initiating palliation is fear, prejudice and, in many times, lack of knowledge of the team and family.

P558

International Study on Carers of patients with heart failure

A Stromberg[1]; R Greene[2]; A Creswell[3]; C Suridjan[4]; E Holzhausen[5]; S Campbell[6]; N Nick Hartshorne-Evans[7]; G Arthur[8]
[1]Linkoping University, Department of Medical and Health Sciences, Division of Nursing Science, Linkoping, Sweden; [2]National Alliance for Caregiving, Bethesda, United States of America; [3]Carers Australia, Deakin, Australia; [4]Carers Canada, Mississauga, Canada; [5]Carers UK, London, United Kingdom; [6]WomenHeart: The National Coalition for Women with Heart Disease, Washington DC, United States of America; [7]Pumping Marvellous, Preston, United Kingdom; [8]The Heart and Stroke Foundation of Canada , Brampton, Canada

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Background: The impact of heart failure on carers is an under-studied area when compared to other conditions like cancer, stroke, mental illness and dementia. The aim of this international study was therefore to describe the effects of caregiving for a person with heart failure on the daily life and well-being of family carers.
Methods: This research study was initiated and implemented by the International Alliance of Carer Organizations (IACO), a coalition of 14 member nations committed to building a global understanding and respect for the vital role of family carers. The study was conducted in Australia, Canada, United Kingdom and United States and IACO collaborated with carer and patient organisations in the four countries. The design was cross-sectional. Data collection using a web-based survey format was conducted between February and March 2017.
Results: The survey included 519 carers, mean age 58 years and 79% women. Half of the carers were partners, 61% had a college or university education. 30% were retired, and 30% worked full time. Three out of four were the primary carer for the person with heart failure and the meantime of care provided was 22 hours/week. The mean age of the persons with heart failure was 69 years. It was a severely

ill group of persons with heart failure whose carers participated in the study, with only 12% not having any other co-morbidities. Carers helped with activities of daily living (ADL) i.e bathing, dressing and instrumental activities of daily living (IADL) i.e cooking, shopping, managing finances, medical and/or nursing tasks. One in five stated that they had chosen to become a carer, the rest had to take on the role (81%). There was no significant correlation between feeling prepared to be a carer and having a choice to be a carer. Half of the carers perceived no control over the heart failure condition, 27% experienced some control and the rest perceived they had good control. Less than 1/3 of the carers felt they were supported by someone to balance their own well-being. Half of the carers did not think caregiving had affected their health, the rest thought it had made it worse. The findings demonstrated tha many similarities in the experiences of carers of persons with heart failure in the four countries participating in the study.
Conclusion: Carers play a vital role in assisting with the implementation and adherence of the treatment regime and self-care for persons with heart failure. It is therefore noteworthy that this survey found that many carers felt unprepared for many of their caregiving tasks and not in control of the heart failure condition. Carers need more education and skill building training as well as psychosocial support to increase preparedness for caring and perceived control over the heart disease. That can both improve carers life situation and well-being as well as give them more tools to support their loved ones with heart failure to improve and maintain self-care behaviour.

P559
Quick screening of nutritional status in an outpatient heart failure unit using de mini nutritional assessment short form tool

B Gonzalez[1]; M Cachero[1]; C Rivas[1]; V Diaz[1]; A Ros[1]; N Benito[1]; M Puertas[1]; A Morales[1]; P Velayos[1]; J Josep Lupon[1]; M De Antonio[1]; M Domingo[1]; P Moliner[1]; E Zamora[1]; A Bayes-Genis[1]
[1]*Germans Trias i Pujol University Hospital, Badalona, Spain*

Background: Nutritional status is an important prognostic factor in patients with heart failure (HF). Malnutrition, independently of the used definition, has been shown to carry worse prognosis above and beyond body mass index in such patients. In a pilot study we observed that the Mini Nutritional Assessment Short Form tool (MNA-SF) was the best approach for the screening of nutritional status in HF outpatients over other tools such as the Malnutrition Universal Screening Tool (MUST) or the Malnutrition Screening Tool (MST).
Purpose: To implement the MNA-SF screening tool in a routine way in a multidisciplinary HF Unit in order to catch those patients with malnutrition or at risk of malnutrition for further evaluation and management by a nutritionist when appropriate.
Methods: The MNA-SF screening tool was introduced in October 2016 in the global nurse evaluation of patients and scheduled to be repeated every 6 months. The scoring ranges from 0 to 14, being considered 0 to7 as malnutrition status, 8 to 11 as being in risk of malnutrition and 12 to 14 as normal nutritional status.
Results: A total of 809 assessments have been performed until November 2017 in 557 patients (mean age 69 ± 11.6 years, 70.5% men, body mass index 28.2 ± 4.7, LVEF 45% ± 13, NYHA class I 6.1%, II 82.6%, and III 11.3%). At first evaluation 15 patients (2.7%) fulfilled the criteria of malnutrition, 88 (15.8%) where at risk of malnutrition and 454 (81.5%) were considered to have normal nutritional status. 252 patients were reassessed at 6.8 ± 1.7 months. Out of the 38 reassessed patients who had malnutrition or were at risk of malnutrition at first evaluation, only 1 fulfilled the criteria of malnutrition while 14 remained at risk of malnutrition. On the other hand, of the 214 patients with normal nutritional status at first evaluation 15 evolved to at risk of malnutrition and 1 to malnutrition. Thus, of the 252 reassessed patients only 2 (0.8%) fulfilled the criteria of malnutrition and 29 (11.5%) were at risk of malnutrition.
Conclusions: The implementation of the MNA-SF as a routine screening tool in a multidisciplinary HF Unit allowed detecting malnutrition and risk of malnutrition in almost one every five ambulatory patients. Malnutrition and risk of malnutrition decreased in reassessed patients at 6 months.

P560
Determination of activities of daily living of individuals with cardiovascular disease

B Betul Bayrak[1]; S Oguz[1]; G Camci[1]; E Beysulen[1]; N Ozturk[1]; S Balci[1]; S Kesdi[1]
[1]*Marmara University, Faculty of Health Sciences, ISTANBUL, Turkey*

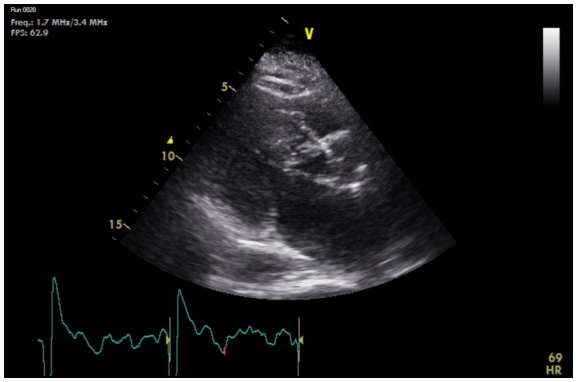
Background: Cardiovascular diseases, which are among the most important causes of death in the world, affect the activities of daily living of individuals in a negative way. For this reason, patients who have cardiovascular disease are insufficient in self-care management.
Purpose: This study was conducted as a descriptive and cross-sectional to determine the activities of dailiy living of individuals with cardiovascular disease.
Methods: The study has been performed between March-April 2017 with 491 patients hospitalized in cardiology wards of two hospitals in Istanbul. Patients who had cardiovascular disease, had no communication problems and were willing to participate in the study were taken into the study. Data were collected with Questionnaire and the Katz Activities of Daily Living (ADL) Scale. The Katz ADL Scale includes washing, dressing, toilet needs, transfer, continence and nutrition sub-dimensions. In activities of daily living scale, 0-6 points dependent, 0-12 points semi independent and 12-18 points as independent are evaluated. In the analysis of data, descriptive statistics, Mann Whitney U and Kruskal Wallis Test were used. Significancy value was evaluated as $p < .05$.
Results: The mean age of the patients was 61.21 ± 14 and 60.5% were male. 88% of the patients were married, 91% were living with their family, 44.2% of their sleep was regular and 86.8% do not exercise. 85% of the patients were adversely affected by the disease. The mean Katz ADL scale of patients was 17.1 ± 2.3. The mean score of bathing and dressing activity of the patients (2,741 ± 0,582 2,794 ± 0,511, respectively) were the lowest. Male (p=.029), married (p=.029), those with regular sleep (p=.003), those without comorbid disease (p= .036) and those who were not adversely affected by disease of the mean Katz ADL score (p=.00) was found to be high.
Conclusion: Patients with cardiovascular disease were independent in their activities of daily living. They were most difficult in bathing and dressing activities.

Basic Science - Cardiac Biology and Physiology

P561
A Clinically and Echocardiographically Demonstrable Dynamic Left Ventricular Outflow Tract (LVOT) Obstruction

S Saad Ahmad[1]; W Khan[1]
[1]*Royal Preston Hospital, Cardiology, Preston, United Kingdom*

Dynamic left ventricular outflow tract (LVOT) obstruction is a distinctive finding on echocardiography and often supports a diagnosis of hypertrophic obstructive cardiomyopathy (HOCM). It is also a clinical entity in its own right and is reproducible with stress. We describe a case of dynamic outflow obstruction in an elderly man



Dynamic LVOT on Echo following exercise

with classical exertional symptoms. Echocardiography was used to demonstrate a variable gradient, with imaging performed at rest and following physical exertion. We will review the patho-physiological changes seen in this condition, both in terms of cardiac structure and the physics of fluid dynamics. Medical treatment is centered around a meaningful understanding of these changes, but there are also surgical and ablative options available. Device therapy with an implantable cardioverter-defibrillator (ICD) is the mainstay of HOCM treatment, particularly when ventricular arrhythmias are evident. A risk stratification for sudden cardiac death from hypertrophic cardiomyopathy is imperative to case by case management.

P562

The single nucleotide polymorphism Q222R in the DNase 1 gene is linked with mortality in patients after ST-elevation myocardial infarction.

A Anna Ondracek[1]; TM Hofbauer[1]; T Scherz[1]; J Mueller[1]; A Panzenboeck[1]; A Mangold[1]; IM Lang[1]
[1]*Medical University of Vienna, Vienna, Austria*

Background/Introduction: Neutrophils are able to release their nuclear content into extracellular space by formation of neutrophil extracellular traps (NETs). NETs are capable to neutralize pathogens, but have also been implicated in autoimmune and thrombotic diseases, including ST-elevation myocardial infarction (STEMI). Deoxyribonuclease (DNase) 1 degrades NETs. DNase 1 Q222R single nucleotide polymorphism (SNP), which impairs DNase 1 function, was associated with an increased incidence of MI. In STEMI, impaired DNase 1 activity was correlated with increased NET burden and infarct size. In a mouse model of coronary artery ligation, DNase 1 treatment decreased infarct size, indicating a potentially therapeutic role. We hypothesized that DNase 1 is crucial to counteract dysregulated NET formation in coronary artery disease (CAD). The Q222R SNP in the DNase 1 gene, resulting in dysfunction of the enzyme, might thereby induce chronic NET burden with influence on long-term outcome.
Methods: We enrolled CAD patients with a history of STEMI, which received primary percutaneous coronary intervention between 2006 and 2016 (n = 711). Genotyping using allelic discrimination was performed to identify DNase 1 Q222R SNP (rs1053874). Mortality data was obtained from the national registry of death. Causes of death were classified according to ICD-10. By multivariable Cox regression, we assessed the influence of DNase 1 SNP on all-cause and cardiovascular mortality, adjusting for the following established cardiovascular risk factors: age, sex, body mass index, diabetes, smoking, hyperlipidemia, renal function as measured by serum creatinine concentration at admission and arterial hypertension.
Results: Homozygous mutation of the DNase 1 SNP was present in 64 (9.0%) patients; 304 (42.8%) and 343 (48.2%) were heterozygous and homozygous for the wild-type allele, respectively. Median survival was 60.0 [interquartile range 30.3; 91.5] months. A total of 133 (18.7%) patients deceased; 78 (11.0%) died of cardiovascular causes. Homozygous mutation of DNase 1 was independently associated with all-cause mortality (hazard ratio 2.05, 95% CI 1.22-3.46, p = 0.006) and cardiovascular mortality (hazard ratio 2.02, 95% CI 1.02-4.01, p = 0.046).
Conclusion: We report a negative influence of the Q222R DNase 1 SNP on survival after STEMI. Our findings argue for a deleterious role of NETs not only in CAD.

Basic Science - Cardiac Diseases

P563

Long-term safety follow-up of patients with advanced heart failure treated with transendocardial delivery of muscle-derived stem/progenitor cells with overexpression of connexin-43

A Adrian Gwizdala[1]; N Rozwadowska[2]; A Cieplucha[1]; A Katarzynska-Szymanska[1]; T Kolanowski[2]; A Malcher[2]; E Straburzynska-Migaj[1]; W Seniuk[1]; Z Oko-Sarnowska[1]; B Perek[3]; K Blaszyk[1]; S Grajek[1]; M Kurpisz[2]
[1]*Poznan University of Medical Sciences, 1st Department of Cardiology, Poznan, Poland*; [2]*Institute of Human Genetics, Poznan, Poland*; [3]*Poznan University of Medical Sciences, Department of Cardiac Surgery, Poznan, Poland*

Background: Patients with advanced heart failure (HF) have poor prognosis despite number of available treatments, including new drugs and devices. Regenerative therapy is continuously an interesting approach to treatment of this condition. Our recently published data demonstrated for the first time that injection of muscle-derived stem/progenitor cells with overexpression of connexin-43 (MDS/PCs-Cx43) in patients with severe HF led to significant improvement of exercise capacity and myocardial viability while inducing no significant ventricular arrhythmias. It could be due to improved electrical coupling of the injected cells and host myocardium and thus better in-situ cooperation between cells.
Objectives: To evaluate the long-term safety of transendocardial delivery (NOGA® MyoStar® intramyocardial injection catheter) of MDS/PCs-Cx43 in patients with advanced HF.
Methods: Thirteen subjects (one female) with advanced HF, NYHA class II-III, with implanted cardioverter-defibrillator, ineligible/disagreeing to other intervention, including transplantation ("no option group") that underwent transendocardial injection of MDS/PCs-Cx43 were enrolled. For safety assessments patents were followed-up for up to 36 months (medical history, physical exam and rhythm monitoring by implanted devices every 12 months).
Results: Total of 3 deaths (23%) were documented. There were 2, 0 and 1 deaths at 12, 24 and 36 months, respectively (one from pancreatic cancer and two form worsening HF). One patient (8%) suffered from sustained ventricular tachycardia (14 months of index procedure) terminated with ICD intervention (anti-tachycardia pacing, ATP) during strenuous exercise; he was further treated with oral amiodarone and no VT recurrence was observed.
Conclusions: The study demonstrated no arrhythmic deaths in patient with severe HF previously treated with injection of Cx-43+ MDS/PCs. Only episode of nonfatal ventricular tachycardia was effectively treated with ATP. These observations may support the thesis that genetic modification (Cx43) of implanted muscle-derived stem/progenitor cells may attenuate the proarrhythmic potential of unmodified skeletal myoblasts due to improved electrical coupling between the injected cells and host cardiomyocytes making the safety acceptable.

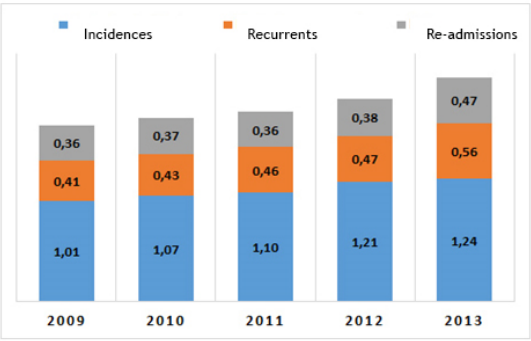
Poster session 1 - Basic Science

Chronic Heart Failure - Epidemiology, Prognosis, Outcome

P584
Long-term natural history of the Heart Failure.

M L Maria Lucia Fernandez Gasso[1]; D Pascual-Figal[2]; L Hernando-Arizaleta[3]; J Palomar-Rodriguez[3]; J Martinez-Diaz[1]; P Ramos-Ruiz[1]; I Garcia-Escribano[1]; G Clavel-Ruiperez[1]; R Soto-Ruiz[1]; J Abellan-Huerta[1]; C Fernandez-Pascual[1]; D Dau-Villareal[1]
[1]Hospital General Universitario de Santa Lucia, Cardiology, Cartagena, Spain; *[2]Hospital Clínico Univeristario Virgen de la Arrixaca, Cardiology, Murcia, Spain*; *[3]Consejería de Sanidad de la Región de Murcia, Servicio de Planificación Sanitaria, Murcia, Spain*

Background: The natural history of the first hospitalization for heart failure (HF), in particular the interaction between survival and re-hospitalizations, is not well established.
Methods: Systematic analysis of all hospitalizations in the Region of Murcia in the period 2003 to 2013. After merging the episodes corresponding to each person, 8.258 different individuals were identified with a first hospitalization due to HF in the period 2009-2013. All patients were followed at least 2 years (median 3.2 years).
Results: In the period 2009-2013, the rates of first hospitalization for HF showed an increase up to 1.24 per thousand inhabitants (2.31% annual percentage change). The first hospitalization accounted for 71% of patients and 57% of hospitalizations for HF. The incidence of readmission at 5 years was 51% for HF, 64% due to cardiovascular causes and 88% to any cause. Survival was significantly lower, 40% at 5 years, to the general population with similar age and sex ($p < 0.001$). Among the 4.368 patients who died, of those without readmissions (15.8%) 58% died in the first six months; and of 84.2% with readmissions, re-hospitalizations were accumulated mainly before death and only in those with a survival longer of two years, a bimodal phenomenon was observed due to early re-hospitalizations after discharge.
Conclusions: The first hospitalization due to HF presents increasing population rates, and its natural history shows a high mortality and re-hospitalization charge, related to time to death. These data support the importance of establishing strategies for end-of-life care with extra-hospital strategies.



P585
Trends in heart failure prevalence and expenditure in portugal

L Santos[1]; ML Lelis[1]; CF Fonseca[2]
[1]Hospital Funchal, Internal Medicine, Funchal, Portugal; *[2]Heart Failure Unit, Hospital de Sao Francisco Xavier, Lisbon, Portugal, NOVA Medical School, Faculdade de Ciências Médicas, Universidade Nova de Lisboa, Lisbon, Portugal*

Background: Heart failure (HF) prevalence in the developed world continues to grow, with growing economic burden of disease. Governments and health organizations must keep track of the costs related to this public health issue. High-income countries devote 1,42% of their annual health care budget for HF direct costs and around 0.06% of their GDP for indirect costs.
Purpose: Given the percentage of annual GDP devoted to healthcare has remained relatively stable we hypothesized that there may be underbudgeting for HF in Portugal.
Methods: We estimated the annual prevalence for HF in Portugal from the age-group prevalences in the 2002 EPICA study. We applied these prevalences to the respective age groups from 2006 to 2016 in order to derive the estimated yearly HF prevalence. Annual expenditure with HF was estimated from the portuguese annual GDP and mean percentage of health budget devoted to HF in high-income countries, from the literature.
Results: Statistically significant correlation between the increase in prevalence and a lowering budget per HF patient ($r=-0,718$, $p = 0.013$) in the past decade. Table 1 shows that adequate financing for HF may be lacking. Conclusion: The ageing process of the portuguese population is determinant to HF prevalence. It is importante to further investigate the actual prevalences and institute measures for prevention of overall cardiovascular disease. Our investigation hints at an ongoing underbudgeting of HF. This must be taken into consideration by governaments and health organizations.

Table 1.

Year	GDP (€)	%GDP for health expenditure	Total health expenditure (€)	Mean % spent of HF (direct)	Estimated direct HF costs (€)	% spent on HF indirect	Estimated indirect HF costs (€)	Estimated overall HF costs (€)	HF prevalence	Mean per patient (€)
2016	1,85179E+11	0,080	14814 MM	0,0142	210 MM	0,0006	111 MM	321 MM	405 193	793,4
2015	1,79809E+11	0,091	16363 MM	232 MM	107 MM	340 MM	400 709	849,1		
2014	1,73079E+11	0,090	15577 MM	221 MM	104 MM	325 MM	396 201	820,4		
2013	1,70269E+11	0,091	15495 MM	220 MM	102 MM	322 MM1	392 189	821,5		
2012	1,68398E+11	0,093	15661 MM	222 MM	101 MM	323 MM	388 449	832,6		
2011	1,76167E+11	0,094	16560 MM	235 MM	106 MM	341 MM	384 198	887,2		
2010	1,79930E+11	0,098	17633 MM	250 MM	108 MM	358 MM	3784 20	947,0		
2009	1,75488E+11	0,098	17198 MM	244 MM	105 MM	350 MM	372 279	938,8		
2008	1,78873E+11	0,093	1664 MM	236 MM	107 MM	344 MM	366 681	936,9		
2007	1,75468E+11	0,090	15792 MM	224 MM	105 MM	330 MM	361 223	912,3		
2006	1,66249E+11	0,091	15129 MM	215 MM	997 MM	315 MM	355 747	884,3		

Trends in estimated heart failure prevalence and total costs in Portugal from 2006 to 2016

Chronic Heart Failure - Diagnostic Methods

P586

Mechanisms responsible for increased circulating levels of galectin-3 in heart disease

X-J Xiao-Jun Du[1]; MN Nguyen[1]; Y Su[1]; D Vizi[2]; AH Ellims[2]; WB Zhao[1]; H Kiriazis[1]; XM Gao[1]; J Sadoshima[3]; AJ Taylor[2]; JR Mcmullen[1]; AM Dart[2]; DM Kaye[2]
[1]Baker IDI Heart and Diabetes Institute, Experimental Cardiology, Melbourne, Australia; [2]The Alfred Hospital, Alfred Heart Centre, Melbourne, Australia; [3]New Jersey Medical School, Department of Cell Biology and Molecular Medicine Rutgers, New Jersey, United States of America

On behalf of: Experimental Cardiology Lab
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Background : Galectin-3 has been utilised as a biomarker for heart disease, however the mechanisms for increment of circulating galectin-3 and its dependency on aetiology or disease-associated conditions, such as inflammation or ß-adrenergic activation, are unclear.
Purpose: To study the mechanisms responsible for elevated circulating galectin-3 levels in animal models of various heart diseases and in patients with cardiomyopathies and heart failure.
Methods : We studied mouse models of dilated cardiomyopathy (cardiac Mst1 overexpression) or fibrotic cardiomyopathy (cardiac ß2-adrenergic receptor overexpression), ischemia-reperfusion (I/R) and treatment with the ß-adrenergic receptor agonist isoproterenol. Plasma and cardiac levels of galectin-3 were measured by ELISA. Myocardial inflammatory cell density was quantified by immunohistochemistry and galectin-3 expression by circulating leukocytes were determined by RT-PCR. Circulating and trans-cardiac gradient of galectin-3 levels were also determined either in mice or cardiomyopathy patients with heart failure.
Results : Relative to controls, all mouse models showed multi-fold increases in cardiac galectin-3 expression while renal function was maintained estimated by cystatin-C levels. In transgenic mouse models of fibrotic cardiomyopathy, I/R or treatment with isoproterenol, plasma levels of galectin-3 and cardiac inflammatory cell infiltration were elevated, including a 3.5-fold increase in galectin-3 gene expression by circulating leukocytes from I/R mice. These models also exhibited parallel changes in cardiac and plasma galectin-3 levels and presence of trans-cardiac galectin-3 gradient indicating cardiac release of galectin-3 into circulation. Despite a 50-fold increase in cardiac galectin-3 content, transgenic mice with dilated cardiomyopathy showed no change in circulating galectin-3 levels nor myocardial inflammatory infiltration. In patients with hypertrophic or dilated cardiomyopathy, plasma galectin-3 increased only in those with impaired renal function, and a trans-cardiac galectin-3 gradient was not present in patients with dilated cardiomyopathy and severe heart failure (NYHA Class III-IV).
Conclusions: : Increase in circulating galectin-3 is dependent on the aetiology of heart disease and occurs by diverse mechanisms. In cardiomyopathy patients, renal dysfunction is responsible for elevated circulating galectin-3 without evidence for cardiac release. In mouse models that exhibit significant cardiac and/or systemic inflammation or ß-adrenergic receptor activation, cardiac release of galectin-3 contributes to elevated circulating levels.

P587

Right ventricular and pulmonary vascular function are influenced by age and volume expansion in healthy humans

E Wolsk[1]; R Bakkestrom[2]; CB Kristensen[1]; KA Myhr[1]; JH Thomsen[1]; L Balling[1]; MJ Andersen[1]; JS Dahl[2]; SJ Shah[3]; F Gustafsson[1]; C Hassager[1]; JE Moller[2]
[1]Rigshospitalet - Copenhagen University Hospital, Copenhagen, Denmark; [2]Odense University Hospital, Odense, Denmark; [3]Northwestern University, Chicago, United States of America

Aims: Patients with heart failure (HF) often show signs of right ventricular (RV) dysfunction. The function of RV coupled with the pulmonary circulation (tricuspid annular plane systolic excursion [TAPSE]: pulmonary artery systolic pressure [PASP]) has been shown to divide HF patients into distinct prognostic strata, however no normative values exist limiting the clinical utility of this measure. We sought to obtain normative values and discern the individual effects of age, gender, and fluid overload on the TAPSE:PASP ratio.
Methods and Results: Sixty healthy subjects aged 20-80 years were enrolled in this prospective study. Right heart catheterization with hemodynamic measurements were performed at rest and following a rapid saline infusion (10 ml/kg, 150 ml/min). Linear regression and Spearman correlation models were used to estimate associations between TAPSE:PASP and relevant variables.
In healthy persons of all ages, the normative TASPE:PASP ratio was median (5th-95th percentile) 1.25 (0.81-1.78) mm/mmHg. The correlation between progressive age and declining TAPSE:PASP was significant (r: -0.35, p = 0.006). Gender did not influence TAPSE:PASP (p = 0.30). Rapid fluid expansion increased central venous pressure from 5 ± 2 mmHg to 11 ± 4 mmHg after fluid infusion (p <0.0001). This resulted in a 32% decrease in the TAPSE:PASP ratio after fluid infusion, compared to baseline (figure 1, p <0.0001).
Conclusion: The TAPSE:PASP ratio was affected by age, but not gender. TAPSE:PASP is not only a reflection of intrinsic RV function and pulmonary vascular coupling, but fluid status dynamically affects this index of RV function. Normative values were obtained for future assessment of HF patients.

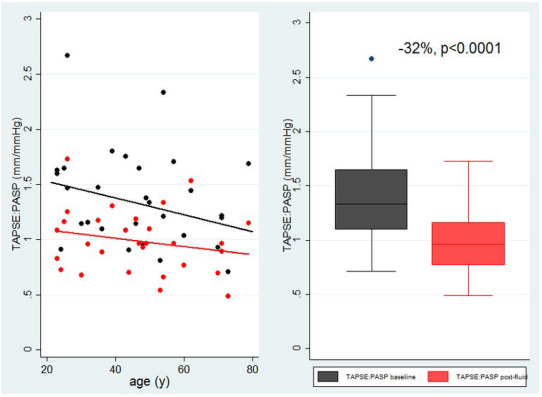


Figure 1

P588

Possible benefits of ultra high field MRI in cardiac diffusion tensor imaging

D Lohr[1]; M Terekhov[1]; AM Weng[2]; A Schroeder[3]; H Walles[3]; LM Schreiber[1]
[1]University Hospital Würzburg, Comprehensive Heart Failure Center (CHFC), Chair of Cellular and Molecular Imaging, Würzburg, Germany; [2]University Hospital Würzburg, Institute of Diagnostic and Interventional Radiology, Würzburg, Germany; [3]Translational Center Regenerative Therapies (TLC-RT), Fraunhofer Institute for Silicate Research (ISC), Würzburg, Germany

Funding Acknowledgements: Financial support: German Ministry of Education and Research (BMBF, grants: 01EO1004, 01E1O1504).

Introduction: In vivo diffusion tensor cardiac magnetic resonance (DT-CMR) has recently been used to characterize myocardial microstructure dynamics during left ventricular wall thickening, showing distinct, abnormal sheetlet function in HCM and DCM patients. However, the necessary trade-off between the number of averages, diffusion weighted directions, and image resolution in clinically used parameter settings have been shown to lead to poor precision of sheetlet and helix angles (HA) of ± 31° and ± 14° respectively. MRI at higher field strength such as 7T may provide higher signal-to-noise ratio (SNR), allowing for improvement of spatial and angular resolution, image quality as well as consistency of diffusion metrics in clinically applied parameter settings.
Purpose: To assess feasibility of DT-CMR at 7T and compare SNR and diffusion metrics in spin echo based diffusion tensor acquisitions of the unfixed, ex vivo porcine heart at 7T and 3T.
Methods: Measurements were performed on 7T and 3T whole body MRI systems using 1Tx/32Rx head coils. Porcine hearts were imaged in physiological saline

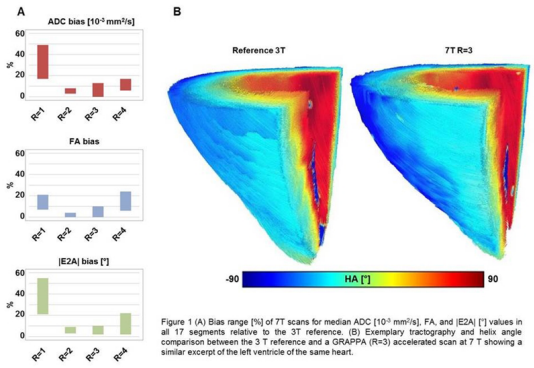


Figure 1 (A) Bias range [%] of 7T scans for median ADC [10^{-3} mm^2/s], FA, and |E2A| [°] values in all 17 segments relative to the 3T reference. (B) Exemplary tractography and helix angle comparison between the 3 T reference and a GRAPPA (R=3) accelerated scan at 7 T showing a similar excerpt of the left ventricle of the same heart.

solution, unfixed, at room temperature within 10 hours after cardiac arrest. MRI with spatial resolution of 1.3x1.3x1.3 mm^3 was performed obtaining 25 and 8 cDTI datasets at 3T and 7T as a reference. Scans at 7T were repeated using parallel imaging acceleration (GRAPPA) factors R = 2, R = 3, R = 4. Apparent diffusion coefficient (ADC), fractional anisotropy (FA), HA and secondary eigenvector angle (E2A) were compared within segmentation according to the American Heart Association (AHA).
Results: DTI data was successfully acquired for all parameter settings used. SNR values in b0 images of scans at 3T and 7T was 34 ± 3 and 45 ± 4 for identical scans. On average DTI analysis was performed for 6 ± 2 slices of apical cap, 8 ± 1 apical, 8 ± 1 mid-cavity, and 8 ± 1 basal slices. Maximal and minimal deviations of ADC [$10^{-3}mm^2/s$], FA, and |E2A| [°] within the AHA segments were used to define a bias range for 7T acquisitions relative to the 3T reference. The smallest bias was found for scans using GRAPPA factor R = 2 (Figure 1). Derived metrics from scans using GRAPPA factor R = 3 showed significant differences in FA in mid-cavity and basal parts. No significant differences were found for scans using GRAPPA factor R = 2.
Conclusion: Feasibility of DTI acquisitions of ex vivo porcine hearts was demonstrated for spin echo based acquisitions with spatial resolution of 1.3x1.3x1.3 mm^3 via comparison with a reference data set measured at 3 T. Derived metrics were statistically similar to the 3T reference data using GRAPPA factors R = 2 and R = 3. The relative SNR gain in 7T acquisitions may benefit clinically used parameter settings for DT-CMR allowing optimization of the trade-off between averages, diffusion directions, and image resolution, especially, when using stimulated echo approaches, which can utilize the increased T1 at higher field strengths.

P589

Myocardial perfusion disturbance precedes LV systolic dysfunction in experimental model of chronic Chagas cardiomyopathy

L F L Oliveira[1]; J T Thackeray[2]; D M Tanaka[1]; J A Marin-Neto[1]; M M D Romano[1]; C D Lopes[1]; A C L Barros-Filho[1]; F F F Ribeiro[1]; J Mejia[3]; C Malamut[4]; F M Bengel[2]; E Cunha-Neto[5]; M L Higuchi[5]; S G Nekolla[6]; M V Simoes[1]
[1]Medical School of Ribeirao Preto - University of Sao Paulo, Ribeirao Preto, Brazil; [2]Hannover Medical School, Department of Nuclear Medicine, Hannover, Germany; [3]Hospital Israelita Albert Einstein, Sao Paulo, Brazil; [4]Nuclear Technology Development Center (CDTN), Radiopharmaceutical Production and Development Unit, Belo Horizonte, Brazil; [5]Heart Institute of the University of Sao Paulo (InCor), Sao Paulo, Brazil; [6]Technical University of Munich, Department of Nuclear Medicine, Munich, Germany

Funding Acknowledgements: São Paulo Research Foundation (FAPESP)

Background: Myocardial perfusion defect (MPD) is a common finding in Chronic Chagas cardiomyopathy (CCC), but it is unclear if the perfusion derangement can precede the left ventricular (LV) systolic dysfunction. We investigated the time-course of myocardial perfusion changes and the correlation with the progression of LV systolic dysfunction in an experimental model of CCC.
Methods: Female Syrian hamsters (n = 40) were infected with 3.5x104 trypomastigotes forms of T. cruzi Y-strain and the surviving animals (n= 22) were submitted to in vivo imaging 2, 4, 6, 8 and 10-months afterwards. Rest high-resolution SPECT imaging using 99mTc-sestamibi was used to assess MPD extension that was analyzed by using polar maps and compared to matched control animal database. The left ventricular (LV) systolic function was assessed by using 2D-echocardiogram. The animals underwent PET imaging for assessment of myocardial inflammation using 18F-FDG under myocardial uptake suppression conditions at 10-months after infection and co-registered with SPECT images. Histological analysis included quantification of myocardial fibrosis.
Results: Compared to control animals, 7 out of 22 (32%) infected animals showed significant LV ejection fraction (LVEF) deterioration after 8-months (69 ± 2% and 61 ± 11%, respectively, p = 0.03), and after 10-months (70 ± 2% vs 54 ± 10%, respectively, p = 0.0002). Individual animals presented MPD at 2-months and progressive deterioration after 6-monts after infection. All animals that died during protocol, presented MPD in the last assessment. LVEF at 10m negatively correlated with MPD at 6m (r= -0.58, p = 0.005), 8m (r= -0.62, p = 0.002) and 10m (r= -0.7, p = 0.0001). Animals with MPD showed higher 18F-FDG uptake topographically correlated with the LV regions with MPD. Segments with MPD in comparison to segments with normal perfusion displayed higher %ID/g (0.15 ± 0.02 vs 0.13 ± 0.03, p= 0.005), SUV (g/cc, 0.28 ± 0.040 vs 0.23 ± 0.05, p < 0.0001) but similar extent of histological fibrosis (21 ± 7.6% vs 22.9 ± 7.1%, p = 0.3). Compared to controls animals, infected animals presented higher interstitial fibrosis (%, 15 ± 6 vs 9 ± 1, p = 0.002), however no transmural scar was revealed.
Conclusions: Rest MPD precedes the development and correlates with the ulterior deterioration of LV systolic dysfunction in experimental CCC. The MPD was topographically associated with elevated 18F-FDG uptake, suggesting a correlation between inflammation and the myocardial perfusion derangement. Our findings suggest that MPD may be a surrogated marker of myocardial inflammation in CCC and raise the possibility of using perfusion imaging for risk stratification and monitoring the course of this myocardial disease.

Chronic Heart Failure - Treatment

P590

Elamipretide restores protein and mRNA expression levels of S100A1 in left ventricular myocardium of dogs with chronic heart failure

RC Gupta[1]; V Singh-Gupta[1]; HN Hani Sabbah[1]
[1]Henry Ford Hospital, Detroit, United States of America

Funding Acknowledgements: Supported by a research grant from Stealth BioTherapeutics, Inc.

Background: S100A1 is a calcium-binding protein predominantly expressed in cardiac and skeletal muscles and localizes to Z-discs and sarcoplasmic reticulum. S100A1 was shown to play a pivotal role in cardiac contractility. More recently, a novel interaction of S100A1 with mitochondrial F1-ATPase was recognized which affects F1-ATPase activity and cellular ATP production. Cardiomyocytes that overexpress S100A1 exhibit high ATP content whereas knockdown of S100A1 decreases ATP levels. Elamipretide (ELAM), a mitochondria targeting peptide, has been shown to improve cardiac contractility and increase the rate of ATP synthesis in left ventricular (LV) myocardium of dogs with advanced heart failure (HF). This study examined the effects of chronic therapy with ELAM on protein and mRNA levels of S100A1 in LV myocardium of dogs with coronary microembolizations-induced HF (LVEF ~30%).
Methods: LV tissue from 14 HF dogs randomized to 3 months therapy with subcutaneous injections of ELAM (0.5 mg/kg once daily, n = 7) or saline (control, CON, n = 7) and LV tissue from 6 normal (NL) dogs was used. Protein levels of S100A1 were determined in LV tissue extract by Western blotting coupled with chemiluminescence and band intensities expressed in densitometric units (du). mRNA expression of S100A1 normalized to GAPDH was measured in RNA from LV tissue using real-time PCR and was expressed as fold change from NL.
Results: Data are shown in the Table. Levels of GAPDH were unchanged among the 3 study groups. mRNA and protein levels of S100A1 were decreased significantly in HF-CON dogs compared to NL dogs. Treatment with ELAM (HF+ELAM) normalized S100A1 mRNA and protein expression.
Conclusions: mRNA and protein levels of S100A1 are decreased in LV of HF dogs and are normalized after chronic therapy with ELAM. The finding supports the observations of improved LV function and rate of ATP synthesis after chronic therapy with ELAM.

mRNA and Protein Expression of S100A1			
	NL	HF-CON	HF+ELAM
S100A1 protein level (du)	470 ± 0.29	2.50 ± 0.37*	3.31 ± 0.17†
S100A1 mRNA (fold change from NL)	1.00	-5.48*	-1.60†

* = p < 0.05 vs. NL; † = p < 0.05 vs. HF-CON

P591

Comparative efficacy of empagliflozin and drugs of baseline therapy in post-infarct heart failure in normoglycemic rats

MV Krasnova[1]; AN Kulikov[2]; SV Okovityi[1]; DYU Ivkin[1]; AA Karpov[3]; AV Tkacheva[1]; DA Vaulina[2]; IG Kayukov[2]; VA Smirnov[2]
[1]Saint-Petersburg State Chemical-Pharmaceutical Academy, Saint-Petersburg, Russian Federation; [2]Saint-Petersburg State Medical University named I.P.Pavlov, Saint-Petersburg, Russian Federation; [3]Almazov National Medical Research Centre, Saint-Petersburg, Russian Federation

Background: Multiple pleiotropic drug effects including a sodium diuretic effect, maintenance of osmotic diuresis due to glucosuria and the decrease of post-load owing to blood pressure decrease have become the basis of the hypothesis on the

Significant changes of echoCG values

	?????? ?1 (CHF)	?????? ?2 (CHF + empagliflozin)	?????? ?3 (??? + ??????????)	?????? ?4 (CHF + ??????????)	?????? ?5 (CHF + ?????????????)
?????? ?1 (CHF)		RA1: 1> 2 MAPSE: 1 <2	LVEDD: 1> 3 LVESD: 1> 3 LVvolD: 1> 3 LA: 1> 3 LAI: 1> 3	-	LA: 1> 5
?????? ?2 (CHF + empagliflozin)	RAI: 2 <1 MAPSE: 2> 1		LAI: 2> 3	IVSEs: 2> 4 MAPSE: 2> 4	MAPSE: 2> 5
?????? ?3 (??? + ??????????)	LVEDD: 3 <1 LVESD: 3 <1 LVvolD: 3 <1 LA: 3 <1 LAI: 3 <1	LAI: 3 <2		FS: 3> 4 EF (T): 3> 4	LVvolD: 3 <5 LAap: 3 <5
?????? ?4 (CHF + ??????????)	-	IVEs: 4 <2 MAPSE: 4 <2	FS: 4 <3 EF (T): 4 <3		-
?????? ?5 (CHF + ?????????????)	LA: 5 <1	MAPSE: 5 <2	LVvolD: 5> 3 LAap: 5> 3	-	

MAPSE - mitral annular plane systolic excursion, LVEDD - left ventricle end-diastolic diameter, LVESD - LV end-systolic diameter, LVvolD - LV end-diastolic volume, RAI - right atrium long position, LAs - left atrium short position, LAI - left atrium long position, EF(T) - LV ejection fraction by the Teichholz method, FS - LV fraction shortening, IVEs - inter ventricular septum at end systole

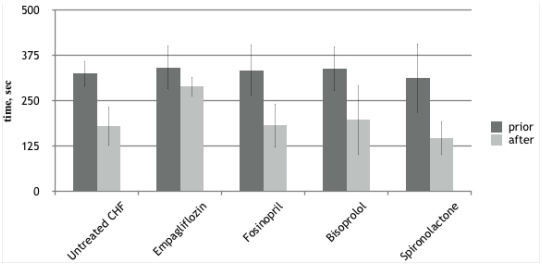
possibility of empagliflozin administration for chronic heart failure (CHF) treatment with the absence of carbohydrate metabolism disorders.

Purpose: The experimental comparative study on empagliflozin efficacy in CHF in normoglycemic settings with the drugs which are generally accepted agents for CHF treatment: angiotensin-converting enzyme inhibitor, ß-blocker and aldosterone antagonist.

Methods: CHF in 50 rats was simulated via permanent ligation of the left coronary artery. 1 month later, the operated animals were randomized under echocardiographic (echoCG) control to 5 equal groups of 10 animals: a group that did not receive any treatment, groups which took empagliflozin, fosinopril, bisoprolol and spironolactone as monotherapy, respectively. 3 months of the therapy, echoCG and treadmill exercise time were analyzed.

Results: The administration of empagliflozin resulted in the retarded progression of left ventricular dysfunction in comparison with the animals not receiving the treatment (Tabl. 1). The tolerance during the treadmill exercise was evidently decreased in 3 months in all study groups of animals. The maximum activity time was the highest in the rats taking empagliflozin (289 ± 27sec), it was significantly higher than in the animals of groups ?1 (180 ± 53sec, $p < 0.05$), ?3 (183 ± 61sec, $p < 0.05$), ?4 (197 ± 95sec, $p < 0,05$), and ?5 (147 ± 46sec, < 0.05) (Fig. 1)

Conclusions: Sodium-glucose co-transporter 2 inhibitor empagliflozin improves tolerance of physical exercise in normoglycemic rats with experimental CHF being superior in this respect to reference agents for CHF treatment.



Maximum activity time at the treadmill

P592

Introducing SGLT2 inhibitors during hospitalization. Safety and outocmes.

S Blasco Turrion[1]; FJ Camacho Jurado[1]; R Castilla Ortiz[2]; I Lobo Torres[1]; A Gomez Lopez[1]; C Collado Moreno[1]; P Gonzalez Perez[1]; JA Sanchez Brotons[1]; S Casquero Dominguez[1]; E Martinez De Morentin[1]; M Maestre Garcia[1]; M Iravedra[1]; J Lozano Cid[1]; P Martinez Romero[1]; FJ Morales Ponce[1]
[1]*Puerto Real Hospital, Cardiology, Puerto Real, Spain*; [2]*Puerto Real Hospital, Internal Medicine, Puerto Real, Spain*

INTRODUCTION: iSLGT2 have shown cardiovascular benefits due not only to a better glycemic control but to weight lo and beter blood pressure and metabolic control. Knowing the limited use of this treatment in Andalucía yet we started a registry of every diabetic patient hospitalized in the Cardiology service and modify their treatment if needed.

METHODS: Prospective and descriptive study of type 2 diabetic patients hospitalized in the Cardiology Service from June 2016 to December 2016, with clinical and laboratory 6-month follow up.

DISCUSSION Out of 750 patients hospitalized 121 were diabetic with 60% male and a mean age of 71 years old. All of them had other cardiovascular risk factors such as hypertension (82%) dyslipidemia (65%) BMI>25 (98%) or smoking history (39%). All were properly treated with beta-blockers, ACE inhibitors, high-intensity statin and antiaggregation drugs. Still 54% of the hospitalizations were due to an acute coronary syndrome, 20% to heart failure (new onset or flare-up) and 20% to arrhythmias. Regarding previous anti-diabetic drugs only 1 patient was already being treated with an iSGLT. As for the rest the majority were treated with metformin and insulin or with the combination of two other oral antidiabetic drugs (most frequently metformin and sulfonylureas).Having said the cardiovascular benefits of the iSGLT2 we started this drugs in every diabetic patient with poor metabolic control. Out of 19 patients that started an iSGLT2 only 1 had an urinary mycotic infection but discontinuation of the treatment was not necessary, 1 patient had an isolated hypoglycemic episode and none suffered from dehydration.There were 4 re-hospitalizations (1 due to hypokalemia,1 due to chest pain with negative ischemic induction test,and 2 due to myocardium infarction) with no deaths in our registry.We also detected a mean weight reduction of 1.2kg ± 2.57, as well as a mean reduction in HbA1c of 0.18 ± 1.9%. Creatinin levels got discreetly better in most of the patients. We also detected a reduction in uric acid (0.18 ± 1.6mg/dl), total cholesterol (30 ± 26mg/dl), LDL (26 ± 31mg/dl) and triglycerides (20 ± 24mg/dl) as well as higher levels of HDL (0.33 ± 20mg/dl). We did not have information about cardiac function at the moment of publication of this study.

CONCLUSION: Following clinical practice guidelines recommendations we started treating diabetic patients with poor metabolic control with SGLT inhibitors with a 6-month follow up, detecting reduction in plasma levels of total cholesterol, LDL, triglycerides and uric acid, as well as HbA1c reduction and weight loss, and also higher HDL plasmatic levels. Up to the publication of this study only 4 patients were rehospitalized with no deaths detected and no important adverse effects. Nevertheless longer tracking period and bigger sample size are needed to validate these findings and evaluate possible long-term adverse effects.

P593

Outcome evaluation of the association of sacubitril/valsartan and iSGLT2 in diabetic patients with heart failure with reduced ejection fraction.

S Blasco Turrion[1]; FJ Camacho Jurado[1]; A Gomez Lopez[1]; I Lobo Torres[1]; R Castilla Ortiz[2]; C Collado Moreno[2]; P Gonzalez Perez[2]; JA Sanchez Brotons[2]; S Casquero Dominguez[2]; M Iravedra[2]; E Martinez De Morentin[2]; M Maestre Garcia[2]; J Lozano Cid[2]; P Martinez Romero[2]; FJ Morales Ponce[2]
[1]*Puerto Real Hospital, Cardiology, Puerto Real, Spain*; [2]*Puerto Real Hospital, Internal Medicine, Puerto Real, Spain*

Introduction: The latest Heart Failure and Cardiovascular Prevention ESC Guidelines have shown the benefits of Sacubitril/Valsartan (LCZ) in reducing rehospitalizations and mortality in patients with heart failure with reduced ejection fraction (HFrEF) that are still symptomatic despite proper treatment with beta-blockers, ACE inhibitors, and MRA drugs. Likewise, these guidelines include iSGLT2, mainly

Empagliflozin, as antidiabetic treatment with important benefits in the prevention and slower progression of heart failure, as well as reducing cardiovascular mortality, due not only to glycemic control but to a better blood pressure and plasma lipid control, and weight reduction. Therefore our goal is to evaluate the progression of patients with HFrED treated with LCZ and an iSGLT2.
Methods: A prospective study of diabetic patients with HFrEF evaluated in the Heart Failure Day-Hospital from September 2016 to December 2017, treated with LCZ and either iSGLT2 or other antidiabetic drugs.
Results: Out of 107 patients evaluated in the Heart Failure Day-Hospital in that period of time, 56 are being treated with LCZ (52%), from which 21 are diabetic patients; 48% are being treated with an iSGLT2 and 52% with either other oral antidiabetic drugs or insulin. In both groups we detected an improvement of their left ventricle ejection fraction, not statistically significant (8.6% ± 10% vs 5.1% ± 8% p = 0.3847) as well as a reduction in plasma NT-proBNP levels (-2229 ± 1329ng/ml vs -2404 ± 1500ng/ml p = 0.7812). Regarding the weight reduction described in pivotal studies, we indeed detected a greater reduction in the patients treated with an iSGLT2 but it was not statistically significant (-2.3 ± 2.9kg vs -0.625 ± 4.5kg p = 0.0963). As for plasma lipid control, we found a greater reduction in total cholesterol and LDL plasma levels in patients treated with other antidiabetic drugs, that was statistically significant (total cholesterol 30 ± 20mg/dl vs -8.6 ± 32mg/dl p = 0.04, LDL 20.6 ± 8mg/dl vs -8.6 ± 24mg/dl p = 0017) while there were no big differences in the increase of HDL plasma levels (-2 ± 7 mg/dl vs 2 ± 14mg/dl p = 0.4255). Likewise, we detected a greater reduction in HbA1c in patients treated with antidiabetic drugs different to iSGL2, statistically significant (-0.15 ± 0.33% vs -0.9 ± 0.77% p = 0.0103). Finally, we did not detect statistically significant differences in complication rates, renal function, ionic or blood pressure control.
Conclusion: In our sample we have not find a statistically significant benefit of the Association of iSGLT2 and LCZ in diabetic patients with HFrEF, in fact, we have detected a worse metabolic control with a disturbing deterioration of plasma lipid control in this patients. Nevertheless, longer tracking period and bigger sample are needed to validate these findings that, at least initially, go against pivotal studies results.

P594

Outcome evaluation of Sacubitril/Valsartan in patients with Heart Failure and reduced ejection fraction with regular follow-up meetings in a Spanish heart failure day-hospital.

S Blasco Turrion[1]; FJ Camacho Jurado[1]; I Lobo Torres[1]; R Castilla Ortiz[1]; A Gomez Lopez[1]; C Collado Moreno[1]; P Gonzalez Perez[1]; JA Sanchez Brotons[1]; S Casquero Dominguez[1]; E Martinez De Morentin[1]; M Maestre Garcia[1]; M Iravedra[1]; J Lozano Cid[1]; P Martinez Romero[1]; FJ Morales Ponce[1]
[1]Puerto Real Hospital, Cardiology, Puerto Real, Spain

Introduction: The latest Heart Failure and Cardiovascular Prevention ESC Guidelines have shown the benefits of Sacubitril/Valsartan (LCZ) in reducing rehospitalizations and mortality in patients with heart failure with reduced ejection fraction (HFrEF) that are still symptomatic despite proper treatment with beta-blockers, ACE inhibitors, and MRA drugs. Therefore our goal is to evaluate the progression of patients with HFrEF treated with LCZ.
Methods: A prospective study of patients with HFrEF treated with LCZ, evaluated in the Heart Failure Day-Hospital from September 2016 to December 2017.
Results: Out of the 107 patients regularly evaluated in the Heart Failure Day-Hospital, 76.4% were male, with a mean age of 66 ± 12 years old. They all had other cardiovascularlar risk factors such as Hypertension (60%), Dyslipidemia (53%), Diabetes (45%) or active smoking (7.5%). 13% of them had had cerebrovascular disease and 54% prior coronary artery disease.
52% of these patients are being treated with Sacubitril/Valsartan, detecting an improvement of left ventricle ejection fraction (6.6 ± 9.2%) and right ventricle function measured by TAPSE (1.16 ± 3.5mm) as well as a reduction in plasma NT-proBNP levels (-3981 ± 11238ng/ml). When compared to those without LCZ we did not find statistically significant differences in weight reduction (-1.29 ± 5kg vs -1.25 ± 5kg p = 0.9671), plasma LDL levels (-20.5 ± 35mg/dl vs -9.7 ± 34mg/dl p = 0.1091) nor plasma HDL levels (4.8 ± 17mg/dl vs 4.7 ± 9.5mg/dl p = 0.97), although there were statistically significant differences in plasma total cholesterol levels, with a greater reduction in patients treated with LCZ (-17 ± 39mg/dl vs 2.6 ± 43mg/dl p = 0.015). We noticed minor hyperkaliemia in 21% of the patients treated with LCZ as well as a 25% of patients without it (p = 0.7477). Finally, regarding complications, there was just 1 death and 2 rehospitalizations due to cardiovascular causes in the group treated with LCZ, while there were 2 deaths and 3 rehospitalizations due to cardiovascular causes in the group without LCZ.
Conclusion: Following the latest Heart Failure Guidelines indications, we started treatment with Sacubitril/Valsartan in patients with reduced ejection fraction that were still symptomatic despite proper treatment with beta-blockers, ACE inhibitors, and MRA drugs, detecting an improvement in cardiac function and reduction in plasma NT-proBNP levels as expected. We also detected a greater reduction in plasma total cholesterol levels, but not in plasma LDL levels. We did not find statistically significant differences in complications or mortality rates until now. Nevertheless longer tracking period and bigger sample are needed to validate these findings.

P595

Effects of irbesartan for renal failure in the patients with chronic heart failure and preserved systolic function and atrial fibrillation

M Muhammad[1]; O Mytrokhina[1]
[1]Dnipropetrovsk medical academy, Dnipropetrovsk, Ukraine

Background: Renal failure is a common disease affecting an increasing number of patients with chronic heart failure (CHF) due to its progression and increased cardiovascular morbidity and mortality. Angiotensin II Receptor Blockers (ARBs) showed renoprotective effects, but the role of ARBs in patients with CHF and preserved systolic function and atrial fibrillation (AF) remains debatable.
Aim: We aimed to evaluate the effects of irbesartan on progression of renal failure in the patients with chronic heart failure and preserved systolic function and atrial fibrillation.
Methods: 31 pts (14 M, 17 F, mean age - 68,63 [45,00;85,00] years) with CHF NYHA I-III class and preserved ejection fraction (LVEF >45%) and AF were enrolled. Pts were divided into 2 groups: 19 (61,29%) pts (1 group) with glomerular filtration rate (GFR) <90 = 60 ml/min/1,73m2 and 12 (38,71%) pts (2 group) with GFR <60 = 30 ml/min/1,73m2. The serum creatinine (SCr) levels were determined in the blood in all pts. GFR was calculated by CKD-EPI formula. All pts received the standard treatment and irbesartan for 12 weeks.
Results: Increased blood pressure (BP) levels correlated to GFR (r=-0,34; p <0,05). After 12 weeks of treatment with irbesartan the SCr levels had been decreased by 9,78 and GFR had been increased by 12% in the 2 group versus 1 group (by 5,45% and 6,82%, respectively (p <0,05)).
Conclusions: The data show, irbesartan therapy may retard progression of CHF and preserved systolic function and AF. Its administration may provide benefits for the reduction of hospitalizations and mortality in its population.

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assessment of physical fitness of patients with heart failure. pilot study

M Malec[1]; M Kaluzna-Oleksy[2]; J Migaj[2]; E Straburzynska-Migaj[2]; A Straburzynska-Lupa[1]
[1]University of Physical Education , Physical Therapy and Sport Recovery, Poznan, Poland; *[2]Poznan University of Medical Sciences, Department of Cardiology, Poznan, Poland*

Background: Heart failure (HF) is a complex pathological process that leads to changes not only in cardiovascular system. Functional and structural changes affect muscular tissue resulting in impairment of functional capacity and leading to lower tolerance of exertion and disability. The Fullerton Fitness Test is a simple diagnostic tool used in rehabilitation of geriatric patients and recently also in people with heart failure, as it reflects changes in fitness and capacity caused by aging.
Aim: The aim of the study was to assess the physical fitness of patients with HF by using Fullerton Fitness Test.
Method: This was a prospective study of 20 men, including 10 with chronic HF with reduced left ventricular ejection fraction (LVEF) (= 40%) in stable clinical state (at least 4 weeks without HF decompensation, defined as no changes in diuretics use), and 10 - control group. They underwent echocardiography with LVEF assessment, laboratory tests with natriuretic peptide evaluation, six-minute walk test (6MWT), and Fullerton Fitness Test, which assessed physical fitness.
Results: Patients with HF had lower LVEF (23.5 ± 7.4 vs. 62.8 ± 4.5, p < 0.001), higher BNP (208.4 ± 201.9 vs. 25.5 ± 19.2, p = 0.0021) and NT-proBNP (1225.6 ± 1055.9 vs. 90.6 ± 139, p < 0.0008). There were no significant differences between the investigated groups as to age (50.90 ± 8.99 vs. 49 ± 9.66, NS) but there was a significant difference in BMI - HF patients had lower BMI (25.33 ± 4.25 vs. 30.96 ± 2.9, NS, p < 0.0015). HF patients showed shorter 6MWT distance (439 ± 146.93 vs. 558.10 ± 62.72, p < 0.0433), longer time of "8-FootUp&Go" (7.42 ± 1.81 vs. 5.74 ± 0.85, p < 0.0433), lower number of repetitions "Chair Stand" (14 ± 5.79 vs. 20.3 ± 5.05, p < 0.0433) and "Arm-Curl" (16.5 ± 5.14 vs. 25.7 ± 4.71, p < 0.0015). Significantly worse results were also obtained in the "BackScratch" (-25.3 ± 17.08 vs. -1.50 ± 5.81, p < 0.0005) and "Chair Sit & Reach" (-17.10 ± 11.82 vs. -4.10 ± 8.02, p < 0,0089). In addition, a positive correlation was observed between LVEF and all test of Fullerton, "6MWT" (r = 0.61,p = 0,004), "Chair Stand"(r = 0.63,p = 0.002), "Arm Curl" (r = 0.7,p = 001), "Chair Sit & Reach" (r = 0.5,p = 0.023), "Back Scratch" (r = 0.71,p < 0.001), " 8-FootUp&Go" (r=-0.59,p = 0.005).
Conclusions: Patients with HF with reduced left ventricle ejection fraction have worse physical performance compared to healthy subjects. The Fullerton Fitness

Test can therefore be used in the comprehensive assessment of patients with heart failure as a repetitive tool for assessing physical fitness.

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Response to cardiac resynchronization therapy improves cognitive function and frailty in older heart failure patients. a prospective, controlled study

S Stefano Tolone[1]; G Pulignano[1]; MD Tinti[1]; D Del Sindaco[1]; A Avella[1]; P De Girolamo[1]; A Di Lenarda[2]; G Barbati[2]; L Tarantini[3]; M Uguccioni[1]
[1]*San Camillo Forlanini Hospital, Heart Failure Clinic, Cardiology1/CCU, Rome, Italy*; [2]*Cardiovascular Center A.S.S. 1 of Trieste, Trieste, Italy*; [3]*San Martino Hospital, Belluno, Italy*

Background: Cognitive impairment (CI) and Frailty are common in older heart failure (HF) patients and are associated with higher hospitalizations rates and worse prognosis. Available evidences suggest that Cardiac Resynchronization Therapy (CRT) could improve cognitive or physical capacity as a consequence of improved cardiac function and, therefore, improved cerebral blood flow. The aim of this study was to assess the effects of CRT on cognitive function and frailty in elderly HF patients.
Material and Methods: Consecutive NYHA II-III HF patients aged >65 years, with EF < 35%, optimized medical therapy with ACE-i/ARB, Beta-blockers and MRA, and life expectancy > 1 year with an indication to electrical device (CRT or ICD) were enrolled. Patients underwent, at baseline and 6 months after device implantation with standard transvenous techniques, a single-blinded clinical, instrumental and multidimensional evaluation of Cognitive function (Folstein MMSE, Trailmaking Test A and B, WAIS Digit Symbol, Verbal Fluency) and frailty (4m gait speed and stand-up time from a chair).
Results: Twenty-nine patients were enrolled: 22 (76%) male, mean age 76 years (65-87), median NYHA class 2.6+0.5 and mean EF 30+4 (22-35). According to ESC guidelines 11 (38%) patients had indication to ICD and 18 (62%) to CRT-D. Two different statistical analysis were performed. In the former the ICD group (n = 11) was compared to the CRT group (n = 18). In the latter ICD and nonresponders to CRT (CRT-NR) patients (n = 17) were compared to CRT responders (CRT-R) (n = 12). There were no significant differences in baseline characteristics between groups, except for QRS duration in CRT and female gender among CRT-R. At 6-month follow-up, compared to ICD group, CRT patients showed a significant improvement of EF, TM-B and TM-A tests, and gait speed. Compared to CRT-NR/ICD group, CRT-R patient showed a more significant improvement of EF, NYHA Class, BNP level, TM-B and TM-A, and gait speed (Figure 1).
Conclusions: Our pilot study suggests that CRT may improve cognitive function and frailty in older HF "responders" patients, with particular regard to executive functions. Assessment of cognitive function and frailty should be recommended before and after device implantation in order to optimize management and evaluate effectiveness.

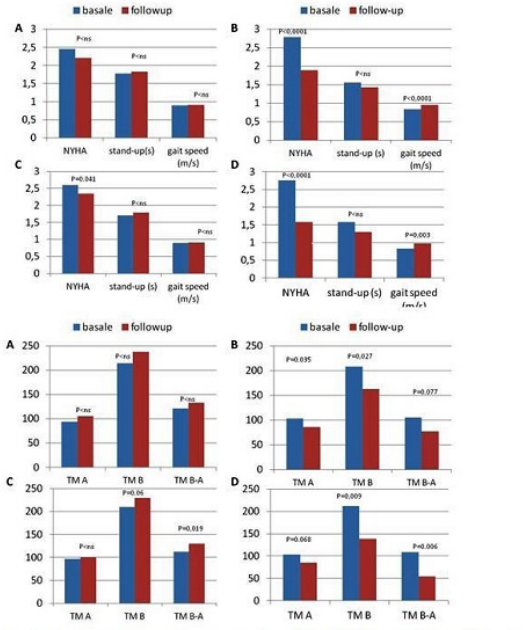

Figure 1. Baseline and follow-up functional capacity, frailty indices and Trial making test A, B and B-A in ICD (A), CRT (B), ICD/CRT-NR (C) and CRT-R patients (D)

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Biventricular stimulation in patients with chronic heart failure with moderate clinical manifestations

ES Atroshchenko[1]; OV Koshlataja[1]; DV Romanovskiy[1]; VA Sujayeva[1]; YP Ostrovskiy[1]
[1]*Republican Scientific and Practical Centre of Cardiology, Minsk, Belarus*

On behalf of: Atroshchenko E.S., Koshlataja O.V., Romanovskiy D.V., Sujayeva V.A., OstrovskiyY.P.

Objective: to assess the effectiveness of CRT (cardiac resynchronisation therapy) implantation in patients with chronic heart failure NYHA functional ?lass II at 12 months
Methods: 52 patients (pts) with ischemic or dilated cardiomyopathy, complicated by CHF NYHA functional ?lass II, LV EF below 35%, QRS duration 150 msec ?nd more and with ECHO confirmed mechanic myocardial dyssynchrony were examined. All patients underwent the LV end-diastolic volume (LVEDV), LV end-systolic volume (LVESV),LV end-systolic diameter (LVESD) LVEF, LV end-diastolic diameter (LVEDD), interventricular delay, dyssynchrony index , all segments max delay were estimated by ECHO. The levels of BNP, the six-minute walk test (6MWT) and life quality (LQ) were measured initially and at 12 months after CRT implantation.
Results: At 12 months LVEDV significantly decreased from 318,41 ± 15,8 ml to 229,06+23,95ml (? < 0,05), LVESV decreased from 241,41 ± 12,9 to 149,6+21,72 (? < 0,05), LVEF increased evidently from 24,17 ± 0,85% to37,81+2,57 % (? < 0,05). Intracardiac hemodynamic changes were accompanied by decreased mechanic dyssynchrony event rate - there was trend to the evident decrease of interventricular delay from 67,7 ± 4,2 to 29,3+6,8msec. (? < 0,05); improved LQ of patients: LQ evidently decreased from 59,9 ± 1,67 scores to 30,8 ± 0,75scores (? < 0,05); 6 MWT increased from 393,2 ± 15,07 m to 477,0 ± 18,43 m; NT-proBNP decreased from 1442,4 ± 277,8 to 287,16 ± 0,75 (? < 0,05).
Conclusions: At 12 months biventricular heart stimulation evidently enhances heart haemodynamic and the clinical conditions of pts, improving exercise tolerance in pts with chronic heart failure NYHA functional ?lass II.

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Aortic telomere length as a potential predictive factor for post transplant allograft function

J Vymetalova[1]; D Dlouha[2]; J Hubacek[2]; V Lanska[3]; I Malek[4]
[1]*Institute for Clinical and Experimental Medicine (IKEM), Cardiac Centre, Cardiovascular Surgery Department, Prague, Czech Republic*; [2]*Institute for Clinical and Experimental Medicine (IKEM), Centre for Experimental Medicine, Prague, Czech Republic*; [3]*Institute for Clinical and Experimental Medicine (IKEM), Statistical Unit, Prague, Czech Republic*; [4]*Institute for Clinical and Experimental Medicine (IKEM), Cardiac Centre, Cardiology Department, Prague, Czech Republic*

Background: Independent of the age, the telomeres may be engaged to the beginning and/or to the progression of cardiovascular diseases. The recipients of orthotopic heart transplantation (OHT) encounters a number of complications which can be connected with the activity of telomerase and length of telomeres. We analyzed how the length of telomeres in aortic DNA correlates with the subsequent post-transplantation development of the organism.
Materials and Methods: During 2005 - 2015 years, we have collected aortic samples of 376 heart recipients (age 50.8 ± 11.8 years) and 383 donors (age 38.6 ± 12.2 years). Relative telomere length in aortic tissue DNA (ArTL) was performed using a quantitative PCR - based method.
Results: Shorter ArTL was detected in heart allograft recipients in comparison to donors (P < 0.0001). Etiology of HF wasn't associated with ArTL of recipients. Patients affected by acute cellular rejection (AR) had significantly shorter ArTL (P < 0.008). Shorter ArTL was detected in patients with implanted mechanical circulatory support before OHT (P < 0.03), and also in subjects who were affected cardiac allograft vasculopathy (CAV; P < 0.05). Overall survival time after heart transplantation was associated only with donors ArTL (P < 0.004).
Conclusions: ArTL differes between donors and recipients independently on sex and age of patients. Changes in ArTL may probably reflect some important mechanisms which contribute to the development of complications after heart transplantation such as AR and CAV.

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Addressing the psycho-educational needs of caregivers of patients with advanced heart failure: a systematic review

L Lorna Cassidy[1]; D Fitzsimons[1]; L Hill[1]; J Mcgaughey[1]; E Greene[1]
[1]*Queen's University of Belfast, School of Nursing and Midwifery , Belfast, United Kingdom*

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Background: Caregivers play a significant role and contribute to the self-care of patients with heart failure. This can be at the expense of their own needs, with limited healthcare resources available to support or reduce caregiver burden. With the increased emphasis on family-centered care there is an urgent need to provide effective psycho-educational care tailored to the needs of caregivers.
Aim: To determine the effectiveness of psycho-educational resources used within published intervention studies for caregivers and thereby inform the components of an intervention.
Methods: A systematic search of PsychInfo, Medline, CINAHL Plus, EMBASE, and SCOPUS databases, citations from relevant articles and expert recommendations was undertaken in November 2017. Randomised controlled trials published in English (2007-2017) with successful psychological outcomes on caregiver burden, caregiver strain, quality of life and depression were assessed. Titles and abstracts were screened, with 39 full texts of potential studies assessed by three independent reviewers. Nine studies were selected and data was subsequently extracted using an inductive approach and methodological quality was assessed.
Results: Nine studies originating from six countries with a total sample size of 1239 participants were included. Qualitative synthesis of the findings identified four themes:
Improved communication by a multidisciplinary team: caregivers desired better communication on the patient's current health status and future treatment plan. Involvement in key discussions and clinical decisions were desired.
Education on heart failure condition and symptoms: caregivers expressed the need for concise written information on how to monitor the patient's heart failure symptoms and what to expect as the condition progresses. Timing of information was vital, with preference being prior to discharge and when the patient became palliative.
Impact of caring on everyday life: practical and problem solving skills to enable the patient to maintain self-care were desired. Communication strategies to help caregivers interact positively with the patient was also considered important.
What to do when symptoms worsen: caregivers wanted knowledge of warning signs indicating deterioration and who, how and when to contact someone in an emergency.
Conclusions: Caregivers have an important and valuable role in the self-care of patients with heart failure. Multidisciplinary teams should involve caregivers in discussions and decisions about the patient's condition. Further research is needed into an intervention amendable to everyday clinical practice.

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Cardioprotective effect of sphingosine 1-phosphate receptor 1 agonist in myocardial infarction and revascularization experimental model

N Ahmed[1]; M Mansoor[2]; D Linardi[3]; M Mansoor[4]; GEBRIE Mebratu[3]; G Rungatscher[3]; G Faggian[3]
[1]University of the Punjab, , Faculty of Health Sciences, Lahore, Pakistan; *[2]King Edward Medical University, Internal Medicine, Lahore, Pakistan*; *[3]University of Verona, Cardiac Surgery Division, Verona, Italy*; *[4]Punjab Institute of Cardiology, Cardiology, Lahore, Pakistan*

Background: Myocardial Infarction is a major health issue and its survival limited by ischemia reperfusion injury leading to heart failure. The mechanism of this phenomenon is not clear because of complicated and complex phathophyiology of this model. In this study, we investigated pharmacological cardioprotective role of Sphingosine 1-Phosphate Receptor 1 agonist an in vivo model of myocardial revascularization.
Methods: We developed in vivo rat models of LAD occlusion and revascularization monitored by invasive hemodynamics measurement. At the beginning of LAD occlusion, animals randomly treated with Sphingosine 1-Phosphate Receptor 1 agonist (Group A, n = 30) or placebo (normal saline) (Group B, n = 30). Half of the animals (Group A1&B1, n = 15 each) were sacrificed after 3 hours and remaining (Group A2&B2) after 14 days of reperfusion. Blood and myocardial tissue were collected for analysis of cardiac biomarkers, inflammatory markers and cell signaling pathways.
Results: Sphingosine 1-Phosphate Receptor 1 agonist treatment activated the cardioprotective reperfusion injury salvage kinase (RISK) and survivor activating factor enhancement (SAFE) pathways leading to decreased myocardial apoptosis and oxidative stress. This improvement contributed in significant recovery of left ventricular systolic and diastolic functions.
Conclusions: Sphingosine-1-phosphate receptor activation with fingolimod increased survival, cardiac function after prolonged myocardial ischemia. Our data strongly support a cardioprotective role for Sphingosine -1–phosphate Receptor-1 agonist activation during reperfusion after myocardial revascularization.

P602

Implantable peritoneal ultrafiltration device: A novel systemic fluid decongestion approach

Y Feld[1]; N Hanani[2]
[1]Sunnybrook Health Sciences Centre, Cardiology, Toronto, Canada; *[2]Paragate Medical LTD, Nazareth, Israel*

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Background: Diuretic therapies aiming to enhance fluid removal in chronic HF are limited due to diuretic resistance in about 30% of the patients. Intravenous diuretics and ultrafiltration as alternatives are associated with side effects, multiple visits and cost. Based on peritoneal dialysis and peripheral ultrafiltration principles, we suggest a novel continuous peritoneal ultrafiltration approach, in which extracellular fluids are slowly prompted through the peritoneal membranes by induction of hydrostatic pressure gradient, into a fully implantable device and cleared to the urinary system. This work tested long term performance and scalability of the concept.
Methods: A flat disk shaped absorption chamber covered by semi-permeable membrane was implanted intraperitoneally in 13 healthy rats (405 ± 33 gr.). Two control rats where implanted with common peritoneal dialysis catheter for comparison of drainage performance. Extracorporeal drainage and sampling of fluids by induction of intermittent hydrostatic vacuum were conducted between 2-3 times a week for period of 4-7 weeks followed by histopathological analysis.
Large model was tested with a fully implantable device in 5 healthy pigs (68.1 ± 5.3kg) up to 6 weeks. Impact of congestion on drainage rate was assessed in another animal by induction of acute venous overload.
Results: In rats, isotonic extracellular fluid was drained at an average rate of 3.2 ± 0.5 cc/kg/hour during follow up period. Unlike designated membrane based chambers, catheters drained 25 folds less per square centimeter. In pigs, the average drainage rate after follow-up was 10 ± 4.9 ml/hr and 210 ± 109 ml/day throughout follow-up period. Overloading central venous pressure acutely from 7 to 16mmHg has doubled drainage rate (0.14 to 0.29 ml/min) despite presence of normal kidney function (increased from 0.4 to 11.7 ml/min). The drained fluid was comparable to serum's electrolytes and toxins, unlike content of secreted Albumin (1.2 ± 0.8 g/dL) that was about one third of the serum Albumin (4.1 ± 0.5 g/dL).
Conclusions: The minimally invasive implantable absorption chamber enables durable systemic extracellular fluids removal through the peritoneal membranes, suggesting of a novel non-aggressive therapy for congested HF patients.

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Chronic application of electrical microcurrent is safe and does not impair cardiac function in sheep

AM Anne-Margarethe Kramer[1]; B Mora[2]; K Macfelda[1]; B Kapellar[1]; K Brandes[3]; K Tillmann[1]; S Hoegler[4]; A Kiss[1]; J Mueller[3]; BK Podesser[1]
[1]Medical University of Vienna, Center for Biomedical Research, Vienna, Austria; *[2]Medical University of Vienna, Anaesthesia, Intensive Care and Analgesia, Vienna, Austria*; *[3]Berlin Heals, Berlin, Germany*; *[4]Veterinary University of Vienna, Department for Pathobiology, Vienna, Austria*

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Background: The application of pulsed electrical signals from CRT or CCM devices improves cardiac function in selected patients beyond the restoration of a synchronized cardiac excitation. In recent publications we have shown that application of direct electrical microcurrent signals improves myocardial function and modifies extracellular matrix components.
Purpose: We wanted to examine whether the chronic application of a moderate microcurrent of 5μA per cm^2 impairs cardiac function to evaluate the upper safety margin for the application of direct microcurrent for the treatment of patients with heart failure.
Methods: By a small left thoracotomy, in five healthy adult sheep (mean weight / age at baseline, 70.8 kg /2.2 years) a epicardial platinum patch electrode (active surface, 36 cm^2) was fixed on the left ventricular free wall by fixation on the pericardium. A coil electrode was implanted transvenously into the right ventricle as counter electrode. Both leads were connected to a battery driven direct microcurrent generator, which supported the leads with a constant current of 180 μA over a mean period of 195 days. Besides a set of different blood chemistry and cell count parameters, left ventricular ejection fraction (LVEF; primary endpoint) and fractional shortening (FS; secondary endpoint) was serially (mean examinations per animal, 12) performed over a follow-up time of 6,5 month by echocardiography and evaluated statistically by non-inferiority testing. Data are given as mean ± SD.
Results: All animals survived the operative procedure and completed the follow-up. Over the observation period the average LVEF increased by 1.4 % from 71.4 to 72.8 % (n.s.). Therefore, the calculated probability to impair the LVEF through microcurrent application by more than 3.9% within 6 months is less than 5 %. The mean FS rose by 4.6 % from 44.8 to 49.4% (P = 0.068, n.s.). A reduction of the FS by more than 5% induced by chronic moderate microcurrent application is

very unlikely (0.05 %). Changes in ECG or signs of infection were not observed. Furthermore, constant levels of hematocrit (32,2% ± 1,8), CK (173,7 U/l ± 50,5) and LDH (415,4 U/l ± 32,5) sustained that no further tissue damage was caused by the chronic application of electrical microcurrent during follow-up compared to baseline levels.
Conclusions: The chronic application of moderate direct electrical microcurrent of 5μA per cm^2 on the hearts of healthy sheep does not compromise heart function. The authors conclude that administration of direct electrical microcurrent for the treatment of heart failure is safe up to a limit of 5μA per cm^2.

Chronic Heart Failure - Prevention

P604
Prevenction of cardiotoxicity during doxorubicin, trastuzumab or pertuzumab treatment by Icz 696 administration in our in vitro model

N Maurea[1]; R Paciello[1]; G Piscopo[1]; G Sorrentino[1]; F Maurea[1]; C Coppola[1]; C De Lorenzo[2]
[1]Istituto Nazionale per lo Studio e la Cura dei Tumori Fondazione Giovanni Pascale - IRCCS, Division of Cardiology, Naples, Italy; *[2]University 'Federico II', Department of Molecular Medicine and Medical Biotechnology , Naples, Italy*

Background: Cardiotoxic effects related to anticancer drugs are among the leading causes of morbidity and mortality in cancer patients treated with Doxorubicin (DX), Trastuzumab (T) and Pertuzumab (P), antineoplastic drugs used in the treatment of breast cancer. Sacubitril-valsartan (LCZ 696), a drug used for the treatment of heart failure in patients with a reduced ejection fraction, is a combination drug, made up of neprilysin inhibitor sacubitril and angiotensin II receptor blocker valsartan.
Purpose: In this study, we aim to assess whether LCZ 696, administered during DX, T or P treatment, reduces in vitro anticancer drugs-related cardiotoxicity, compared to Valsartan (V), used as a control drug.
Methods: Our in Vitro model, the H9C2 rat cardiomyoblasts, were seeded in 96-well plates at a density of 1 x 104 cells/well and incubated at 37°C with 5% CO2 for 16 hours. After the addition of 200 nM of T, P or DX in the culture medium, cells were incubated for further 72 hours. Cells were then treated in the absence or presence of 10 μM of LCZ 696 or V for additional 3 days. Cells viability was evaluated by trypan blue exclusion test; the percentage of viable cells compared to control untreated cells express cell survival.
Results: LCZ 696 reduced significantly T, P and DX related toxicity in H9C2 cardiomyoblasts as evidenced by the higher percentage of viable cells treated with combinations of T, P or DX with LCZ 696 with respect to cells treated with T, P or DX alone ($p < 0.001$).
V reduced significantly T and DX related toxicity in H9C2 cardiomyoblasts treated with combinations of T or DX and V with respect to the cells treated with T or DX, used as single agents ($p < 0.001$). However, there was no significant reduction of toxicity when H9C2 cells were treated with P + V.
Thus, both LCZ 696 and V reduced significantly DX related toxicity when administered to H9C2 cardiomyoblasts after the antineoplastic treatment (no significant difference between LCZ 696 and V treatment, $p = 0.6$).
Moreover, LCZ 696 was significantly more effective than V ($p < 0.001$) in reducing both T and P related toxicity when administered to cultures of H9C2 cardiomyoblasts after antineoplastic treatments.
Conclusions: These results show that LCZ 696 administration, during DX, T or P treatment, significantly increases the viability of treated cells, thus reducing cardiotoxic effects of these drugs, as demonstrated by our in vitro experiments. The future purpose is to test LCZ 696 in in vivo models as well, in order to assess its capability to blunt left ventricular dysfunction after antineoplastic treatments.

Chronic Heart Failure - Clinical

P605
Prognostic role of structural changes of large arteries and peripheral blood flow in patients with chronic heart failure

I Shkurat[1]
[1]Institute of Heart, Kyiv, Ukraine

Purpose: To investigate the dependence of structure of a.femoralis (a.F) and peripheral blood flow (PBF) on severity and 12-months survival prognosis of chronic heart failure (CHF).
Methods: Ultrasonography of a.F, a.dorsalis pedis (a.DP) were performed in 129 patients (age 56.6 ± 1.2 years; 89 males) with stable CHF (NYHA II-III) and LVEF < 40% and in 40 age-matched healthy subjects. Diameter (D), intima-media thickness (IMT) of a.F, velocities (Vps and Ved) in a.DP were measured; index of relative wall thickness (RWT) of a.F: RWT = IMT/D; index of peripheral resistance (RI): RI=(Vps-Ved)/Vps. Kaplan-Meier 12-months survival analysis was performed for RWT as well as for Vps, Ved, RI in a.DP based on 'below median vs. above median' approach.
Results: In pts with CHF IMT and RWT were significantly higher (IMT: 0.99 ± 0.16 vs 0.59 ± 0.09mm, $p < 0.001$; RWT: 0.16 ± 0.03 vs 0.10 ± 0.01unit, $p < 0.001$). Vps and Ved in a.DP were significantly lower in pts with CHF (39.3 ± 2.1 vs 56.4 ± 6.6cm/s, $p < 0.01$ and 5.2 ± 0.8 vs 12.9 ± 1.7cm/s, $p < 0.01$, respectively), and RI in a.DP was significantly higher (0.83 ± 0.04 vs 0.77 ± 0.02unit, $p < 0.01$). These changes become more pronounced in pts with NYHA class III-IV than in NYHA class II (Vps 32.3 ± 1.9 vs 35.7 ± 2.1cm/s, $p = 0.03$, Ved 5.8 ± 0.7 vs 6.9 ± 1.3cm/s, $p = 0.03$ and RI 0.84 ± 0.03 vs 0.82 ± 0.02unit, $p = 0.04$, respectively). Kaplan-Meier 12-months survival analysis was performed in relation to the RWT ($p = 0.038$), Vps in a.DP ($p = 0.04$), Ved in a.DP ($p = 0.037$) and RI in a.DP ($p = 0.04$). Significantly lower survival was apparent in pts with RWT>0.16, Vps < 36?m/s, Ved < 6?m/s, RI>0.84unit.
Conclusions: The present study indicates that remodeling of peripheral blood vessels is accompanied by decrease peripheral arterial blood flow and by increase in resistance of resistive vessels in patients with CHF. RWT, Vps, Ved and RI in a.DP may be used for mortality risk stratification in patients with CHF.

P606
Reversibility of heart failure-specific changes in systemic metabolomics through mechanical cardiac unloading in end-stage HF patients

MS Marion Susanna Hilse[1]; R Pistulli[1]; T Kretzschmar[1]; M Franz[1]; T Bekfani[1]; S Moebius-Winkler[1]; M Kiehntopf[2]; S Neugebauer[2]; J Gummert[3]; H Milting[3]; PC Schulze[1]
[1]University Hospital of Jena, Internal Medicine I, Dept. of Cardiology, Jena, Germany; *[2]University Hospital of Jena, Institute of Clinical Chemistry and Laboratory, Jena, Germany*; *[3]Heart and Diabetes Center NRW, Bad Oeynhausen, Germany*

Aims: Metabolism is impaired in advanced heart failure (HF) and mechanical unloading through implantation of left ventricular assist devices (LVADs) is known to improve clinical symptoms and hemodynamics in patients with end-stage HF. The aim of this study was to systematically evaluate systemic metabolic changes in end-stage HF patients before and after LVAD therapy in comparison to non-diseased controls.
Methods: 181 serum metabolites were assessed in serum of 40 end-stage HF patients (n = 20 ICM, n = 20 DCM, mean EF 21.5 ± 6.0 %, LVEDD 69.4 ± 12.3mm) before and after LVAD implantation as well as 20 controls using liquid chromatography tandem mass spectrometry. Metabolomic measurement in HF patients were repeated at 30 days and 100 days post-LVAD implantation. Principal component analyses (PCA) with heatmapping of measured metabolites were performed in order to assess group differences in metabolites.
Results: Following LVAD implantation, echocardiographic parameters of HF patients improved (100 d post-LVAD: EF from 21.5 ± 6.0 to 26.1 ± 6.7 %, $p = 0.003$; LVEDD 69.4 ± 12.3 to 59.6 mm ± 14.5 mm, $p < 0.0001$). A clear separation of HF patients and control individuals but not between HF subgroups was evident in the PCA analyses of serum metabolites. In HF patients compared to controls, we found a significant decrease of phosphatidylcholines and sphingolipids (2.7-fold, $p < 0.0001$) as well as an increase in acylcarnitines (3.0-fold, $p < 0.0001$). There were no significant intergroup differences preceding LVAD or at 30 days following LVAD implantation. In DCM, but not ICM patients, phosphatidylcholines increased after 100 days LVAD therapy (1.6-fold, $p = 0.01$). Such partial reversibility was not observed for acylcarnitines or other metabolites.
Conclusions: In line with our previous observations, we found distinct alterations of serum metabolites in advanced HF patients. Following LVAD therapy, a partial reversibility of these metabolic alterations, in particular involved in fatty acid metabolism, occurs in patients with DCM. Further studies are needed to explore possible metabolic differences between ischemic and non-ischemic HF as well as their response to LVAD therapy.

Chronic Heart Failure - Other

P608
Budget impact of IV iron therapy with ferric carboxymaltose in patients with chronic heart failure and iron deficiency in France

M Mathilde Faller[1]; FO Champs[1]; H Moutier[1]; K Levesque[2]; S Bourguignon[1]; A Cohen-Solal[3]
[1]IQVIA, Health Economics and Outcome Research, paris, France; *[2]Vifor Pharma, Health Economics and Outcome Research, paris, France*; *[3]Hospital Lariboisiere, Cardiology, Paris, France*

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Introduction: Iron deficiency (ID) is highly prevalent in patients with systolic chronic heart failure (CHF). CHF with ID is a major cause of hospitalization and represents a major cost for national healthcare budgets. The ESC recommends intravenous (IV) iron therapy with ferric carboxymaltose (FCM) as the only treatment against ID for such patients.
Purpose: This analysis aims to evaluate the budget impact of IV iron therapy with FCM for patients with systolic CHF and ID, from the French public health insurance perspective.
Methods: A budget impact model was adapted to forecast the budget impact over a 5-year horizon, as the difference of costs between two scenarios: one where patients can be either treated for ID by 1000 mg of FCM annually, or not treated for it, and the other where patients are not treated for ID. Cost saving can be through NYHA class improvement, lower rate of hospitalizations, and shorter length of stay. Clinical data were extrapolated from pooled data from four randomized controlled FCM trials (FER-CARS-01, FAIR-HF, EFFICACY-HF and CONFIRM-HF) using regression models. The time horizon was extended to 5 years by applying transition probabilities estimated from CONFIRM-HF. Our model used data from the FCM arms of these trials for patients treated with FCM, and data from the placebo group for patients not treated for ID. Epidemiological parameters for France were derived from the literature. To document costs, the French Diagnostic-Related Groups and hospital activity from the national hospitalizations database (PMSI), as well as national recommendations were used. Market shares of FCM were based on forecasts. Secondary scenario and univariate sensitivity analyses assessed the influence of various factors, including FCM dose, cost of other medication, hospitalization, or outpatient visits by NHYA levels.
Results: In the primary analysis, the modelled 5-year cost difference between the scenarios with and without FCM in a population of 189 334 prevalent and incident patients with CHF+ID was −881 834€, giving a negative budget impact of increased use of FCM for health insurance. The cumulative savings resulted from lower hospitalization costs due to CHF worsening (-€35.8M€) and follow-up (-2.9 M€). These CHF cost savings outweighed costs for FCM treatment (37.7 M€). In sensitivity analyses, the budget impact varied from -16 M€ to +146 M€ if the hospitalization rate for patients not treated for ID either improved or reduced by 25%. Other factors with a budget impact were the dose used (+36 M€ with a dose of 1679 mg), the absence of hospitalization cost differentiation between NYHA classes (−12 M€ if costs are differentiated), and administration settings (-34 M€ if another administration setting is used).
Conclusion
Increased use of FCM in France is expected to meet a medical need in patients with CHF+REF and ID with a minimum economic impact on the French public healthcare system.

P609
Flow-mediated vasodilatory response in patients with chronic heart failure

I Shkurat[1]
[1]*Institute of Heart, Kyiv, Ukraine*

Purpose: To establish the dependence of endothelium-mediated vasodilatory response on severity, etiology of CHF, depending on the availability of the phenomenon of insulin resistance and 12-months survival prognosis of CHF.
Methods: We examined 106 hemodynamically stable CHF patients (pts), NYHA II-IV, LVEF < 40%. Hypertensive heart disease (HHD) was established in 66 pts and dilated cardiomyopathy (DCMP) in 40 pts. 42 pts (’40%) had IR. Diameter of a.brachialis (D) was detected ultrasonographically before (D1) and after (D2) standard forearm cuff test. Flow-mediated vasodilation (FMV) was calculated by formula: (D2-D1)/D1 × 100%. Insulin resistance index (HOMA-IR) was calculated according to the formula: fasting insulin (microU/L) x fasting glucose (nmol/L)/22,5. IR was based on the value of the index HOMA^{3}2,77. Kaplan-Meier 12-months survival analysis was performed for FMV based on ‘below-median vs above-median’ approach.
Results: In CHF pts FMV was significantly impaired in comparison to age-matched controls (6,8 ± 0,5% vs 11,04 ± 1,3%, p < 0,01). More pronounced impairment of FMD in III-IV NYHA class pts than in II NYHA class was observed (6,3 ± 0,8% vs 7,1 ± 1,1%, p = 0,03). In DCMP FMV was significantly worse than in HHD (5,5 ± 0,8% vs 7,4 ± 1,3%, p < 0,001) despite comparable LVEF (p = 0,47) and NYHA class (p = 0,62) in both groups. In IR pts FMD was significantly lower than in pts without IR (5,2 ± 0,8% vs 7,9 ± 1,3%, p < 0,03). Respectively, significant correlation relationship was found between HOMA index and FMV (rho=-310,p = 0,004). 12-months survival was significantly better in group with better (above-median) FMV (93% of pts alive vs 85% of pts alive in below-median group, p = 0,047), although LVEF in both groups were comparable (33,5 ± 8,1% vs 32,1 ± 7,3%, p = 0,32).
Conclusions: In CHF FMV is pronounsly impaired, particularly in NYHA III-IV, DCMP pts and IR pts. The better FMV responders demonstrated the better 12-months survival than worse responders despite comparable LVEF in both groups.

Acute Heart Failure - Pathophysiology and Mechanisms

P610
Myocardial infarction is sufficient to increase GLP-1 secretion leading to improved left ventricular contractility and mitochondrial respiratory capacity

M Michael Lehrke[1]; S Diebold[1]; J Moellmann[1]; F Kahles[1]; E Haj-Yehia[1]; A Nickel[2]; C Maack[2]; N Marx[1]
[1]*RWTH University Hospital Aachen, Cardiology, Aachen, Germany*; [2]*DZHI, Cardiology, Würzburg, Germany*

Background and aims: The incretin hormone GLP-1 holds cardioprotective efficacy and was recently found to be increased by inflammatory stimuli. This study was performed to characterize the secretion of GLP-1 in response to myocardial infarction in mice and investigate its functional relevance.
Background and aims: The incretin hormone GLP-1 holds cardioprotective efficacy and was recently found to be increased by inflammatory stimuli. This study was performed to characterize the secretion of GLP-1 in response to myocardial infarction in mice and men and investigate its functional relevance.
Materials and Methods: GLP-1 plasma levels were assessed in 143 patients following myocardial infarction and 15 controls. Myocardial infarction (MI) was induced by permanent LAD ligation in 6 week old, male C57BL/6J mice, the dipeptidylpeptidase-4 (DPP-4) inhibitor linagliptin (3 mg/kg p.o., bid) was given for 3 days before to LAD ligation, GLP-1 and exendin-9 (both 100 nM/kg i.p.) were given for 1 day before LAD ligation, experiments were performed in wild type and GLP-1 Receptor KO mice.
Results: GLP-1 plasma levels were elevated in patients at days 1-3 after myocardial infarction, but not thereafter. Induction of Myocardial infarction in mice led to a significant increase of circulating GLP-1 concentrations (from 7.9 pM to a maximum of 20.8 pM after 6 hours; n = 6; p < 0.05 in comparison to baseline and sham control). Prevention of GLP-1 degradation by pretreatment with linagliptin increased left ventricular contractility (10101 ± 1690 dp/dt by Millar catheter) relative to control (7830 ± 1445 dp/dt; p < 0.05 n = 8) 6h post MI, while antagonism of the GLP-1 receptor (exendin-9; 100 nM/kg i.p., 1 day pretreatment) worsened contractility (6469 ± 944 dp/dt; p < 0.05 n = 7). Further, linagliptin failed to improve left ventricular function in GLP-1 receptor KO mice demonstrating a GLP-1 receptor-dependent effect. Mechanistically we found linagliptin or GLP-1 pretreatment to similarly increase myocardial AMPK-activation in non-infarcted tissue (1.6 fold induction by linagliptin; p < 0.01 n = 6; 1.5 fold induction by GLP-1; p < 0.04 n = 4;), which was associated with improved respiratory capacity of isolated mitochondria from non-infarcted myocardial tissue (2 fold induction by GLP-1; p < 0.04 n = 6; 1.7 fold induction by DPP-4 inhibition; p < 0.04 n = 7) detected by Clark electrode.
Conclusion: Myocardial infarction is a GLP-1 secreting stimulus, which improves left ventricular function in a GLP-1 receptor dependent manner. This is amplified by linagliptin dependent DPP-4 inhibition leading to AMPK-activation and improved mitochondrial respiration of cardiomyocytes in non-infarcted tissue.

Acute Heart Failure - Diagnostic Methods

P611
Circular RNA MICRA predicts heart failure after acute myocardial infarction

M Vausort[1]; A Salgado-Somoza[1]; L Zhang[1]; Y Devaux[1]
[1]*Luxembourg Institute of Health, CVRU, Strassen, Luxembourg*

On behalf of: On behalf of the Cardiolinc network (www.cardiolinc.org)
Funding Acknowledgements: Ministry of Higher Education and Research of Luxembourg and Society for Research on Cardiovascular Diseases.

Background: Predicting heart failure (HF) development after acute myocardial infarction (AMI) would allow tailoring healthcare to each individual. Yet, this task is still challenging due notably to limited accuracy of current biomarkers such as brain natriuretic peptides (BNP) in this setting. In our search of novel biomarkers, we previously identified a circular RNA named MICRA (Myocardial Infarction-associated Circular RnA) which was associated with HF after AMI.
Purpose: Here, we addressed the ability of MICRA to risk stratify AMI patients according to the 3-group classification of HF defined by the ESC: HF with reduced ejection fraction (HFrEF, EF < 40%), mid-range EF (HFmrEF, EF 40-49%) and preserved EF (HFpEF, EF > 50%). In addition, we addressed the function of MICRA in lymphocytes.

Methods: MICRA expression was measured by quantitative PCR using divergent primers in whole blood samples obtained at reperfusion in 472 AMI patients. Left ventricular EF was determined at 4 months using echocardiography. Multivariable analyses with ordinal regression were conducted to determine the ability of MICRA to classify patients into 3 EF groups.
Results: Eighty seven patients (18%) had HFrEF, 106 (22%) had HFmrEF and 279 (59%) had HFpEF at 4 months. Expression levels of MICRA were lower in patients with HFrEF compared to patients with HFmrEF and HFpEF ($p < 0.001$), and were comparable between patients with HFmrEF and HFpEF. MICRA classified patients into 3 EF groups with an adjusted odds ratio [95% confidence interval] of 0.78 [0.64-0.95]. Patients with low levels of MICRA were at high risk of reduced EF. Computation of the Akaike Information Criteria and bootstrap internal validation attested that MICRA improved the predictive value of a multivariable clinical model including BNP ($p = 0.012$). In AMI patients, MICRA was positively associated with lymphocytes count ($p < 0.0001$) and T cell markers CD4 and CD8. In vitro experiments in Jurkat T cells showed an overexpression of MICRA upon stimulation by anti-CD3/CD28 ($p = 0.003$), which was accompanied by a blunting of cell proliferation. These results suggest a potential implication of MICRA in T-cell proliferation/activation/differentiation.
Conclusion: These results confirm and strengthen the ability of MICRA to predict HF and improve risk stratification after AMI. MICRA is expressed by T lymphocytes and may find utility in future prognostication strategies aiming to personalize healthcare of AMI patients (Figure).

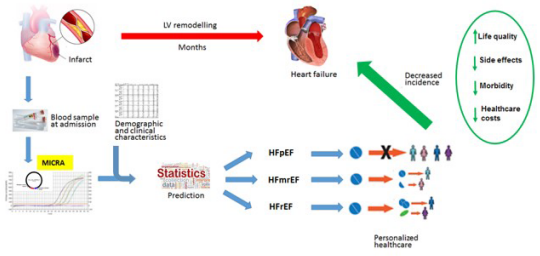

Figure: MICRA is a novel prognostic biomarker for personalized healthcare of acute myocardial infarction patients.

P612
Cardiac enriched lncRNAs as a novel class of biomarkers for heart condition and prediction of heart failure

E Eric Schordan[1]; L Zhang[2]; S Danilin[1]; S Ounzain[3]; D Atar[4]; P Leszek[5]; H Firat[1]; T Pedrazzini[3]; Y Devaux[2]
[1]Firalis SAS, Molecular Diagnostics, Huningue, France; *[2]CRP-Sante, Cardio Vascular Research Unit, Luxembourg, Luxembourg*; *[3]University Hospital Centre Vaudois (CHUV), Experimental Cardiology Unit, Lausanne, Switzerland*; *[4]Ulleval University Hospital, Department of Cardiology B, Oslo, Norway*; *[5]Institute of Cardiology, Heart Failure and Transplantology Department, Warsaw, Poland*

On behalf of: On behalf of the Cardiolinc™ network (www.cardiolinc.org).
Funding Acknowledgements: EUREKA Eurostars E!11020

Background: In recent years, long non-coding RNAs (lncRNAs) have emerged as a new type of non-coding RNAs with potential as biomarkers in various cardiovascular pathologies. In contrast to other non-coding RNAs such as microRNAs, lncRNAs lack strong sequence conservation across species but can be highly tissue-specific. Cardiovascular disorders such as coronary artery disease, acute myocardial infarction (AMI) and heart failure (HF) are leading causes of mortality and morbidity in the modern World. A consensus emerged that more personalized healthcare would allow stopping the "epidemic" raise of the burden of cardiovascular disease, especially HF. However, to move forward towards personalized healthcare, novel biomarkers reflecting cardiac function and able to aid in diagnosis, prognosis, monitoring of drug effects and disease activity, are needed.
Purpose: In the present study, we aimed to identify cardiac-enriched lncRNAs associated with HF which can be used as biomarkers.
Methods: We performed deep sequencing in 26 cardiac biopsies from failing (11 end-stage ischemic cardiomyopathy and 10 end-stage non-ischemic cardiomyopathy) and non-failing (n = 5) human hearts.
Results: An average of 211 M reads of total-RNA-Seq librairies were generated. From these data, we identified a panel of 3353 lncRNAs that were either cardiac-enriched or differentially expressed between failing and non-failing hearts, including 1036 novel lncRNAs (i.e. not described in GENCODE database). To test their potential as biomarkers, we performed RNA-Sequencing in whole blood collected in PAXgene tubes in 57 AMI patients and in plasma samples collected from AMI patients and control subjects. We found that out of the 3353 lncRNAs identified in cardiac biopsies, 2171 were detectable in whole blood samples and 2669 in plasma samples. Moreover, cardiac lncRNAs were up-regulated in patients with AMI compared to controls. Interestingly, we identified 150 lncRNAs differentially expressed between patients developing HF 1 month after AMI compared to patients not developing HF.
Conclusion: These results motivate the development of a molecular diagnostic kit for the measurement of cardiac enriched lncRNA based on capture probes technology for a for high throughput targeted sequencing approach that can be applied on large cohort of patients to assess cardiac lncRNAs.

P613
Cyclin dependent kinase inhibitor 1 C is a female-specific marker of left ventricular function after acute myocardial infarction

T Lalem[1]; L Zhang[1]; M Scholz[2]; R Burkhardt[3]; V Saccheti[1]; A Teren[4]; J Thiery[3]; Y Devaux[1]
[1]Luxembourg Institute of Health, CVRU, Strassen, Luxembourg; *[2]University of Leipzig, Institute for Medical Informatics, Statistics and Epidemiology, Leipzig, Germany*; *[3]Leipzig University Hospital, Institute of Laboratory Medicine, Clinical Chemistry and Molecular Diagnostics, Leipzig, Germany*; *[4]Heart Center of Leipzig, Leipzig, Germany*

On behalf of: On behalf of the Cardiolinc™ network (www.cardiolinc.org)
Funding Acknowledgements: Ministry of Higher Education and Research and the Society for Research on Cardiovascular Diseases of Luxembourg.

Background: A significant proportion of patients develop left ventricular (LV) remodelling leading to heart failure after acute myocardial infarction (AMI). Being able to identify these patients would represent a step forward towards personalized medicine. Since men and women with AMI have different clinical profiles, risk factors, pathophysiology and outcome, it is important to find ways to risk stratify patients in a gender-specific manner.
Purpose: To determine the ability of cyclin dependent kinase inhibitor 1C (CDKN1C) to risk stratify AMI patients, in a gender-specific manner.
Methods - CDKN1C expression was measured in blood samples obtained at admission in a test cohort of 447 AMI patients and a validation cohort of 294 patients. The study end-point was LV function assessed by the ejection fraction (EF) at 4-month follow-up. Patients were either classified as having a reduced EF (rEF, < 40%), mid-range EF (mrEF, 40-49%) or preserved EF (pEF, > = 50%).
Results - In the test cohort, CDKN1C was lower in rEF patients compared to mrEF and pEF patients. This observation was specific to women (Figure 1). Furthermore, CDKN1C was a significant univariate predictor of LV function only in women with an odds ratio (OR) [95% confidence interval (CI)] of 0.56 [0.37-0.83]. In multivariable analyses adjusted for [age, body mass index, white blood cells count, CPK, cTnT, Nt-proBNP, ischemic time (i.e. delay between chest pain onset and reperfusion), gender, history of AMI, diabetes, hypertension, hypercholesterolemia, smoking and infarct type (STEMI vs NSTEMI)], CDKN1C was a strong predictor of LV function in women (OR [95% CI] 0.44 [0.23-0.82]) but not in men (0.90 [0.70-1.16]). On the opposite, Nt-proBNP was associated with LV function in men (1.85 [1.37-2.47]) but not in women (1.06 [0.55-2.0]). CDKN1C increased the predictive value of the clinical model as attested by a decrease of the Akaike information criterion (AIC). This effect was present in women ($p = 0.006$) but not in men ($p = 0.41$). Of note, contrarily to the area under the curve, the AIC is penalized by the number of covariates, thus avoiding model overfitting. A decreased AIC indicates an improvement of prediction. The incremental predictive value of CDKN1C specifically in women was confirmed using bootstrap internal validation. The female-specific association of CDKN1C with LV function after AMI was validated in the independent cohort: OR [95% CI] 0.18 [0.04-0.90] in women and 0.67 [0.29-1.58] in men.
Conclusion: CDKN1C is a novel female-specific biomarker of LV function after AMI. If replicated in additional patient cohorts, this finding may help personalizing healthcare of AMI patients, in a gender-specific manner.

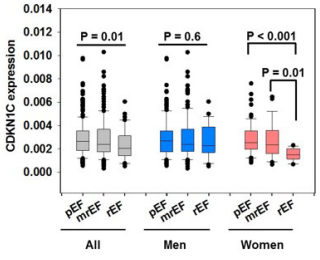

Figure 1. Expression of CDKN1C in the three EF groups, in all patients of the test cohort (n=447) and in men (n=338) and women (n=109) separately.

Acute Heart Failure - Treatment

P614

Omecamtive mecarbil evokes electromechanical dissociation in the rat: beyond positive inotropy

GA Fulop[1]; T Csipo[1]; L Nagy[1]; A Kovacs[1]; SL Helgadottir[1]; R Porszasz[2]; B Horvath[3]; P Nanasi[3]; A Olah[4]; T Radovits[4]; B Merkely[4]; I Edes[5]; Z Csanadi[5]; Z Papp[1]; A Toth[1]

[1]University of Debrecen, Faculty of Medicine, Disivion of Clinical Physiology, Debrecen, Hungary; *[2]University of Debrecen, Faculty of Medicine, Department of Pharmacology and Pharmacotherapy, Debrecen, Hungary*; *[3]University of Debrecen, Faculty of Medicine, Department of Physiology, Debrecen, Hungary*; *[4]Semmelweis University, Heart and Vascular Center, Budapest, Hungary*; *[5]University of Debrecen, Faculty of Medicine, Department of Cardiology, Debrecen, Hungary*

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Background: The cardiac myosin activator omecamtiv mecarbil (OM) improves the contractility of the failing heart via increased number of acto-myosin interactions and prolonged systole. These promising cardiotonic effects of OM have been reported in preclinical and phase I/II clinical investigations. However, there is limited preclinical information on OM.
Purpose: Here we investigated the alternative cardiac mechanisms of action of OM beyond positive inotropy.
Methods: In vivo effects of OM were studied on Wistar-Kyoto rats by left ventricular (LV) hemodynamic analysis (n = 10), echocardiography (n = 10) and blood pressure measurement by carotid artery catheterization (n = 10). OM was administered through a jugular venous canule in increasing doses from baseline (BASE) up to 200, 600 and 1200 μg/kg cumulative doses. In vitro effects of 0.1 and 1 μM OM were tested on isolated LV myocytes. Action potential characteristics, calcium transients and unloaded cell shortening were studied on isolated canine (n = 9), and force generation was studied on human donor (n = 9) cells.
Results: LV systolic function was improved upon treatment with OM (ejection fraction, %: BASE: 70 ± 2; 200 μg/kg: 72 ± 4; 600 μg/kg: 78 ± 5; 1200 μg/kg: 82 ± 8; and dP/dtmax, mmHg/s: BASE: 9102 ± 597; 200 μg/kg: 9633 ± 533; 600 μg/kg: 10683 ± 594; 1200 μg/kg: 11055 ± 437). At the same time, we found dose-dependent deleterious effects of OM on diastolic function: decrease of E/A ratio (BASE: 2.0 ± 0.1; 200 μg/kg: 1.7 ± 0.1; 600 μg/kg: 1.4 ± 0.1; 1200 μg/kg: non measurable) and dP/dtmin (mmHg/s: BASE: -11622 ± 607; 200 μg/kg: -10548 ± 710; 600 μg/kg: -10704 ± 810; 1200 μg/kg: -9751 ± 679), and increase of isovolumetric relaxation time (ms: BASE: 22.3 ± 1.3; 200 μg/kg: 31.7 ± 2.3; 600 μg/kg: 35.1 ± 1.8; 1200 μg/kg: 50.7 ± 4.2) and tau (ms: BASE: 9.2 ± 0.4; 200 μg/kg: 10.4 ± 0.5; 600 μg/kg: 12.6 ± 0.1; 1200 μg/kg: 15.4 ± 0.7). These results are in accordance with the dose-dependent effects of OM on skinned myocytes enhancing not only Ca2+-dependent active force, but Ca2+ sensitivity (pCa50) and Ca2+-independent passive force of the contractile machinery. In vivo at 1200 μg/kg OM evoked an electromechanical dissociation in 76.6% of cases (n = 23 of total 30): with continuous ECG every effective contraction was followed by an ineffective one. In line with this phenomenon, at the myocyte level, we found alternating action potential, calcium transient and cell shortening upon administration of 1 μM OM at high pacing frequencies (4 and 5 Hz). Finally, the above mentioned cardiac alterations at high (1200 μg/kg) dose led to a significant decrease of blood pressure (vs. BASE: systolic: -59 ± 9%; diastolic: -63 ± 11%).
Conclusion: OM improves LV systolic function, but induces diastolic dysfunction even at low doses in the rat. In addition, OM can evoke periodical electromechanical dissociation beyond myosin sensitization.

P615

Predicting mortality in patients with ECMO: is the SAVE score applicable in our population?

N Nahikari Salterain Gonzalez[1]; R Manrique Anton[2]; J Ibero Valencia[1]; E Iglesias Colino[1]; JJ Gavira Gomez[1]; G Rabago Juan-Aracil[2]

[1]University of Navarra, Cardiololgy, Pamplona, Spain; *[2]University of Navarra, Cardiac Surgery, Pamplona, Spain*

Introduction and Objectives.
The newly created SAVE score has overcome previous scores in predicting survival after an urgent veno-arterial extracorporeal membrane oxygenator implantation (vaECMO).
The objective of our study was to assess the applicability of this new tool in our population.
Material and Methods.
All patients in cardiogenic shock who underwent a vaECMO implantation in our center between January 2007 and December 2017 were included. The SAVE score was calculated retrospectively for each patient. Data were collected from the hospital ventricular assist devices database.
We evaluated: 1) the total mortality of the group, 2) the classification and mortality of our series according to the SAVE score and 3) the utility of this score in our population.
Results: Thirty-two patients were included, 56% being above 63 years old. The most frequent cardiomyopathy was ischemic heart disease (47%) and the indication for ECMO implantation in 69% of them "bridge to transplant", qualified as "other" in the SAVE diagnosis variable. 56% had acute kidney injury prior to implantation and 44% liver dysfunction. In 91% of the cases, peripheral access was preferred. The Levitronix Centrimag was the most frequently used device. The majority of patients were included in the higher risk group of the score.
The in-hospital mortality was 53% (16 patients with the device in situ and one weeks after explantiation). The distribution of patients for each group of the classification and mortality is shown in Table 1.
Conclusions.
Our results are comparable to those published in international registries. Even though the profile of our patients may be different from those included in the score, both the distribution of patients per group and the mortality resembles the SAVE score. The use of this score is feasible in our setting but further experience may be needed.

Table 1. Mortality.

SAVE score	CUN		
Classification	Mortality (%)	N	Mortality n (%)
I	25	0	0
II	42	5	0
III	58	5	2(40)
IV	70	12	6 (50)
V	82	10	9 (90)

Coronary Artery Disease - Pathophysiology and Mechanisms

P616

Measuring coronary artery calcium with high-pitch computed tomography acquisition: is it as consistent as prospective acquisition

L-L Lan-Linh Truong[1]; F Erthal[1]; O Clarkin[1]; A Hossain[2]; Y Yam[1]; J Inacio[3]; BJW Chow[1]

[1]University of Ottawa Heart Institute, Cardiac Imaging, Ottawa, Canada; *[2]University of Ottawa Heart Institute, Cardiovascular Research Methods Centre, Ottawa, Canada*; *[3]The Ottawa Hospital, Radiology, Ottawa, Canada*

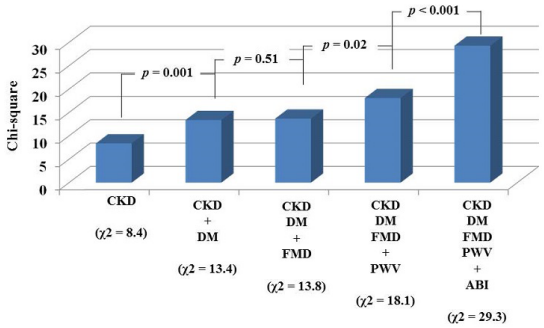
Background and Purpose: The detection of coronary artery calcification (CAC) with computed tomography (CT) is a reliable method for detecting coronary atherosclerosis. Traditional prospective ECG-triggered CAC image acquisition exposes patients to radiation doses of approximately 1-2mSv. A new technique using high-pitch ECG-triggered acquisition reduces radiation doses to approximately 0.3mSv. However, it has the detriment of increasing image noise, which may impact the reliability of CAC measurements. The purpose of this study is to understand the inter-observer variability associated with prospective and high-pitch acquisition protocols and the effect of patient habitus on CAC measurements.
Methods: 9741 patients undergoing CAC imaging a between 2006 and 2016 were screened. Readers measured CAC of these patients using the Agatston method. Readers were blinded to each other's CAC measures. Inter-observer agreement was assessed using linear-regression model and Bland-Altman plot. Inter-observer variability across different BMI groups was assessed by percentage difference.
Results: Inter-observer correlation was excellent (r = 0.999) and agreement was very good for both prospective and high-pitch acquisition methods (r = 0.999 and 0.998 respectively). Variability in CAC measurements was directly related to patient size. This finding was true for both prospective ECG-triggered and high-pitch acquisition models. The variability between readers was less in the high-pitch population.
Conclusion: Inter-observer variability of CAC measurements increased with patient body habitus. Prospective ECG-triggered acquisition, despite having a higher radiation dose, yielded the highest variability.

P617

Severity and complexity of coronary artery disease assesssed by comparison of multimodality evaluation of atherosclerosis : Pulse wave velocity ,flow-mediated dilation and ankle-brachial index

Y Y Yun Young Choi[1]; JS Woo[1]; HO Kim[1]; HM Chung[1]; JM Lee[1]; SJ Kim[1]; WS Kim[1]; KS Kim[1]; W Kim[1]; JB Kim[1]
[1]*Kyunghee University, cardiology, Seoul, Korea Republic of*

Background: Flow-mediated dilation (FMD), Ankle-brachial index (ABI) and Pulse wave velocity (PWV) have been used as noninvasive modalities for evaluating atherosclerosis. This study was revealed that which non-invasive atherosclerosis tests could predict complexity and severity of coronary artery disease (CAD).
Methods: From January 2010 to November 2013, 1,630 stable angina patients who performed non-invasive arthrosclerosis evaluation (FMD, ABI, PWV) with diagnostic Coronary angiography (CAG) were enrolled in this study. The primary end point was differences of non-invasive tests according to CAD severity (number of diseased vessel) and complexity (syntax score).



Incremental prediction of CAD complexity

Results: Patients with high syntax score (= 23) showed significantly low values of FMD and ABI and high PWV. CAD extent was significantly associated with ABI ($p < 0.001$). However, there was no significant correlation of CAD extent and FMD ($p = 0.17$), PWV ($p = 0.06$). Non-invasive tests showed incremental predictive values of CAD complexity (Figure) Conclusion: Different non-invasive tests could be useful to predict CAD severity and complexity in a complementary manner regardless of its purpose in patients with stable angina.

Coronary Artery Disease - Treatment

P618

Psychological stress aggravates the vulnerability of atherosclerotic plaques in ApoE knockout mice via SDF-1 /CXCR4 signalling

Z-Y Huang[1]; C-L Peng[2]; Y-Y Liu[3]; X-B Wang[4]; M-P Huang[3]; L Lu[1]; D-H Liang[2]
[1]*The First Affiliated Hospital, Guangzhou University of Chinese Medicine, Guangzhou, China People's Republic of*; [2]*School of Traditional Chinese Medicine, Southern Medical University, Guangzhou, China People's Republic of*; [3]*Department of Traditional Chinese Medicine, Zhujiang Hospital, Southern Medical University, Guangzhou, China People's Republic of*; [4]*Department of Cardiology, Zhujiang Hospital, Guangzhou, China People's Republic of*

On behalf of: Psychosomatic treatment of cardiovascular disease

Background: Psychological stress has been recognized as a key risk factor for acute coronary syndrome (ACS). However, little information is available on the mechanism underlying psychological stress-induced vulnerable plaque formation. Here, we report the aggravation of vulnerable plaques via the SDF-1/CXCR4 biological axis imbalance, which is caused by psychological stress.
Purpose: Our purpose is to provide new insights for early psychological prevention and treatment of ACS.
Methods: The mice were subjected to chronic unpredictable mild stress (CUMS) or administered with AMD3100 (2.5mg/kg/day, i.p.) together for 12 weeks. Animals were evaluated for behavioral changes, such as anxiety-related behaviour by high plus maze, behavioral despair by forced swim test, and exploratory behaviors by an open field test. CRP mRNA in liver, along with lipid metabolism, NEUT%, norepinephrine (NE), IL-6, SDF-1/CXCR4 indexes in serum were investigated. The changes of atherosclerosis plaque in the aortic arch and the aorta were observed by oil red O staining and HE dying. Moreover, the expression of SDF-1 and CXCR4 in aorta was examined by immunofluorescence assay and western blotting assay.
Results: Our results showed that CUMS not only significantly increased the levels of plasma lipid, NEUT%, norepinephrine (NE), IL-6 and reduced SDF-1/CXCR4 indexes, but also accelerated depressive-and anxiety-like behaviors and vulnerable plaque formation in mice. The immunofluorescence assay results showed that SDF and CXCR4 were significantly down-regulated in the aortic arch of the stressed mice. The protein levels of SDF-1 and CXCR4 in the platelets, aorta were decreased under CUMS intervention. AMD3100 significantly aggravated the CUMS-induced changes in CUMS mice.
Conclusions: Psychological stress is a crucial factor that causes SDF-1/CXCR4 biological axis dysfunction and growing vulnerable plaque.

P619

Heart failure after acute coronary syndrome: demographic and clinical predictors.

I Ines Almeida[1]; H Miranda[1]; J Chin[1]; C Sousa[1]; S Almeida[1]; D Mesquita[1]
[1]*C.H.Barreiro-Montijo , Lisboa, Portugal*

Introduction: Heart failure (HF) is an important complication that can derive from the acute coronary syndrome (ACS), however its prevalence has been decreasing when associated with the implementation of new therapeutics.
Objective: Evaluation of predictor factors of HF in patients (P) with ACS.
Materials and Methods: Retrospective analysis of the P data admitted with ACS included in multicentric register between 2012-2017. Comparison of the implemented double antiaggregation strategy (CLOPI versus TICA) and evaluation of the endpoint HF.
Results: 10135 P with ACS were admitted, of which 15.9% developed HF during the internment. The average age was of 73 +/- 12 years, 64.4% of the P were the masculine genus. The comorbidities more prevalent were arterial hypertension (76.4%) and dyslipidemia (59.7%). 2.1% of the admitted P already had a previous diagnosis of HF. In comparison with the P that did not develop HF, the average value of the brain natriuretic peptic was superior to (844 +/- 840 vs 302 +/- 556 pg/ml, $p < 0.001$) and presented an ejection fraction inferior to (43+/-12 vs 53 +/- 11%, $p < 0.001$). 17% were medicated with CLOPI and 9.7% with TICA ($p < 0.001$). The patients treated with CLOPI presented HF with greater frequency during the internment (85.6% vs 91.9%, $p < 0.001$, OR 1.90) than those medicated with TICA (14.4% vs 8.1%, $p < 0.001$, OR 0.53). The therapeutic with TICA is associated with a lower probability of developing HF in respect to CLOPI (p 0.002, OR 0.71). Other associated factors to HF were antecedents of valvular disease, peripheral arterial disease, renal disease, the presentation in dyspnea or cardiac arrest; the presence of tachycardia or hypotension; the persistent elevation of the ST segment in the electrocardiogram; and the previous utilization of diuretic pharmacies.
Conclusion: The presence of systemic arterial vascular disease, ACS with atypical presentation and the presence of clinical and electrocardiographic markers of seriousness and therapeutic with clopidogrel, when compared with ticagrelor, looks to be predicting factors of development of HF during the internment.

P620

Prognostic impact of the antiaggregation strategy implemented in acute coronary syndrome

I Almeida[1]; H Miranda[1]; J Chin[1]; C Sousa[1]; D Mesquita[1]; S Almeida[1]
[1]*C.H.Barreiro-Montijo , Lisboa, Portugal*

Introduction: The patients (P) with acute coronary syndrome (ACS) must go through double antiaggregation therapeutic with acetylsalicylic acid (ASA) and an inhibitor PY12 (IPY12). According to the recommendations of the European Society of Cardiology of 2017, the preferable IPY12 are the ticagrelor (TICA) and the prasugrel, being the clopidogrel (CLOPI) recommended if unavailable or counter indication for the first.
Objective: Prognostic impact evaluation of the second antiaggregate pharmacies choice - CLOPI versus (vs) TICA - in the P with ACS.
Materials and Methods: Retrospective analysis of the P data admitted with ACS included in multicentric register between 2012-17. Compared intra - hospitable morbimortality and multivaried analysis accomplished for the second antiaggregate choice impact evaluation.
Results: 10157 P were admitted, having been administrated CLOPI in 75.7% of them. The P medicated with CLOPI were older (66 +/- 13 vs 62 + / - 12 years, $p < 0.001$), with predominance of the masculine genus and with more previous coronary disease. During the internment, the P under CLOPI were more medicated with antagonists of vitamin K (2.4 vs 0.6%, $p < 0.001$), however the prescription of ASA at the discharge date was inferior (94.1 vs 97.6%, $p < 0.001$). The P under TICA were more frequently submitted to reperfusion (91.4 vs 85.6%, $p < 0,001$), the majority percutaneous angioplasty (98.7 vs 93.3%, $p < 0.001$) being overlapping in

the two groups the prevalence of multivessel disease and the involvement of the left main or anterior descendant artery. Of the evaluated endpoints, the P medicated with CLOPI presented a greater ratio of heart failure (HF) (17 vs 9.7%, $p < 0.001$) and atrial fibrilation (AF) (5.5 vs 3.2%, $p < 0.001$). The major hemorrhage ratio was inferior in the patient group medicated with CLOPI (1.4 vs 1.6%, p 0.047) however the intra-hospitable mortality was superior (3.2 vs 1.5%, $p < 0,001$).

Conclusion: The P medicated with CLOPI were older and with more prevalence of important comorbidities. The utilization of TICA was associated to a greater ratio of hemorrhagic events major but a minor occurrence of complications, namely HF and AF, and intra - hospitals mortality. This data shows the real life the impact of the new IPY12 in the patients with ACS.

HF-DACH Poster session

Chronic Heart Failure - Pathophysiology and Mechanisms

P564

Cardiotoxicity versus Diastolic Dysfunction: Distinct Features in Biopsy-Proven AL and ATTR Cardiac Amyloidosis

F Felix Escher[1]; S Schneiderbauer-Porod[2]; J Doerler[1]; M Zaruba[1]; C Ensinger[3]; C Ebner[2]; G Poelzl[1]

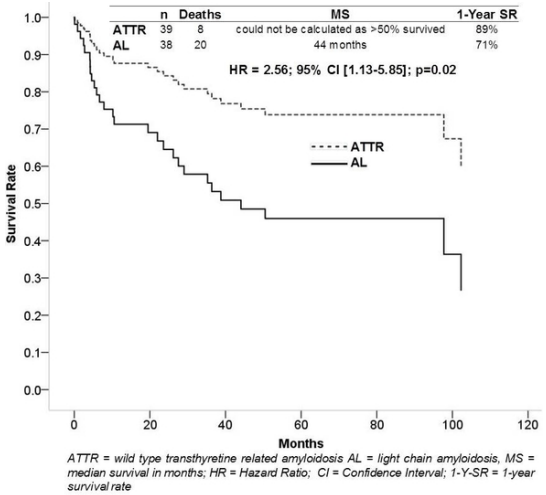
[1]Innsbruck Medical University, Department of Cardiology and Angiology, Innsbruck, Austria; *[2]Elisabethinen University Teaching Hospital, Department of Cardiology, Linz, Austria*; *[3]Innsbruck Medical University, Institute of Pathology, Innsbruck, Austria*

Introduction: Amyloidosis is a severe, systemic disease associated with poor survival. Prognosis depends primarily on cardiac involvement and the underlying amyloid subtype. Cardiac light-chain amyloidosis (AL) is associated with worse survival compared to transthyretine-related amyloidosis (ATTR). However, reasons for this difference in prognosis are still poorly understood.
Purpose: It was the aim of our study to retrospectively compare survival between patients with cardiac AL and ATTR amyloidosis and to evaluate subtype-specific characteristics that might explain differences in survival between groups.
Methods: 77 patients with biopsy-proven amyloidosis (AL: n = 38, ATTR: n = 39) diagnosed and managed in two medical centres between 03/2001 - 12/2017 were analysed. Data were obtained from health records, phone calls and public death registers. The endpoint was defined as death from any cause. Univariate cox regression analysis was used to compare survival and T-Tests and Fisher's Exact tests were used to evaluate mean values and frequencies.
Results: AL patients had a significant worse overall survival compared to ATTR patients (HR= 2.56 [95%CI = 1.13-5.85]; p = 0.02, 1-year survival-rate 71% vs. 89%, median survival time 44 months in the AL group vs. median survival could not be calculated for the ATTR group as more than 50% survived). LV-EF was still preserved and not different between groups (p = 0.34). Characteristics of diastolic dysfunction such as LV posterior wall thickness (p <0.001), LV mass (p <0.001), and percentage of patients with atrial fibrillation (p = 0.001) were significantly higher in ATTR compared to AL patients. In contrast, troponin T as a marker for cardiotoxicity from amyloid deposition was significantly higher in AL patients (p = 0.02).
Conclusions: Survival is worse in individuals with AL amyloidosis despite less cardiac amyloid deposits compared to individuals with ATTR amyloidosis. Differences in prognosis may be explained by cardiac toxicity from light chain deposition in AL rather than diastolic dysfunction in ATTR. However, extensive extra-cardiac involvement and severe infectious complications may add to higher mortality in AL and need further investigation.

Cardiac Characteristics

Variables	AL Amyloidosis (n = 38)	ATTR Amyloidosis(n = 39)	P Value
cTnT (µg/L) (mean ± SD)	0.091 ± 0.02	0.051 ± 0.03	0.02
LV Mass (g) (mean ± SD)	246.9 ± 14.8	334.1 ± 18.1	<0.001
PWD (mm) (mean ± SD)	14.7 ± 2.31	17.1 ± 2.95	<0.001
LV EF (%) (mean ± SD)	51.7% ± 12.6	49.1% ± 10.5	0.34
AF (n) (%)	5 (13.2%)	20 (51.3%)	0.001

cTnT = cardiac Troponin T, PWD = Posterior Wall Thickness; AF = Atrial Fibrillation



ATTR = wild type transthyretine related amyloidosis AL = light chain amyloidosis, MS = median survival in months; HR = Hazard Ratio; CI = Confidence Interval; 1-Y-SR = 1-year survival rate

Univariate Cox Regression Analysis

P565

Sublingual microcirculation in patients with continuous- flow ventricular assist devices

P P Wadowski[1]; B Steinlechner[2]; D Zimpfer[3]; T Schloeglhofer[4]; H Schima[4]; M Huelsmann[5]; R Wurm[5]; T Gremmel[1]; R Koppensteiner[1]; C Schoergenhofer[6]; B Jilma[6]

[1]Medical University of Vienna, Division of Angiology, Department of Internal Medicine II, Vienna, Austria; *[2]Medical University of Vienna, Division of Cardiothoracic and Vascular Anaesthesia and Intensive Care, Vienna, Austria*; *[3]Medical University of Vienna, Department of Cardiac Surgery, Vienna, Austria*; *[4]Medical University of Vienna, Center for Medical Physics and Biomedical Engineering, Vienna, Austria*; *[5]Medical University of Vienna, Division of Cardiology, Department of Internal Medicine II, Vienna, Austria*; *[6]Medical University of Vienna, Department of Clinical Pharmacology, Vienna, Austria*

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Background: The implantation of continuous - flow ventricular assist devices (VAD) is suggested to evoke angiodysplasia contributing to adverse events like gastrointestinal bleeding.
Purpose: To investigate possible systemic microvascular changes we evaluated in vivo capillary density and glycocalyx dimensions in patients with chronic heart failure and VAD support vs. standard treatment.
Methods: Forty- two patients with VAD support were compared to fifty- three patients with ischemic and non-ischemic CHF and standard pharmacotherapy in a prospective cross- sectional study. Sublingual microcirculation was visualized using a Sidestream Darkfield videomicroscope and functional and perfused total capillary densities quantified. A reduced glycocalyx thickness was measured by an increased perfused boundary region (PBR).
Results: Mean time after VAD implantation was 20.9 ± 16.6 months; patients were treated with centrifugal-flow devices (n = 31) and axial-flow devices (n = 11). Median functional capillary density was markedly lower in patients with VAD therapy (196 vs. 245/mm2, p = 0.024); in addition total perfused capillary density was also rarefied, though not significant (19% difference). Glycocalyx dimensions were similar in both groups.

Conclusion: Improvement of hemodynamic conditions in patients with continuous-flow VAD treatment leads to an alteration of shear forces, which might contribute to capillary density rarefaction.

Chronic Heart Failure - Diagnostic Methods

P566

Klotho is induced in human cardiomyopathy independently of circulating klotho levels

S K Santhosh Kumar Ghadge[1]; G Poelzl[1]; M Messner[1]; B Haubner[1]; P Wuertinger[2]; A Griesmacher[2]; J Doerler[1]; C Ensinger[3]; H Ulmer[4]; MM Zaruba[1]
[1]Innsbruck Medical University, Department of Internal Medicine III, Innsbruck, Austria; *[2]Innsbruck University Hospital, Central Institute for Medical and Chemical laboratory Diagnosis, Innsbruck, Austria*; *[3]Innsbruck Medical University, Department of Pathology, Innsbruck, Austria*; *[4]Innsbruck Medical University, Department of Medical Statistics, Informatics and Health Economics, Innsbruck, Austria*

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Introduction: Klotho is an antiaging protein which exerts cardioprotection. In the kidney, trans-membrane Klotho acts as essential co-receptor of fibroblast growth factor 23 (FGF23) which has been linked to the cardiac remodeling, advent and progression of chronic heart failure (CHF). In the heart, soluble Klotho (sKlotho) protects from stress induced hypertrophy and systolic dysfunction independently of FGF23. Since the role of sKlotho in CHF is barely understood, we aimed to analyze the association of FGF23 and sKlotho upon progression of heart failure and analyzed Klotho expression in human non-ischemic cardiomyopathy (CMP).
Methods and Results: Serum levels of sKlotho and FGF23 were measured in 287 patients with CMP. Tissue samples from CMP (n = 10) and non-failing control hearts (n = 10) were analyzed for Klotho expression using 3'RACE-PCR, qRT-PCR, immunoblotting, and immunohistochemistry. In tertile-based sex-stratified analysis, individuals in the third FGF23 tertile were 4.1 times (95%CI 1.42-12.38; p = 0.009) more likely to reach an endpoint of death, heart transplantation or assist device implantation compared to first tertile. No relationship was found between sKlotho and the combined endpoint (hazard ratio 0.76 [0.45-1.2]; p = 0.299). Instead, Klotho mRNA encoding the full-length form was upregulated in human DCM hearts. Immunoblotting and immunohistochemistry confirmed upregulation of sKlotho associated with increased expression of proteases involved in cleavage of Klotho like ADAM10, ADAM17, and BACE1 in DCM hearts suggesting local cleavage of Klotho in the heart.
Conclusions: Our data indicate that in contrast to FGF23, serum sKlotho is not associated with disease severity or progression in CHF. Instead, Klotho is expressed and upregulated in diseased hearts, suggesting local cardioprotective paracrine effects.

P567

Neprilysin (CD10) expression on peripheral leukocytes in chronic heart failure patients

J Johannes Novak[1]; H Arfsten[1]; A Cho[1]; G Goliasch[1]; PE Bartko[2]; G Strunk[3]; M Huelsmann[1]; N Pavo[1]
[1]Medical University of Vienna, AKH - Vienna, Cardiology Clinic, Cardiology, Vienna, Austria; *[2]Medical University of Vienna, Vienna, Austria*; *[3]Research Institute for Complex Systems - Complexity-Research, Vienna, Austria*

Background: Neprilysin inhibition (NEPi) has been shown to reduce hospitalization and all-cause mortality in patients with heart failure and reduced ejection fraction (HFrEF). Since then circulating NEP concentration (sNEP) has been discussed controversially as a biomarker. Neprilysin (CD10) is known to be present on the surface of monocytes and lymphocytes as well as at higher levels on neutrophils in healthy subjects and implicated in the inflammatory response. The possible impact of NEP expression on peripheral leukocytes on sNEP levels and prognostic measures in HFrEF have not been investigated yet.
Methods: We prospectively enrolled 99 consecutive patients with stable HFrEF, who were clinically followed-up routinely. Laboratory markers including NT-proBNP were assessed. sNEP and NEP (CD10) expression on peripheral blood cells were measured by FACS analysis for all patients. The association between NEP expression and laboratory parameters as well as with sNEP levels were determined.
Results: Figure1 shows characteristic FACS expression results for patients with HFrEF with high and low expression intensities of CD10. NEP was markedly expressed on granulocytes with 94.8% (IQR 90.5-97.4) and measureable on B-cells and monocytes with 8.5% (IQR 5.3-13.5) and 0.8% (IQR 0.4-1.5) of CD10+ cells of the respective leukocyte subtype. NEP expression on T-cells was not detectable. The mean fluorescence intensity (MFI) of CD10 was 5461 (IQR 4028-6904) for granulocytes, 640 (IQR 535-740) for B-cells and 1589 (IQR 1395-1975) for monocytes. An inverse correlation of NT-proBNP could be proven with the MFI of CD10+granulocytes (r=-0.46, p < 0.001) but not with the MFI of CD10+B-cells (r=-0.13, p = 0.191) or CD10+monocytes (r = 0.07, p = 0.477). Figure2 depicts differences in MFI for CD10+granulocytes according to tertiles of selected variables, i.e. NT-proBNP, albumin, hemoglobin and butyryl-cholinesterase. sNEP concentrations were 2425pg/ml (IQR 1559-3349). sNEP concentrations correlated positively with the expression of CD10 on granulocytes (r = 0.22, p = 0.030) and with the MFI of CD10+granulocytes (r = 0.306, p = 0.003).
Conclusions: CD10 expression levels on neutrophils might reflect a distinct systemic inflammatory disposition, with low expression levels accompanying a more severe disease state reflected by NT-proBNP. Granulocyte CD10 expression correlates to measurable sNEP levels.

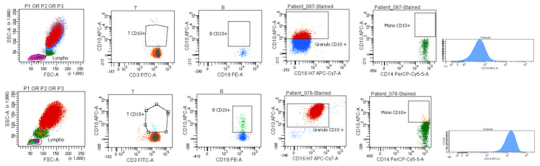

Figure 1

P568

Circulating Neprilysin is not a prognostic biomarker for cancer patients

N Noemi Pavo[1]; H Arfsten[1]; A Cho[1]; G Goliasch[1]; PE Bartko[1]; R Wurm[1]; C Mayrhofer[1]; M Raderer[1]; C Zielinski[1]; M Huelsmann[1]
[1]Medical University of Vienna, Vienna, Austria

On behalf of: Herzinsuffizienz MUW

Background: The circulating form of the membrane-bound zink-metalloendopeptidase neprilysin (cNEP) as a biomarker in heart failure has been discussed controversially in recent studies. However, evidence emerges that NEP is not only implicated in the homeostasis of vasoactive peptides, but also plays a key role in tumor biology. NEP could therefor represent another link between the heart and cancer which might be of special interest in the field of cardiooncology. Concentrations of cNEP have not yet been assessed in cancer patients.
Aim: The aim of the study was to determine cNEP levels in an unselected cohort of treatment-naïve cancer patients and to investigate the association of cNEP levels with biomarkers of the heart, other organ systems and inflammatory state as well as the effect of cNEP on prognosis.
Methods: 555 consecutive patients with primary diagnosis of cancer without prior anticancer therapy were enrolled prospectively. NEP levels were determined in venous plasma samples alongside routine laboratory parameters, a set of cardiac biomarkers, i.e. N-terminal pro-B-type natriuretic peptide (NT-proBNP), high-sensitive TroponinT (hsTnT), mid-regional pro-atrial natriuretic peptide (MR-proANP), mid-regional pro-adrenomedullin (MR-proADM), C-terminal pro-endothelin-1 (CT-proET1) or Copeptin, and inflammatory parameters, i.e. C-reactive protein (CRP), interleukin-6 (IL-6) and serum amyloid A (SAA). All-cause mortality was defined as primary endpoint.
Results: cNEP showed a wide distribution in the total cohort with a median of 276pg/ml (IQR 0-5981), displaying a weak correlation with age [r=-0.12, p = 0.023]. cNEP showed a modest but consequent inverse rank-correlation with the inflammatory status [r=-0.14, p = 0.007 for CRP; r=-0.20, p < 0.001 for IL-6 and r=-0.18, p < 0.001 for SAA], however seemed not to be related to the functional parameters of other organ systems as the heart [r=-0.05, p = 0.367 for NT-proBNP; r=-0.10, p = 0.075 for hsTnT; r=-0.03, r=-0.02, p = 0.664 for MR-proANP; r=-0.05, p = 0.387 for MR-proADM; r = 0.07, p = 0.168 for CT-proET1 and r=-0.01, p = 0.864 for Copeptin], kidney or liver. cNEP was not associated with overall survival in the total cohort [adj.HR for ln(cNEP) 1.00, 95%CI:0.94-1.06, p = 0.887], and neither in the subgoups of solid tumors nor myeloproliferative disease, but in myelodysplatic malignancies [adj.HR for ln(cNEP) 1.27, 95%CI:1.01-1.61, p = 0.044]. Figure 1 shows the Kaplan-Meier analysis according to cNEP tertiles.
Conclusions: cNEP shows a wide distribution in human plasma of cancer patients. cNEP levels are comparable between different tumor entities and stages and lack association with outcome but for myelodysplastic disease. Moreover, no association could be revealed between cNEP and other organ system, especially the heart, assessed by a set of established cardiac biomarkers.

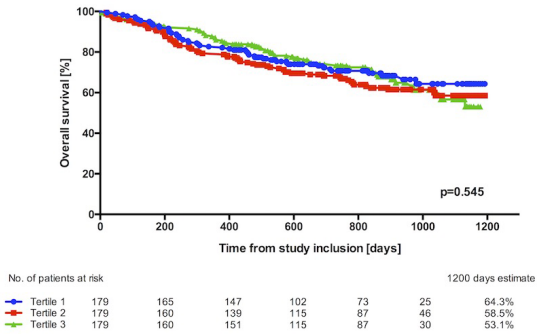

Figure 1

P569

Diagnostic accuracy of 99m-DPD SPECT scintigraphy in TTR-Amyloidosis

M Manuel Ebert[1]; F Escher[1]; J Doerler[1]; MM Zaruba[1]; C Ensinger[2]; C Uprimny[3]; AP Kroiss[3]; G Poelzl[1]
[1]Innsbruck Medical University, Department of Internal Medicine III, Cardiology and Angiology, Innsbruck, Austria; *[2]Innsbruck Medical University, Institute of Pathology, Innsbruck, Austria*; *[3]Innsbruck Medical University, Clinic for Nuclear Medicine, Innsbruck, Austria*

Introduction: Two-dimensional bone scintigraphy with 99m technetium 3,3-diphosphono-1,2-propanedicarboxylic acid (99mTc-DPD) is recommended to discriminate transthyretin amyloidosis (ATTR) from other forms of cardiac amyloidosis (CA), e.g. light chain amyloidosis (AL). Three-dimensional imaging with Single Photon Emission Computed Tomography (SPECT) may improve diagnostic accuracy in these patients. It was the aim of our study to evaluate the diagnostic accuracy of 99mTc-DPD SPECT scintigraphy in patients with CA using semi-quantitative (Perugini-Score) and quantitative measurements.
Materials and Methods: SPECT scintigraphy with 99m-DPD was performed in a total of 17 patients (m = 14 [82.4 %], f = 3 [17.6 %]). All patients underwent endomyocardial biopsy for histologic and immunohistochemical evaluation. Three groups were generated according to the final diagnosis: ATTR (n = 7), AL (n = 5), no CA (n = 5). Semi-quantitative assessment of SPECT scintigraphy was performed using the Perugini Grading System. Quantitative assessment was based on measuring intensity of tracer uptake in predefined areas of the left ventricle (LV) and right ventricle (RV). Finally, intensity of tracer uptake was correlated with serum troponin T values.
Results: Perugini-Score 0 was assigned to 10 patients (58.8 %), Perugini-Score 1 and 2 to no patient, and Perugini-Score 3 to seven patients (42.2 %) by a physician unaware of the final diagnosis. All patients with Perugini-Score 3 were finally diagnosed with ATTR by endomyocardial biopsy resulting in a positive predictive value (PPV) and negative predictive value (NPV) of 1, respectively. All patients with ATTR showed an increased tracer uptake in RV, although uptake was lower compared to LV (p = 0.001). Correlation of troponin T with intensity of tracer uptake was significant in RV (p = 0.02) and of borderline significance in LV (p = 0.073).
Conclusion: Our data indicate an exceptional high diagnostic accuracy for 99mTc-DPD SPECT scintigraphy in the diagnosis of ATTR. In addition, this technique allows for detection of amyloid deposition in the right ventricle that correlates well with troponin T levels. Further studies are needed to evaluate a possible association of RV tracer uptake with long-term prognosis in CA.

P570

Correlation of strain and strain-rate imaging and left ventricular function in ischemic and non-ischemic chronic heart failure patients

K Klemens Ablasser[1]; M Gangl[1]; E Kolesnik[1]; L Kattnig[1]; M Manninger[1]; D Scherr[1]; D Von Lewinski[1]; F Fruhwald[1]; N Verheyen[1]
[1]Medical University of Graz, Department of Cardiology, Graz, Austria

Background: Left ventricular ejection fraction (EF) is the standard method for assessing the left ventricular function in heart failure (HF) patients.

Speckle-tracking echocardiography allows to quantitative determine myocardial deformation by strain and strain-rate imaging.
Purpose: The purpose of this investigation was to analyse the relationship between global longitudinal strain (GLS), global strain rate (GSR) and ejection fraction (EF) in a prospective cohort of ischemic and non-ischemic CHF patients.
Methods: Heart failure patients with mid-range reduced EF (HFmrEF) or reduced EF(HFrEF) were enrolled in the study. They had to be in a stable disease condition, as defined by absence of unplanned hospitalization or change in medication or device therapy within the previous month or major surgery within the previous 3 months. Patients also had to be on ESC guideline conform medication. Patient history, physical examination and an extensive echocardiography exam were performed. Manual longitudinal strain was calculated using EchoPAC (General Electric Medical Systems, Horten, Norway) by a single and blinded examiner. LVEF was measured using Simpson's biplane method.
Results: Overall, 103 patients were enrolled, however 19 patients were excluded from this analysis due to inadequate echocardiography image quality. Participants were 76% male with a mean age 61.0 years. Mean EF was 35,7 % (SD +/- 9,5 %), mean GLS was -9.6 % (SD +/- 4.5 %) and mean GSR -6,67 (SD +/- 0,21). Aetiology was 70.0 % ischemic vs 30.0 % non-ischemic heart failure.

There was a significant correlation between GLS and EF (Pearson r = 0.620, p < 0.001) as well as GSR and RF (Pearson r = 0.595, p < 0.001). However in a multivariate regression analysis only GLS, but not GSR, remained significantly correlated with EF (adjusted beta-coefficient= 0.429, p = 0.043).

In the subset of patients with an ischemic cardiomyopathy both GLS (Pearson r = 0.716, p < 0.001) and GSR (Pearson r = 0.714, p < 0.001) remained highly correlated to EF. However, in patients with non-ischemic heart failure significant correlation could only be demonstrated between EF and GSR (Pearson r = 0.334, p = 0.003), but not EF and GLS (Pearson r = 0.338, p = 0.17).
Conclusion: In CHF results from speckle tracking echocardiography correlate highly with EF, which also held true for GLS in a multivariate regression analysis.

However, in a subset of patients with a non-ischemic aetiology of CHF GSR show a better correlation to EF. Therefore, different measurements of left ventricular function might be best suited for different aetiologies of heart failure.

P571

Correlation of global longitudinal strain and NT-proBNP in ischemic and non-ischemic chronic heart failure patients

M Gangl[1]; E Kolesnik[1]; L Kattnig[1]; V Habenicht[1]; M Manninger[1]; J Schmid[2]; D Scherr[1]; F Fruhwald[1]; D Von Lewinski[1]; N Verheyen[1]; K Klemens Ablasser[1]
[1]Medical University of Graz, Department of Cardiology, Graz, Austria; *[2]Medical University of Graz, Department of Radiology, Graz, Austria*

Background: In chronic heart failure (CHF) NT-proBNP and left ventricular ejection fraction (LVEF) by echocardiography are standard diagnostic as well as follow-up markers and are known to correlate with prognosis. Speckle-tracking echocardiography is a more recent technique to quantify myocardial deformation as a measurement of left ventricular function with potential benefits over LVEF.
Purpose: The purpose of this investigation was to analyse the cross-sectional relationship between 2D speckle tracking-derived global longitudinal strain (GLS) and NT-proBNP plasma levels in a prospective cohort of ischemic and non-ischemic CHF patients.
Methods: We enrolled 103 patients with chronic heart failure. Major inclusion criteria were age over 18 years, stable disease with absence of unplanned hospitalization or change in medication or device therapy in the previous month or major surgery in the previous 3 months. CHF treatment had to be according to the recommendations of the ESC CHF guidelines 2016 and LVEF had to be below 50%.
Patient history, physical examination and an extensive echocardiography exam were performed. Lab results included NT-proBNP. Manual longitudinal strain was calculated using EchoPAC (General Electric Medical Systems, Horten, Norway) by a single and blinded examiner. LVEF was measured using Simpson's biplane method.
Results: Of 103 patients included in the trial, 19 patients were excluded from the analysis due to poor echocardiography image quality or missing lab
Results: The baseline characteristics included mean age 61.0 years and 76% male. Mean GLS was -9.6 % (SD +/- 4.5 %) and median NT-proBNP 1269.5 (IQR 379.5 - 2759.5) ng/ml. The CHF aetiology was 70.0 % ischemic vs 30.0 % non-ischemic.
There was a significant negative correlation between GLS and NT-proBNP (Pearson r = 0.239, p = 0.029), this was not significant for LVEF and NT-proBNP (Pearson r = 0.149, p = 0.228).In a multivariate regression analysis adjusted for age, sex, NYHA classification and HF aetiology, GLS remained significantly correlated with NT-proBNP (adjusted beta-coefficient= 0.289, p = 0.011). Furthermore, in contrast to LVEF, GLS showed a significant correlation to NT-proBNP in patients with ischemic (Pearson r = 0.266, p = 0.049) as well as non-ischemic aetiology of heart failure (Pearson r = 0.434, p = 0.034).
Conclusion: Global longitudinal strain, not LVEF, was significantly correlated with NT-proBNP in patients with CHF, independently of age, sex, symptoms or heart

failure aetiology. This shows that speckle-tracking might be superior to LVEF for the assessment of left ventricular function in CHF.

P572

Estimation of NTproBNP and overhydration (ECF excess) during the 12-channel routine ECG

F Skrabal[1]; K Skrabal[1]; M Penatzer[2]
[1]*Institute for Cardiovascular and Metabolic Medicine, Graz, Austria*; [2]*Barmherzige Schwestern, Innere Medizin 1, Wien, Austria*

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Background: The diagnosis of chronic heart failure (CHF) in clinical practice is no triviality. We have developed a 12 channel ECG which combines the Einthoven, Wilson and Goldberger leads with segmental impedance spectroscopy and impedance rheography in six body segments (thorax, abdomen and the four extremities) using only one additional double electrode at the neck (Combyn ECG). Using this technology it is possible to measure the acceleration of blood and also the relation of extracellular to intracellular water (ECF/ICF ratio) during the routine ECG in these 6 body segments. These two parameters combined may be used for estimation of NTproBNP levels.
Purpose: We evaluated prospectively the sensitivity of the methodology to estimate NTproBNP in unselected outpatients.
Methods: 195 patients (91 without CHF, 104 with CHF) were evaluated. The measured NTproBNP plasma levels were compared with the output of the Combyn ECG using discriminant function analysis. The following cut offs for groups 1 to 4 were used: NTproBNP (1) < 120, (2) 120-400, (3) 400-1000, (4) >1000 pg/ml.
Results: Participants of the study without CHF and with NTproBNP levels < 120 pg were allocated to group 1 and 2 (74.7 and 17.6%, respectively; total 92.3%), patients with CHF and NTproBNP >1000 pg were allocated to group 3 and 4 (20.8 and 58.3%, respectively; total 79.1%). Patients with NTproBNP levels between the above extremes were detected with lower sensitivities (table).
Conclusions: NTproBNP is an (over-)stretch release hormone, overstretch also leads to an impaired acceleration of blood which can be measured by the Combyn ECG. Based on these physical principles (i.e. an inverse correlation between NTproBNP levels and blood acceleration and a positive correlation between NTproBNP levels and ECF excess) our prospective study shows promising sensitivity for estimating NTproBNP levels solely by recording of the 12 channel Combyn ECG.

Table

Discrimination Analysis: Classification Results in %, cross validated

	Predicted Group				
Groups based on NTproBNP (pg/ml)	1	2	3	4	Sum
1: NTproBNP < 120	74.7	17.6	6.6	1.1	100
2: NTproBNP 120-400	22.4	53.1	20.4	4.1	100
3: NTproBNP 400-1000	12.9	22.5	32.3	32.3	100
4: NT proBNP > 1000	4.2	16.7	20.8	58.3	100

Chronic Heart Failure - Treatment

P573

Therapeutic response of peritoneal dialysis as a therapy for refractory heart failure and congestive right ventricular dysfunction

N Noemi Pavo[1]; R Yarragudi[1]; H Puttinger[1]; G Strunk[2]; A Bojic[1]; A Vychytil[1]; M Huelsmann[1]
[1]*Medical University of Vienna, Vienna, Austria*; [2]*Research Institute for Complex Systems - Complexity-Research, Vienna, Austria*

Background: In patients with refractory heart failure (HF) peritoneal dialysis (PD) is associated with improved functional status and decrease in hospitalization. However, previous studies did not focus on right ventricular dysfunction as important pathophysiologic component of cardiorenal syndrome.

Methods: In a prospective cohort study PD was started in 40 patients with refractory right HF (with/without left HF). Refractoriness to conservative therapy was defined as persistent right heart congestion/ascites with intensified diuretic treatment and/or = 2 hospitalizations within 6 months because of cardiac decompensation despite optimal medical treatment, and/or acute renal failure during intensified conservative treatment of cardiac decompensations.

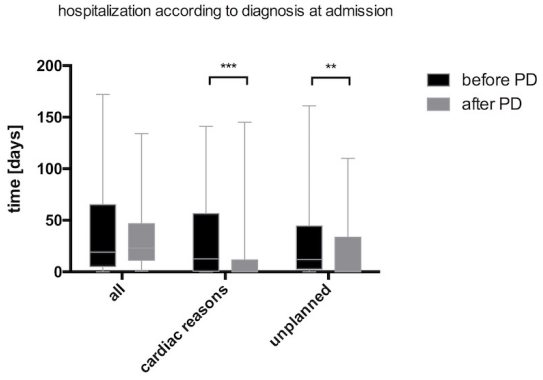


Figure 1

Results: Patient survival was 55.0% at 1 year, 35.0% at 2 years and 27.5% at 3 years. The number of hospital days declined after initiation of PD for both cardiac [13 (IQR 1-53) days before vs. 1 (IQR 0-12) days after PD-start of PD, p < 0.001] and unplanned reasons [12 (IQR 3-44) days before vs. 1 (IQR 0-33) days after PD-start, p = 0.007] (Figure 1). Using a combined endpoint including survival time of = 1 year and either improvement in quality of life or decline in hospitalizations we found that patients with extended ascites, higher systolic pulmonary artery pressure, more marked impairment of right ventricular function and tricuspid valve insufficiency, higher residual renal function as well as those who could perform PD without assistance most benefited from this therapy.
Conclusions: Patients with more pronounced backward failure, less marked residual renal functional impairment and those not depending on assistance for therapy are likely to profit most from PD.

P574

Baroreflex-activation-therapy in advanced heart failure: do patients accept an additional device-based therapy when symptomatic under optimized treatment?

D Denise Guckel[1]; KJ Gutleben[1]; D Horstkotte[1]; G Noelker[1]
[1]*Herz- und Diabeteszentrum NRW, Ruhr-Universität Bochum, Clinic for Cardiology, Bad Oeynhausen, Germany*

Background/Introduction: Baroreflex-Activation-Therapy (BAT) is a new promising treatment option for patients (pts) suffering from advanced heart failure (HF) with reduced left ventricular ejection fraction (HFrEF) to improve functional status and quality of life. Data on the acceptance of this novel therapeutic device are lacking. Comparative clinical data on outcome of pts implanted with BAT devices in comparison to control HFrEF pts are scarce as well.
Purpose: The aim of our study is to analyse the acceptance of this novel therapeutic device and to evaluate the outcome of pts implanted with a BAT device in comparison to HFrEF pts solely treated with a guideline directed medical therapy (GDMT). Beyond that we intend to examine to which extent possible factors (e.g. cardiac resynchronisation therapy (CRT), atrial fibrillation, sacubitril/valsartan or sleep apnoea) might influence the response to BAT.
Methods: In this single centre prospective study, 38 HFrEF pts (67 ± 1.8 years) (mean ± SEM) (32 males) eligible for BAT (EF 27 ± 1 %, NYHA III, NT-proBNP 2302 ± 460 pg/ml, 6-minute hall walk distances (6MWD) 281 ± 23 m) were included. Baseline pts answered a questionnaire focussing on the acceptance of BAT. Follow-up visits (FU) were scheduled after 3, 6 and 12 months. Primary efficacy endpoints will include an improvement in quality of life (EQ-5D-5L), New York Heart Association (NYHA) functional class, ejection fraction, hospitalisation rate due to recurrent heart failure symptoms, NT-proBNP levels and 6MHWD. Pts refusing BAT served as a control group.
Results: 34 pts (87%) completed the questionnaire concerning their acceptance of BAT. 32 of these pts (95%) were unaware of this novel therapeutic option and were interested in BAT, 12 of them (38 %) wanted to be implanted directly, 11 pts (34 %) expected further information before treatment. The majority of pts interested in BAT

(16 pts, 50%) wanted to make sure that no other competing therapeutic options were available. 3 pts (9%) strictly denied the option of a BAT therapy because of potentially unexpected adverse effects caused by the implantation, but none of the pts refused BAT due to other reasons. 10 pts (30%) could not yet decide and hence requested further information (6 pts, 20%) and time for consideration (4 pts, 12%). Eight pts have already been implanted with a BAT device. All pts were interested in regular visits at our centre due to their severe heart failure.

Conclusion: To the best of our knowledge, we are the first to analyse the acceptance of BAT in pts suffering from advanced HFrEF. From our limited data BAT seems to be a broadly accepted but previously unknown therapeutic tool in HFrEF pts. Details on mid-term clinical outcome will be available and presented at the meeting.

Coronary Artery Disease - Pathophysiology and Mechanisms

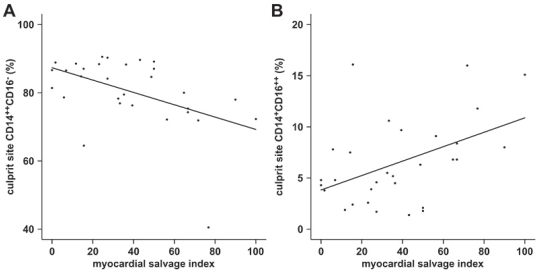
P575

Non-classical monocytes at the culprit lesion site of ST elevation myocardial infarction patients are connected to improved outcome

A Andreas Mangold[1]; T Hofbauer[1]; S Thomas[1]; A Ondracek[1]; C Testori[2]; A Panzenboeck[1]; F Sterz[2]; I Lang[1]
[1]*Medical University of Vienna, Department of Internal Medicine II, Division of Cardiology, Vienna, Austria*; [2]*Medical University of Vienna, Department of Emergency Medicine, Vienna, Austria*

Funding Acknowledgements: Austrian Science Fund (APKLI209)

Background: Myocardial infarction (MI) is a major cause of acute and chronic heart failure. The pathomechanisms of myocardial salvage and scar formation are incompletely understood. We have previously shown that neutrophils release neutrophil extracellular traps (NETs) at the culprit lesion site (CLS). Coronary NET burden correlated significantly with increased infarct size in ST elevation MI (STEMI) patients. It was shown that macrophages are critical for the clearance of NETs. Monocytes are circulating macrophage precursors and play a critical role after myocardial ischemia/necrosis. Monocytes are sub-grouped according to their CD14/CD16 expression into classical (CD14++CD16-), intermediate (CD14++CD16+) and non-classical (CD14+CD16++) monocytes. These subsets fulfill diverging roles in inflammation; especially patrolling non-classical monocytes are important for the efficient removal of cell debris after tissue damage. The chemotactic fractalkine receptor CX3CR1 is highly expressed on non-classical monocytes. We sought to investigate monocyte subsets at the CLS of STEMI patients.



Monocyte subsets and myocardial salvage

Methods: In the course of a clinical trial, in which out of hospital-initiated therapeutic hypothermia was tested in STEMI patients (STATIM trial, n = 120, submitted), we determined monocyte subsets in thrombectomy specimens from the CLS compared to femoral blood samples (n = 30) using flow cytometry. Cardiac magnet resonance (CMR) was performed in these patients 4 ± 2 days after STEMI. The primary endpoint of this trial was myocardial salvage index (MSI). In a second STEMI population (n = 36), we performed a detailed expression marker analysis of respective subsets at the CLS compared to the femoral site. NET surrogate markers (citrullinated histone 3 [citH3], double-stranded deoxyribonucleic acid [dsDNA]) were measured in CLS and femoral plasma using immunometric assays. Enzymatic infarct size (CK-MB area under the curve [CK-MB AUC]) was determined in all patients.

Results: Therapeutic hypothermia had no effect on MSI or other outcome measures. Classical monocytes were significantly decreased at the CLS and correlated negatively with MSI, whereas non-classical monocytes where significantly increased and correlated positively with MSI. In the second STEMI population, CX3CR1 expression of non-classical monocytes correlated negatively with CK-MB AUC and with citH3 and dsDNA. These NET surrogate markers correlated positively with CK-MB AUC, as previously published.

Conclusion: These data indicate that non-classical monocytes accumulate at the CLS and contribute to myocardial salvage, potentially via effective clearance of cell debris and NETs. CX3CR1 appears to be highly important in this process.

P576

Fibrocytes accumulate at the culprit lesion site in STEMI and are functionally impaired by neutrophil extracellular traps

A Anton Frueh[1]; T Hofbauer[1]; T Scherz[1]; A Ondracek[1]; A Panzenboeck[1]; M Schneider[1]; C Feist[1]; L Kascha[1]; A Mangold[1]; IM Lang[1]
[1]*Medical University of Vienna, AKH - Vienna, Cardiology Clinic, Vienna, Austria*

Introduction: Inflammation is important in the pathogenesis of ST-elevation myocardial infarction (STEMI). Neutrophil extracellular traps (NETs) are enriched at the culprit lesion site (CLS) of patients. Fibrocytes, mesenchymal progenitor cells with both leukocyte and fibroblast properties, accumulate in cardiac tissue of a murine ischemia/reperfusion model and contribute to tissue repair and Collagen-I deposition. In advanced atherosclerotic plaques, expression of bone morphogenic protein receptor II (BMPRII) is lost. We studied fibrocyte frequencies and their BMPRII expression at the CLS of STEMI patients.

Methods: We drew blood samples from the CLS and femoral site during primary percutaneous coronary intervention from STEMI patients (n = 50, male = 78%, mean age = 61 ± 13y). Fibrocytes were characterized using flow cytometry. Double-stranded (ds)DNA, a surrogate marker of NETosis, was measured in plasma using PicoGreen®. To assess the influence of NETs on Collagen-I and BMPRII expression, fibrocytes were stimulated in vitro with isolated NETs.

Results: Fibrocytes were increased two-fold at the CLS compared to femoral blood. No differences were found in BMPRII expression between CLS and femoral blood. dsDNA was highly increased at the CLS and negatively correlated with both Collagen-I and BMPRII expression of fibrocytes. In vitro treatment of fibrocytes with NETs induced a decrease of Collagen-I and BMPRII. DNase 1, which degrades NETs, abolished this effect.

Conclusion: We report the accumulation of fibrocytes at the CLS and STEMI. Furthermore, our data suggest a functional link between NETs and fibrocytes, leading to Collagen-I and BMPRII downregulation. NETs might thereby impair reparative functions of fibrocytes after STEMI.

Coronary Artery Disease - Treatment

P577

Abstracts role of irisin in ischaemia reperfusion injury in isolated heart of albino rats

S M Salah Mohamed Ibrahim[1]
[1]*university, cairo, Egypt*

Background: Irisin, a newly identified myokine, is critical in modulating body metabolism, thermogenesis and reducing oxidative stresses. Lower plasma level of irisin in patients with acute myocardial infarction (AMI) was reported. Nevertheless, the significance and functional role of irisin in the modulation of myocardial ischemia and reperfusion injury are not clear.

Purpose: This study was designed to explore possible effect of irisin on ischemia-reperfusion injury in isolated heart of adult male albino rats and to explain the possible involved mechanisms, in a trial to clarify irisin expected cardioprotective effect.

Methods: This study was carried out on thirty sex adult male albino rats which were divided equally (n = 12) into 3 groups: Group I (ischemia-reperfusion I/R group); hearts were stabilized then subjected to (I/R) protocol, Group II (Irisin pre-conditioning group); Irisin was infused for 20 minutes before hearts were subjected to ischemia and Group III (Irisin post-conditioning group); Irisin was infused for 20 minutes at the beginning of 60 minutes of reperfusion. Cardiac performance indicators as left ventricular pressure (LVP), +max (LV dp/dt), -max (LVdP/dt), in addition to heart rate were recorded. Lactate dehydrogenase (LDH), creatine kinase-MB (CK-MB), superoxide dismutase (SOD) and C-reactive protein (CRP) were measured in the collected perfusate and cardiac Malondialdehyde (MDA) was measured. Finally, Nitro blue tetrazolium stain was used to detect the necrotic tissue percentage to the whole left ventricular mass.

Results: In group III (post conditioning group), there was a significant increase of the studied cardiac parameters compared to group I (I/R). Irisin significantly increased LVP, +max (dp/dt), -max (dp/dt) and HR in comparison with I/R group. This was associated with a significant decrease in LDH and CK-MB levels, a significant increase in SOD level and a significant decrease in MDA and CRP levels. Moreover, Irisin caused a significant decrease in percentage of necrotic tissue to the whole left ventricular mass. Regarding group II, no significant changes were detected in all parameters when compared to group I.

Conclusion: Irisin could protect against ischemia/ reperfusion injury in vitro through its antioxidant and anti-inflammatory properties, by limiting the infarction area, only

if given as a post conditioning factor after I/R. Those results open the way to include Irisin among the strategies for management of cardiac infarction during reperfusion.

Myocardial Disease - Clinical

P578

The damage-associated molecular pattern S100A8/S100A9 as a potential biomarker in patients with active myocarditis

I Irene Mueller[1]; U Kuehl[2]; T Vogl[3]; B Pieske[2]; S Van Linthout[1]; C Tschoepe[2]
[1]Berlin-Brandenburg Center for Regenerative Therapies, Charite - Campus Virchow Klinikum, Berlin, Germany; *[2]Charite - Campus Virchow-Klinikum (CVK), Department of Cardiology and Pulmonology, Berlin, Germany*; *[3]University of Muenster, Department of Immunology, Munster, Germany*

Background: The alarmin S100A8/S100A9 is a damage-associated molecular pattern molecule and has been shown to be of importance under inflammatory disorders such as arteriosclerosis and coronary heart disease. Clinical evidence highlights that high plasma levels of S100A8/S100A9 are a risk factor for future cardiovascular events.
Purpose: We aimed to evaluate the potential of serum S100A8/S100A9 levels as a prognostic biomarker in patients with endomyocardial biopsy (EMB)-proven active myocarditis (A-MC) vs non-ischemic dilative cardiomyopathy (DCM) and controls.
Methods: S100A8/S100A9, high sensitivity C-reactive protein (hsCRP) and n-terminal (NT) pro-brain natriuretic protein (BNP) levels were analyzed in serum and plasma of A-MC (n = 27; ejection fraction (EF): 38.8% ± 14%) and DCM patients (n = 16; EF: 22.5% ± 4.7%), and controls (n = 51; EF: 60% ± 5%) by specific ELISAs. Patients serum and plasma were collected at time point (T) 1, where also EMBs were collected. EMB S100A8, S100A9, and NLRP3 mRNA levels and the number of invaded inflammatory cells in EMBs were determined by real-time PCR and immunohistology stainings, respectively. Ejection fraction (EF) was determined at T1 and T2 by echocardiography and the improvement/deterioration in EF between T1 and T2 was calculated.
Results: Serum S100A8/S100A9 was not increased in DCM vs controls. In contrast, serum S100A8/S100A9 levels were 3.7-fold ($p < 0.0001$) higher in A-MC patients vs controls. At the cut-off of 570 ng/ml, S100A8/S100A9 levels showed a diagnostic specificity and sensitivity of 77% and 89%, respectively, vs controls. Alarmin levels correlated with hsCRP ($r = 0.588$, $p < 0.012$), but not with plasma NT pro-BNP levels ($r = -0.210$, $p = 0.3013$). The peripheral increased alarmins correlated strongly with the mRNA expression of S100A8 ($r = 0.731$, $p = 0.0006$) and S100A9 ($r = 0.702$, $p = 0.0011$) and moderately with lymphocyte function-associated antigen 1 presence (LFA1; $r = 0.435$, $p = 0.0233$) in EMBs of A-MC patients. In A-MC patients, EMB mRNA expression of inflammasome 3 (NLPR3), known to belong to the intracellular signaling of alarmins, correlated with EMB S100A8 ($r = 0.6$, $p = 0.024$) and S100A9 ($r = 0.66$, $p = 0.012$) mRNA expression. Clinically, alarmin serum levels correlated with the EF T1 ($r = 0.6032$, $p = 0.0011$) and moderately with the EF improvement/deterioration (EF T2 - EF T1 7.8% ± 6.5%) over time ($r = 0.498$, $p = 0.0415$) in A-MC patients. For hsCRP ($r = 0.363$, $p = 0.151$) and NT pro-BNP ($r = -0.180$, $p = 0.5046$) levels such latter correlation did not exist.
Conclusions: The S100A8/A9-NPLR3 axis is activated in human A-MC, but not in DCM patients, and reflected by increased serum S1008/S100A9 levels. S1008/S100A9 serum levels are increased under these conditions like some other inflammatory tissue and plasma markers such as hsCRP, but correlated best with the change in LV function. We conclude that the measurement of S100A8/S100A9 serum levels can provide an additional value for the diagnosis and monitoring of A-MC.

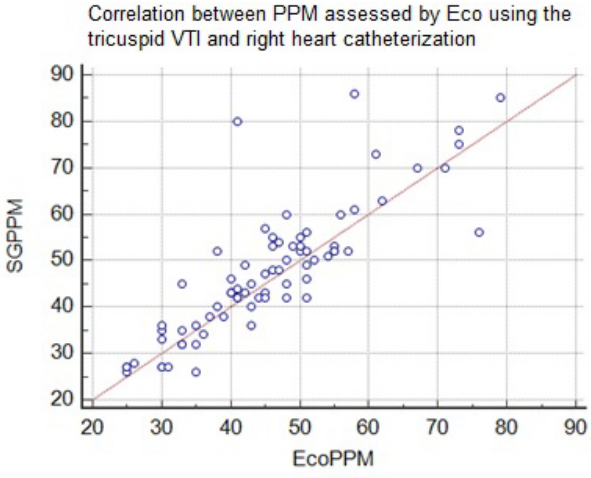
Pulmonary Circulation, Pulmonary Embolism, Right Heart Failure - Clinical

P579

Accuracy and precision of mean pulmonary pressure assessed by echocardiography among patients with pulmonary hypertension

D A Crippa[1]; A Ferro[2]; MG Romero[1]; H Gomez Santa Maria[2]; N Gonzalez[2]; A Lavalle Cobo[2]; G Damianich[2]; F Nehme[1]; I Constatin[1]; MA Gonzalez[2]; H Grancelli[2]; V Daru[3]; M Sztejfman[4]; C Giuliani[4]; A Lescano[1]
[1]Finochietto Clinic, Cardiovascular Imaging, Buenos Aires, Argentina; *[2]Finochietto Clinic, Cardiology, Buenos Aires, Argentina*; *[3]Finochietto Clinic, Buenos Aires, Argentina*; *[4]Finochietto Clinic, Interventional cardiology, Buenos Aires, Argentina*

Background: Non-invasive estimation of pulmonary pressures by Doppler echocardiography (DE) is an important management tool for pulmonary hypertension (PH) patients. Previous reports suggested the use of the velocity-time integral (VTI) of the tricuspid jet for estimating the mean pulmonary pressure (MPP). However, there is limited information regarding precision and accuracy of the VTI tricuspid reflux in patients with HP.
Porpuse: Estimate the concordance between mean pulmonary pressures assessed by DE using the tricuspid VTI and right heart catheterization (RHC)
Material and Methods: Patients with confirmed PH diagnosis (MPP = 25mmHg) that underwent RHC between March 2012 and May 2016 from three heart failure services were included in the analysis. The echocardiographic studies were performed using two ultrasound systems (Esaote Vivid mylab 5s and 30 Gold) equipped with a 3.5MHz transducer. The MPP was obtained by adding the tricuspid jet VTI to the right atrial pressure (RAP), estimated by the inferior vena cava diameter and inspiratory collapse. Hemodynamic confirmation was obtained by a RHC with a Swan-Ganz catheter to asses pulmonary pressures. RHC and DE were performed with less than 24 hs of difference between them and the physicians performing the RHC were blind to echocardiography results. The MPP obtained by the two methods were compared using Lin's concordance correlation coefficient and Bland Altman plot. MPP was categorized in 11 groups per 10 mmHg increase and quadratic weighted kappa was performed for qualitative agreement measures.



Results: A total of 98 patients with confirmed diagnosis of PH were included. Mean age was 57.5 years (SD 19) and 73% were women. PH group (G) distribution was GI 64; GII 16%; GIII 8%; GIV 8% and GV 6%. 79% had heart failure, 26% syncope and 23% chest pain; mean distance in the 6 minute walk test was 326 meters (SD 137). Mean RHC pressures (mm Hg) were: MPP 48 (SD 15), Systolic pulmonary pressure (SPP) 76 (SD 20), Diastolic pulmonary pressure (DPP) 34 (SD12), transpulmonary gradient 35, RAP 10 (SD 5,1). Mean cardiac index was 2,7 liters/min/mts2 (= 2,2, 25%). Analysis of DE data shown: mean TAPSE 18mm (DS 4), SPP 73mmHg (DS 16) and MPP 45,6mmHg (SD 12,1). The concordance correlation coefficient resulted in 0.83 (95% CI 0.74-0.88), with a Pearson r of 0.84 (precision) and a Cb correction factor of 0.97 (accuracy). The Bland Altman plot shows a mean difference of 2mmHg and SD of 7,6mmHg. Although related to a small number of observations, DE underestimated pulmonary pressures above 70mmHg MPP. The k resulted in 0.80 (95% CI 0.70-0.90).
Conclusion: A moderate to high concordance in MPP assessment between a noninvasive technique (tricuspid VTI) and right heart catheterization was observed among patients with PH. These results supports the use of DE as a reliable diagnosis measure of MPP among patients with PH. Further research may be needed to assess accuracy in very high PH patients (MPP above 70mmHg).

Diabetes and the Heart

P580

RAS Antagonists and beta blockers stabilize HbA1c and improve insulin resistance in patients with diabetes free from cardiac disease

R Raphael Wurm[1]; M Resl[2]; S Neuhold[3]; H Arfsten[1]; N Pavo[1]; M Clodi[2]; A Luger[4]; M Huelsmann[1]
[1]Medical University of Vienna, Department of Internal Medicine II, Division of Cardiology, Vienna, Austria; *[2]Convent of the Brothers of Mercy Hospital Linz, Department of Internal Medicine, Linz, Austria*; *[3]Medical University of Vienna, Department of Anaesthesia, General Intensive Care and Pain Control, Vienna, Austria*; *[4]Medical University of Vienna, Department of Endocrinology, Vienna, Austria*

Background: Sacubitril/Valsartan improves glycemic control in patients with diabetes and heart failure. Conversely, the translational PONTIAC trial showed that first line heart failure drugs, i.e. renin-angiotensin-system (RAS) antagonists and beta blockers, improve outcome in patients with diabetes free from cardiac disease.
Purpose: Here we sought to assess the effects of RAS antagonists and beta blockers on HbA1c and HOMA in the PONTIAC population.

Methods: The PONTIAC trial enrolled 300 patients with stable diabetes free from cardiac disease. They were randomized to either intensified treatment with RAS antagonists and beta blockers titrated to reach guideline recommended target doses, or control for one year. In this post-hoc hoc analysis, we included patients in whom complete insulin profiles were available. We compared changes in HbA1c, and in insulin resistance via the homeostatic model assessment (HOMA), between baseline and one year of follow up.
Results: We included 195 patients (100 control, 95 treatment). The mean age of the cohort was 66 ± 9 years, mean duration of diabetes was 15.4 ± 12.6 years.
After one year, HbA1c increased significantly in the control group (6.7% to 7.0%, p < 0.05) while there was no change in the treatment group (7.2% to 7.1%, p = n.s.). Correspondingly, HOMA did not change in the control group (13.2 to 13.6, p = n.s.), while it decreased significantly in the treatment group (19.1 to 14.9, p = 0.047).
Discussion: Despite treatment, diabetes tends to worsen over time. Here we show that treatment with RAS antagonists and beta blockers can halt this deterioration and improve insulin resistance in patients free from cardiac disease. Potential mechanisms include improved peripheral circulation or a positive effect on subclinical heart failure. Future trials to evaluate heart failure drugs as preventive measures in patients with diabetes appear warranted.

Baseline characteristics

	Control (n = 100)	Intervention (n = 95)	p-value
Male n (%)	64 (64.0)	64 (67.4)	0.731
Age (mean (sd))	66.22 (9.40)	67.72 (7.82)	0.230
Duration of diabetes (median [IQR])	12.50 [5.75, 20.00]	10.00 [5.00, 20.00]	0.607
BMI (median [IQR])	29.10 [25.35, 32.92]	27.70 [25.60, 33.00]	0.682
Insulins, n (%)	38 (38.0)	43 (45.3)	0.377
Oral antidiabetic therapy n (%)	70 (70.0)	69 (72.6)	0.804
eGFR (median [IQR])	81.40 [68.40, 96.20]	82.00 [72.70, 93.80]	0.757

BMI - body mass index; eGFR - estimated glomerular filtration rate.

Cardiovascular Pharmacotherapy

P581
Withaferin A attenuates inflammatory response and cardiovascular dysfunction induced by LPS

C Chintan Koyani[1]; C Trummer[2]; I Plastira[2]; M Lechleitner[2]; H Sourij[3]; S Frank[2]; W Sattler[2]; E Malle[2]; D Von Lewinski[1]
[1]Medical University of Graz, Division of Cardiology, Graz, Austria; *[2]Medical University of Graz, Institute of Molecular Biology and Biochemistry, Graz, Austria*; *[3]Medical University of Graz, Division of Endocrinology and Diabetology, Graz, Austria*

Background: Prevalence of diabetes is steeply rising in developing countries. Along with hyperglycaemia, other diabetic complications including impaired cardiovascular function, elevated inflammatory cytokines (primarily derived from monocytes/macrophages) and higher susceptibility to develop infection are detrimental and require substantial clinical attention. Withaferin A, a steroidal lactone derived from Withania somnifera belonging to Solanaceae family, has recently been identified as a potent anti-diabetic agent with positive effects against weight gain.
Purpose: In the present study we aimed to evaluate the effects of withaferin A against LPS-induced inflammation (in cardiomyocytes and macrophages) in vitro, and cardiovascular dysfunction (aortic ring contractile function and survival) and sepsis in vivo.
Methods: Murine cardiomyocyte (HL-1) and macrophage (RAW 264.7) cell lines were used to study intracellular signalling. C57BL6 mice were used to clarify the effects of withaferin A on LPS-induced cytokine release, cardiac and vascular dysfunction, and survival.
Results: Withaferin A (1 μM) impaired LPS-induced p42/44 MAPK and p65 activation in both cell lines. Inhibition of STAT1/3/6 phosphorylation was observed only in macrophages. As a consequence, LPS-induced cytokine (TNFa, IL-4/6/10) production and iNOS expression became apparent in response to LPS. Myography data revealed protective effect of withaferin A (10 mg/kg, i.p.) against LPS-impaired endothelial relaxation and significantly improved survival rate (˜40%) in septic mice. Conclusion: Our data reveval therapeutic potential of withaferin A against LPS-induced cardiovascular damage, inflammation and mortality.

Basic Science - Cardiac Biology and Physiology

P582
Protein tyrosine phosphatase non receptor type 22 (PTPN22) function impacts neutrophil extracellular trap formation

L Lisa Kascha[1]; T Hofbauer[1]; M Winter[1]; A Panzenboeck[1]; K Distelmaier[1]; S Scherz[1]; A Ondracek[1]; C Feist[1]; A Mangold[1]; IM Lang[1]
[1]Medical University of Vienna, Department of Cardiology, Internal Medicine II, Vienna, Austria

Background: Neutrophils undergo NETosis via peptidylarginine deiminase 4 (PAD 4) activation and release extracellular traps (NETs) into the extracellular space to combat pathogens. NETs also have a significant role in thrombotic disease. Coronary NET burden correlates positively with infarct size in ST-elevation myocardial infarction (STEMI) patients. It was reported that a missense mutation (R620W) in the protein tyrosine phosphatase non receptor type 22 (PTPN22) results in abrogated PAD4 inhibition and consecutively leads to enhanced NETosis. Deoxyribonuclease (DNase) is a natural counter mechanism against NETs.
Purpose: We analyzed the effect of PTPN22 deficiency on NET formation in a murine model and studied the R620W single nucleotide polymorphism (SNP) in coronary artery disease (CAD) patients with regard to outcomes.
Methods: Blood was drawn from PTPN22 knockout (KO) mice, NETosis was induced by ionomycin and compared to wildtype (WT) mice (each n = 10). NETotic neutrophils were measured by flow cytometry. DNase activity in murine plasma samples was measured by an in-house built activity assay. Furthermore, we tested the R620W SNP in 711 CAD patients who suffered from ST elevation myocardial infarction using allelic discrimination polymerase chain reaction (PCR).
Results: PTPN22 KO mice displayed significantly reduced NETosis compared to WT. Interestingly, PTPN22 mice had a significantly increased plasmatic DNase activity, which correlated with reduced NETosis. CAD patients carrying the R620W showed no altered mortality compared to controls.
Conclusion: In contrast to present literature, we found decreased NETosis in PTPN22 KO mice. In this ongoing project, we will further evaluate NETosis and DNase in connection to PTPN22.

Cardiac Resynchronization Therapy

P583
Underuse of Cardiac resynchronization in Austria, and the role of dedicated heart failure clinics for implementation.

M Marianne Gwechenberger[1]; M Huelsmann[1]; D Moertl[2]; G Poelzl[3]; L Kaltenbach[4]; C Gangl[1]
[1]Medical University of Vienna, Vienna, Austria; *[2]University Hospital Sankt Poelten, Sankt Poelten, Austria*; *[3]Medical University of Innsbruck, Innsbruck, Austria*; *[4]Innsbruck Medical University, Innsbruck, Austria*

Background: Cardiac resynchronization therapy (CRT) is a well established therapy in patients with heart failure and has been proven to reduce morbidity and mortality. However, there is still a gap between the number of patients with an indication for a CRT (according to the guidelines) and its actual utilization, with wide variations between different countries.
Purpose: Aim of the study was to investigate the utilization of CRTs in Austria in general and in the heart failure registry which is conducted in dedicated heart failure clinics.
Methods: The calculations are based on a previously published models: Roughly 1-2% of the general population suffer from heart failure, of whom 10% have a class I indication for CRT, leading to 1000-2000 eligible patients per million inhabitants. Due to varying guideline definitions 24.5-30% if the population have a class I and IIa indication, leading to 24500-3000 eligible patients per million inhabitants. The actual number of patients treated with a CRT was calculated from the sum of CRT implantations over five years (normalized / million). Statistics Austria was used as a source. The CRT penetration was defined as CRT patients treated with a CRT divided by the prevalence of patients eligible for CRT. The normalized implant rates increased over the years. The Austrian Working Group on Heart Failure has established a registry in for all patients referred to dedicated heart failure clinics with a planned follow-up after 12 ± 3 months. For this analysis we assessed the rate of patients with a CRT at the follow up visit.
Results: In Austria the normalized implant rates increased over the years, leading to 752.2 patients normalized per million population (2012-2016) that received a CRT device. Therefore the estimated CRT penetration range was 37.6-75.2% for the class I indication and 25,1-30.7% for class I and IIa indication. In the heart failure registry 16,2% of all patients received a CRT-device at 1 year follow up. However 12.1% with an indication for a CRT remained without device.
Conclusion: Although implant rates increased over the years, the CRT penetration range is still needs optimization. The implementation of CRT recommendation seems to be higher in dedicated heart failure clinics.

Poster Session 1 - Clinical Cases

Chronic Heart Failure - Pathophysiology and Mechanisms

P621
Anagrelide induced cardiomyopathy: a case report

A Tsipis[1]; N Skandalakis[1]; N Kanakakis[1]; N Pilatis[1]; E Petropoulou[1]
[1]*IASO General Hospital, Department of Cardiology, ATHENS, Greece*

Introduction: Anagrelide is a synthetic quinazoline derivative that has been shown to reduce platelet production and the risk of thrombosis in patients with thrombocythaemia associated with myeloproliferative disorders. Anagrelide inhibit platelet cyclic adenosine monophosphate cyclic phosphodiesterase (cAMP) and platelet aggregation. Phosphodiesterase inhibitors are associated with positive inotropy, vasodilatation and cardiac arrhythmias. Experimental studies have shown that treatment with anagrelide produces myocardial necrosis and apoptosis.
Material and Methods: We report a case of an 80-year old woman with essential thrombocythaemia developed anagrelide induced cardiomyopathy. The patient had no cardiovascular risk factor and the cardiac function was normally prior to treatment. After anagrelide introduction, patient appears worsening dyspnoea, fatigue and palpitations.
Results: Echocardiography revealed decreased left systolic dysfunction and left ventricular enlargement. The serum levels of brain natriuretic peptide were elevated. It was decided that this condition was due to anagrelide administration and the treatment was interrupted. Three months later, following treatment for heart failure, the patient presents improved left ventricle systolic function and BNP was normalized.
Conclusions: Cardiotoxicity secondary to anegralide treatment manifests as congestive heart failure and cardiac arrhythmias. Mechanism by anegralide induced cardiotoxicity involves inhibition of cAMP, interference with mitochondrial metabolism, myocardial necrosis and apoptosis. Anagrelide should be used with caution in patients with heart disease. A pretreatment cardiovascular examination is recommended along with careful monitoring during treatment in all patients with or without heart disease.

P622
Use of sacubitril/valsartan beyond guidelines

H Altay[1]; S Pehlivanoglu[1]
[1]*Baskent University Istanbul Hospital , Cardiology, Istanbul, Turkey*

A 54 year-old-man applied to our outpatient clinic for progressive dyspnea and dizziness. He had had aortic valve replacement surgery 18 years ago. Further workup in early 2014 revealed an echocardiogram with left ventricular ejection fraction (LVEF) of 20 % and cardiac angiography with no significant coronary disease. Cardiac resynchronization therapy (CRT) device was implanted 3 years ago. He did not respond to CRT device favourably and he has been on atrial fibrillation (AF) for the last two years. He was on medical therapies that included, carvedilol, spironolactone, tolvaptan, furosemide and warfarin. He had been started ARNi one month ago but could not tolerate because of hypotension. Physical examination was notable for blood pressure 85/60 mmHg, no peripheral edema, and cool peripheral extremities. Decreased breath sounds were heard at the base of her left ungs. Notable admission labs included creatinine (cr) 1,56 mg/dl, blood urea nitrogen (BUN) 74 mg/dl, estimated glomerular filtration rate (eGFR) 59 ml/minute, sodium 130 mmol/L and amino terminal pro-brain natriuretic peptide (NT-proBNP 750 pg/mL. An echocardiogram demonstrated LVEF 15 %, severe tricuspid regurgitation, systolic pulmonary artery pressure 50 mmHg and normal aortic prosthesis function. His ECG revealed AF with left bundle branch block. A chest radiograph revealed left-sided pleural effusion. He was diagnosed with low output HF and hospitalized. The patient was transitioned to digoksin with carvedilol discontinued. She was started dobutamine infusion in addition to a thoracentesis for pleural effusion. Dobutamine was weaned off at day 4. On Day 5, sacubitril/valsartan was initiated at the dose of 24/26 mg b.i.d and followed for 2 more days in the hospital. The patient maintained adequate blood pressure and urine output meantime. He was discharged with sacubitril/valsartan and digoksin . Sacubitril/valsartan was titrated to dose of 49/51 mg b.i.d mg b.i.d. after one month postdischarge. At 6 months after discharge, on clinic visits she has been without signs of decompensated or low output HF.
In a patient with valvular cardiomyopathy, stage D HFrEF and low cardiac output profile, we describe the successful use of sacubitril/valsartan after failed attempts to use due to hypotension. The hypotensive effects of these drugs may potentially explain the lack of benefit or potential harm that may be observed in advanced HF patient who have already low blood pressure. Additional lowering of SBP in a patient with baseline hypotension may result in organ hypoperfusion, worsening renal function, cardiac ischemia, and reductions in cardiac output further.
Conclusion and implications for clinical practice
Given the long-term favourable findings of sacubitril/valsartan and our experience with this patient, sacubitril/valsartan may be a potential option for advanced HF patients with low cardiac profile after a trial of intravenous inotrop support.

P623
Questions and doubts about ARNI therapy in a patient with heart failure: a real life experience

D Kosuta[1]; T Furlan[1]; S Poznic[1]; A Adamlje[1]; B Leskovar[1]
[1]*Trbovlje General Hospital, Department of Internal Medicine, Trbovlje, Slovenia*

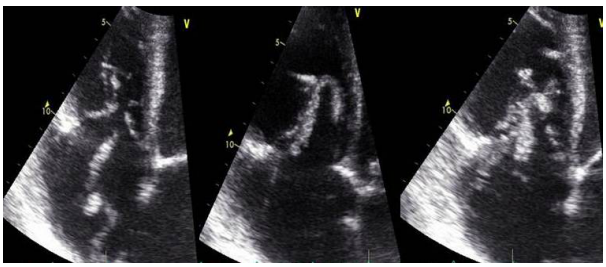
Introduction: ARNI (angiotensin receptor-neprilysin inhibitor) is considered a breakthrough therapy in heart failure with reduced ejection fraction since it has been shown to have a great prognostic impact. However, the administration and titration of the drug in real life carries multiple doubts that are not easy to solve.
Case presentation: We are presenting the case of a 77-year-old gentleman with ischemic heart disease, diabetes mellitus type 2, chronic kidney disease, with a pacemaker-defibrillator implanted due to intermittent 3rd degree AV block and a history of myocardial infarction. In May 2015, he was enrolled in our outpatient clinic due to heart failure with reduced ejection fraction (20 - 30%). Despite optimised medical treatment with maximum tolerated doses of standard drugs and several applications of levosimendan, he remained symptomatic, his functional status was NYHA class III, so we decided to start ARNI therapy.
Discussion: At the beginning of the therapy his pulse rate was around 100 beats/minute despite ivabradine and digoxin and his blood pressure was within normal range. After initiation with the lowest dose of sacubitril/valsartan (24/26 mg twice daily) we observed an increase in the ejection fraction by 10%, a systolic and diastolic pressure drop to 96/65 mmHg and a drop in the heart rate to 87 beats/minute. We considered stopping the drug because of hypotension however, since the patient was feeling good and did not have any symptoms of hypotension, we continued with the therapy. Moreover, the reduction of heart rate was an indicator of an improved hemodynamic status, which allowed the heart to meet the organism's needs for oxygen at a lower heat rate. When the systolic pressure reached values over 100 mmHg again, we increased the dosage. The patient would not tolerate a high dose increase at once, because his pressure was still on the lower side and his renal function was impaired, so we did it with a stepwise approach over a six months period. We increased the dose for 24/26 mg per day every month till we reached the recommended dose, with check-ups every two to four weeks. Each time we increased the dose, we noticed an initial drop in blood pressure, which increased again after a while, and a consistent lowering of the heart rate. During this period of time patient's lean body mass raised for about 12%, he was feeling increasingly better, his performance status improved to NYHA class II according to the six-minute walking test and he has maintained a good functional status ever since.
Conclusion: ARNI therapy has a great impact on the prognosis of patients with heart failure with reduced ejection fraction and its pros outweigh minor cons. Therefore patients experiencing asymptomatic hypotension should not discontinue ARNI but they should rather be thoroughly monitored and ARNI titration scheme should be individually tailored with a stepwise approach.

P624

Dilated cardiomyopathy with severe left ventricular dysfunction and right atrial thrombi secondary to thyrotoxicosis.

S Antit[1]; I Slama[1]; S Chenik[1]; S Belakhel[2]; A Mestiri[2]; I Boussabeh[1]; M Thameur[1]; L Zakhama[1]; S Benyoussef[1]
[1]*Interior Security Forces Hospital, Department of Cardiology, Marsa, Tunisia*; [2]*Interior Security Forces Hospital, Department of medicine interne, Marsa, Tunisia*

Introduction: Hyperthyroidism can affect variously the cardiovascular system. The cardiovascular findings range from sinus tachycardia to atrial fibrillation and from a high cardiac output state to rarely congestive heart failure due to impaired systolic left ventricular function and it is associated with a higher risk of thrombo-embolism events. Thrombosis of the right atrium is extremely rare, and to the best of our knowledge, only two cases are described in the literature. We report a rare case of right atrial thrombi in a patient with Graves'disease induced dilated cardiomyopathy with severe left ventricular systolic dysfunction.
Case report: A 45-year-old man with a past medical history of diabetes mellitus, thrombophlebitis of the right lower limb in 2011 and Graves'disease since 2008. He was admitted in our department of cardiology for acute heart failure associated to a recurrent thrombophlebitis of the right lower limb. On clinical examination, he appeared very anxious and had fine tremors in hands, exophthalmos associated with a large goiter. Cardiovascular system examination revealed left ventricular gallop, bilateral basal crackles and clinical signs of right heart failure. Electrocardiogram showed a sinus rhythm, incomplete right bundle branch block. Transthoracic echocardiography (TTE) revealed a dilated left atrium, moderately dilated left ventricle with severe global systolic dysfunction (Ejection Fraction: 20%). The right cavities were also dilated and there was severe right ventricular dysfunction and pulmonary hypertension (52mm Hg). There was significant mitral and tricuspid insufficiency. The patient was managed with intravenous diuretics, bisoprolol, spironolactone, anticoagulation therapy and anti-thyroid drugs.
One week later, a repeat TTE showed large highly mobile snake-like echogenic masses in the right atrium partially adherent to the tricuspid valve and floating in the right ventricle and the inferior vena cava. The diagnosis was between thrombi or vegetations. The patient didn't present fever (37°C) and the laboratory tests didn't show inflammatory syndrome. Despite optimal anticoagulation range, the diagnosis of atrial thrombi was made and we associated antiplatelet agent to anticoagulation therapy. A further TTE (after 7 days) showed totally regression of the atrial thrombi. The patient was discharged on optimal medical therapy, asymptomatic, with a recommendation of radioactive iodine treatment.
Conclusion: In summary, we should keep in mind the possibility of atrial thrombus with Graves'hyperthyroidism, especially patients that have heart failure or atrial fibrillation. In such case, performed echocardiography was warranted. And, if intra-cardiac mass identified, careful differential diagnosis are needed.



Snake-like thrombi in the right atrium.

P625

Case 5-Fluorouacil-Induced Myocardial Infarction and Recurrent Stent Thrombosis; An Unusual Case

B Benedicte Lefebvre[1]; S Dandona[1]; I Malcolm[1]; N Mousavi[1]
[1]*McGill University Health Centre, Cardiology, Montreal, Canada*

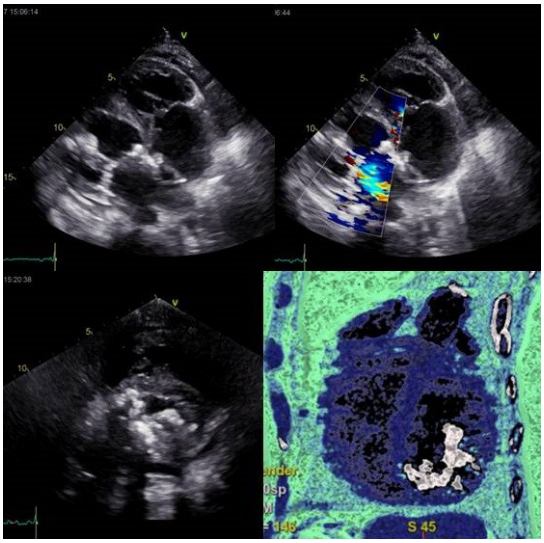
A 66 year-old gentleman known for diabetes mellitus and no other cardiac risk factors presented to the emergency room with retrosternal chest pain of a few days duration. He was known for stage IV colon cancer and had undergone resection of primary tumour and liver metastases. The patient had been treated with 1 cycle of 5-Fluorouacil (5-FU) 2 weeks prior to admission. Anterior ST Elevation MI was diagnosed and the patient immediately underwent an angiography, which revealed 100% occlusion of the left anterior descending artery (LAD), with patent remaining coronaries. Deployment of the stent to the LAD lesion relieved the patient's symptoms. However, 12 hours after the procedure, chest pain and anterior ST segment elevation recurred despite dual antiplatelets therapy with aspirin and Clopidogrel. The patient was emergently brought back to the cath lab. In-stent thrombosis was diagnosed and a new stent was inserted after aspiration of clots. Clopidogrel was replaced with Ticagrelor. Throughout the following days, the patient had residual chest pain and ST segments remained elevated despite the troponin level trending down. Echocardiogram showed a left ventricular ejection fraction (LVEF) of 20-25% with septal, anterior and apical akinesis. He was returned to the cath lab on day 6 as mild chest discomfort was still present. He was found to have recurrent in-stent thrombosis despite adequate treatment and well-apposed stents. The decision was made by the interventionalist not to perform another angioplasty as clot aspiration was impossible and a new stent would have to be inserted back into the left main. A cardiac MRI was done to assess for viability of the anterior wall. It showed massive haemorrhagic infarction of the entire LAD territory without viability with LVEF of 21%, right ventricular ejection fraction of 20% and apical thrombus. From these results, 2 dilemmas arose. First, should we anticoagulate for the apical clot given the haemorrhagic transformation and would we risk myocardial rupture? Second, should we insert an implantable cardioverter defibrillator (ICD) without waiting the recommended amount of time as the ejection fraction is unlikely to recover? Given that the patient was returning to a community center and had episodes of non-sustained ventricular tachycardia, we elected to insert the ICD prior to transferring the patient. The patient passed away right after the procedure of unclear circumstances.
5-FU is an antimetabolite chemotherapeutic agent with potential for cardiotoxicity. The mechanism is not well understood but is thought to be secondary to myocardial ischemia due to coronary vasospasm, thrombosis or arteritis provoked by dysregulation of endothelial nitric oxide synthase and upregulation of protein kinase C. Here we present an extreme case of 5-FU toxicity in a patient with increased prothrombotic state due to underlying malignancy and also, difficult clinical decisions for anticoagulation and early ICD insertion

P626

The legend of a stone heart

M Maia Rusu[1]; A Ionescu[1]; T Constantinescu[2]; T Barascu[3]; B A Popescu[1]; C Ginghina[1]; R Jurcut[1]
[1]*Institute of Cardiovascular Diseases Prof. C.C. Iliescu, Bucharest, Romania*; [2]*"Marius Nasta" Institute Of Pneumology, Bucharest, Romania*; [3]*Fundeni Clinical Institute, Bucharest, Romania*

Introduction: Exposure to radiation is associated with a risk of radiation-induced heart valve damage characterised by valve fibrosis and calcification. There is a latent interval of 10-20 years between radiation exposure and development of clinically significant heart valve disease. Risk is related to radiation dose received, younger age at the time of irradiation, interval from exposure and use of concomitant chemotherapy.



Clinical case: A 38-year-old man was admited to our clinic with moderate exertional dyspnea, fatigue and a syncope during exercise. The medical history revealed: left pulmonary sarcoma at the age of 4 years old (in 1982) treated with radiotherapy

(16 sessions of cobaltotherapy in a 6 months interval), chemotherapy (medication not known) and left total pneumonectomy. At admission, laboratory tests showed an increased BNP levels (1426 pg/ml) and mild dyslipidemia, with normal calcium and parathormon levels.The transthoracic echocardiography found a normal LV systolic function with severe calcifications of the papillary muscles, apical segments of inferior septum and inferior wall asociated with severe mitral regurgitation probably related to radiotherapy during childhood. It also revealed a severe tricuspid valve regurgitation, severe pulmonary hypertension and small amount of pericardial fluid. A thoracic computed tomography with contrast was performed to exclude pulmonary thromboembolism, which described severe cardiac calcifications, right bazal pulmonary emphysema, mediastinal adenopathies. Pneumological evaluation found a hypertrophic right lung herniated in left hemythorax, without patological changes at CT examination (fibrosis or bronchiectasis), only right bazal emphyzema. The patient had severe ventilator dysfunction with prevalence of restrictive component. In this case pulmonary hypertension the most probably is determined by the left cardiac stuctural changes (severe mitral regurgitation postradiotherapy), so it has a limited indication for pulmonary vasodilator therapy and cardiac catheterization. Cardiac reevaluation after 4 months revealed an improvement in clinical state, a decrease of BNP level to 1031pg/ml. In case of clinical worsening, the patient has an indication for valve replacement, but we should be aware about periprocedural complications in conditions of left pneumectomy and severe calcifications of mitral subvalvular apparatus.

Conclusions: Radiation exposure is a risk factor for development of clinically significant valvular heart disease. Cancer survivors who received mediastinal radiotherapy require vigilance and screening for valvular heart disease many years after curative treatment. Although the majority of patients are initially asymptomatic, a proportion of patients will require valve surgery. Physicians must be aware of post-radiation cardiac complications, recognize at-risc patients, and screen such patients for symptoms and signs of cardiac disease.

P627

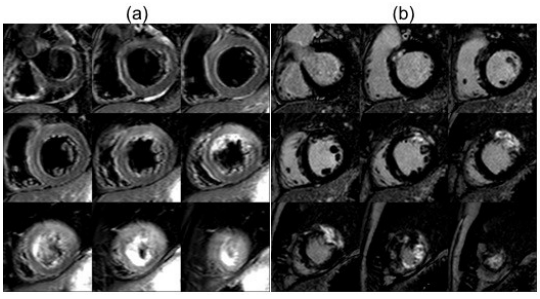
A case of bleomycin induced myocarditis

M Sweeney[1]; GD Cole[1]; CM Plymen[1]
[1]*Imperial College Healthcare NHS Trust, London, United Kingdom*

We report the case of a 26-year-old man with no preceding medical history who presented with metastatic embryonal carcinoma of the right testicle. Following orchidectomy, he commenced adjuvant combination chemotherapy with bleomycin, etoposide and cisplatin with curative intent.

On day 5 of the first cycle of chemotherapy, he experienced severe retrosternal chest pain associated with vomiting and sweating. An ECG at the time demonstrated widespread saddle-shaped ST-segment elevation in the inferior and lateral leads and serum troponin increased from 28 ng/L (Ref: = 34 ng/L) on admission to 18,520 ng/L at 12 hours. A cardiac MRI demonstrated normal overall left ventricular systolic function, however, there were regional wall motion abnormalities in the anterior and anterolateral walls and apex associated with myocardial oedema (panel a) and there was widespread late gadolinium enhancement (panel b) suggesting a diagnosis of acute myocarditis. Within 24 hours the chest pain was improving and serum troponin was downtrending. He was symptom free by day 3 of admission and was discharged on regular ibuprofen and colchicine.

The aetiology of myocarditis remained unclear. An autoimmune screen was negative, common viral markers demonstrated no acute viral infections and the temporal relationship between starting chemotherapy and onset of symptoms made a reaction to chemotherapy the most likely cause. Bleomycin was suspected as the causative agent due to a number of case reports of an acute chest pain syndrome following its administration.



Cardiac MRI at presentation

After discussion with the treating oncologist, it was felt that omitting bleomycin would not significantly reduce the efficacy of the chemotherapy. Therefore given the significant troponin rise in a young patient, this was withheld from future cycles. We did not start prognostic heart failure therapy as the overall LV function remained normal despite the wall motion abnormalities.

6 months after initial presentation, the metastatic deposits had resolved and tumour markers were negative. He remained asymptomatic from a cardiac perspective and repeat cardiac MRI demonstrated improvement of the wall motion abnormalities with only mild hypokinesia of the lateral wall and apex. The myocardial oedema had almost completely resolved and late gadolinium enhancement was markedly improved.

No conclusive diagnosis has been made in any of the previous cases of bleomycin induced chest pain and this is the first reported case to have a cardiac MRI performed following an acute reaction which may provide insight into the aetiology of previously reported cases. This case highlights the importance of multi-disciplinary team working when managing cardio-oncology patients where decisions to alter life-saving chemotherapy need to be made on a patient-by-patient basis with careful consideration of the severity of the cardiotoxicity and the anti-neoplastic benefit which would be lost by excluding a suspected cardiotoxic chemotherapy.

Chronic Heart Failure - Diagnostic Methods

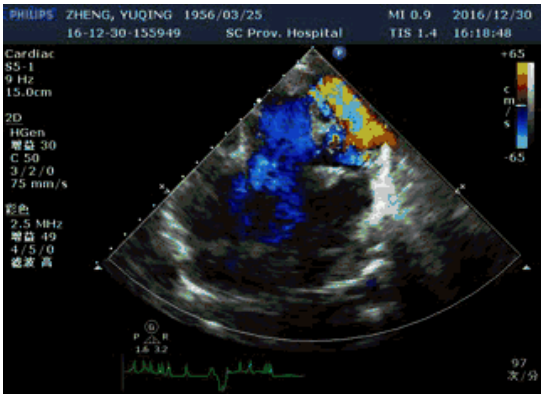
P628

Anomalous origin of the left coronary artery from the pulmonary artery in an old female

G Geqi Ding[1]
[1]*Sichuan Academy of Medical Sciences & Sichuan Provincial People's Hospital, Department of Cardiovascular Ultrasound and Non-invasive Cardiology, Chengdu, China People's Republic of*

A 60-year-old female referred to our center due to paroxysmal nocturnal dyspnea and orthopnoea. During the 2 days prior to admission, she had suffered progressive dyspnea with chest pain. she had suffered dyspnea on exertion from one year previously, which was in New York Heart Association (NYHA) functional class II, without any history of chest pain and syncope. At presentation, blood pressure was normal and a holosystolic murmur of grade III/VI at the left sternal border were detected. A twelve-lead electrocardiogram showed a rapid atrial fibrillation rhythm with ST-T changes. Chest X-ray showed marked cardiomegaly and pulmonary venous congestion. Lab data showed NT-proBNP was elevated (9000 pg/ml).

Transthoracic echocardiography demonstrated severe left ventricular and atrium enlargement with moderate dysfunction [LVEDD = 63mm, LA diameter = 61mm, left ventricular ejection fraction (LVEF) = 45%] and moderate to severe mitral and tricuspid insuffciency along with 36 (mmHg) increased systolic pulmonary artery pressure. There was regional wall motion abnormality in the anterior and lateral wall and multiple dilated coronary branches with abundant color doppler signals in both right and left territories through the inferior wall and apex extending by septal toward the anterior and basal. The origin of the right coronary artery from the right sinus of Valsalva was seen; however, the left coronary branches were connected to the backward of pulmonary artery and the color doppler was presence of "steal blood phenomenon".



Electrocardiographically-gated multi-detector computed tomographic (CT) angiograp-hy revealed anomalous origin of the left coronary artery from the

pulmonary artery (ALCAPA) with a retrograde ?ow from the left coronary artery to the pulmonary artery and extensive collateral vessels at the left ventricle.
Diuretic intravenous treatment for 7 days and metoprolol for ventricular rate control, trimetazidine for myocardial metabolism improvement, The patient's congestive symptoms were decreased and clinical situation improved stable, but she refused to have surgery due to the high risk. she was discharged 10 days after admission in a stale status, with all previously reported parameters within normal limits. At discharge, she was followed by cardiologist and cardiac surgeons, and her clinical situation one year later is stable without signs and symptoms of heart failure.
Possible differential diagnosis: In this case two main possibilities need to be differentiated: coronary artery fistula and ALCAPA. The origin of left coronary is correct in coronary fistula and the flow is antegrade which is no steal phenomenon.
Conclusion: This case illustrates an congenital coronary origin anomaly cause of acute heart failure (ALCAPA)that might be underdiagnosed in clinical practice (especially in patients with chronic comorbidities) and emphasizes the importance of echocardiography for management of heart failure.

Chronic Heart Failure - Treatment

P629
The case of sudden cardiac death at patient with heart failure and reduced ejection fraction in long-term period after stem cell therapy

D Dina Shorikova[1]; A Gabrielan[2]; E Shorikov[1]
[1]Bucovinian State Medical University, Chernivtsy, Ukraine; [2]National Institute of Surgery and Transplantology n. a. O. O. Shalimov, Kyiv, Ukraine

Case Summary: Patient M., 63 years old, was hospitalized in clinic with the substantial decreased tolerance to exercise stress, class NYHA IV of heart failure (HF) was diagnosed. The patient's ejection fraction was 18% and local contractility index was set at 2,63 points. The mean blood pressure during 24-hour monitoring was 124/78 mmHg. Heart rate was 68 bpm, the ECG showed normal sinoatrial rate. Plasma NT-proBNP was measured at the level of 2970 pcg/ml. Blood TORCH-infection markers were negative. On the basis of conservative medicamentous treatment, which consist of carvedilol 12,5 mg daily, ramipril - 2,5 mg daily, spironolactone 50 mg daily, the procedure of steam cells transplantation from cord blood was applied. After 6 month of controlled follow-up was reported the diminishing of clinical symptoms and signs of HF, NYHA III class was set and the EF increased up to 28%, the NT-proBNP level decreased down to 757 pcg/ml on the basis of the reaching of the maximal tolerated doses of prescribed drugs. The patients returned to the stable previous work in the office and started gradually maximize everyday physical activity.
After 6 and a half month the patient was urgently hospitalized in cardiologic department with the episode of paroxysmal ventricle monomorphic tachycardia. The episode was quickly stopped by administration of bolus dose (800 mg) of amiodarone with the continued use of 400 mg daily maintenance dose of it. The investigation of the TORCH markers became positive by finding of cytomegalovirus and Epstein-Barr infection.
After the 8 month after transplantation of steam cord blood cells the acute viral respiratory infection was diagnosed in patient, and on this background sudden cardiac death was occurred. The possible cause of lethal incident was the fatal ventricle rhythm disturbance.
Questions: 1. Is there an association between fatal rhythm occurrence and steam cord cells transplantation? 2. What is the role of TORCH infection markers in the origin of lethal rhythm disturbance? 3. Should we prevent the development of the dangerous heart rhythm disorders after transplantation of steam cells of cord blood?
Discussion: Steam cells transplantation is followed by stable level of some adverse effects. Firstly, the proarrhythmogenic activity was typical for steam cells, mostly expressed in skeletal mioblasts. Secondly, the manifestation of persistent viral infection is also characterized the live cycles of polipotent heamathopoetic cells, embryogenic cells and mesenchymal adipose tissue steam cells. The diagnosis of lethal arrhythmias and routine use of daily ECG-monitoring in patients after steem cells transplantation especially after acute viral respiratory infection now remains an open-ended question. Also the estimation of the influence of TORCH-infection on HF patients with low ejection fraction follow-up keeps actual

P630
An unusual case of explantation of a left ventricular assit device.

O Oyvind Reitan[1]; B Kornhall[1]; C Meurling[1]; E Grins[1]; B Bronden[1]
[1]Lund University Hospital, Department of Cardiology, Lund, Sweden

Case description: A 60 year old lady suddenly became ill with irradiating chest pain. ECG showed sinus tachykardia, RBBB and anterior ST-elevation. The patient was referred to our hospital for coronary angiography, which was performed 8 hours after debut.
The angiogram showed a LM stenosis, LAD and RCA ocklusion and a Cx stenosis. Ultrasound showed a normal-sized LV with contractions only in the basal segments. An acute CABG, with intra aortic balloon pump (IABP) support was done.
The postoperative stay on the thoracic intensive care unit was stormy with repetitive episodes of pulmonary edema, ventricular fibrillations, despite the continuous use of IABP, different inotropes and anti arrhytmic drugs. Ultrasound showed an ejection fraction (EF) of 15 %.
After 2 weeks it was decided to provide the patient with a left ventricular assist device (LVAD). Post
LVAD-implantation the arrythmias disappeared and the patient recovered and could be transferred to the ward for training but also be examined as a possible candidate for heart transplantation (HTx).
However, her vascular system showed extensive calcified arterial vessels especially in the pelvic arteries and she was therefore found not eligible for a HTx.
After discharge the patient did well on the pump. She was treated with RAAS blockade and betablocker to keep the mean blood pressure between 70-90mmHg. After some months, the patient started to produce pulse and the blood pressure increased. Continous examinations of the heart with ultrasound were performed showing neither dilatation of the left ventricle nor development of an aneurysm which is common in an LAD-related myocardial infarction. The native heart function was tested in a controlled manner in the echo-lab by reducing the speed of the pump gradually untill non-support. The heart thereby took over the pump work without any discomfort for the patient.
After approximately 3 years on pump, the LVAD started to give unexpected larms, which turned out to be due to cable brake. It was decided to explant the pump and replace it with a second one. The pump was explanted and the native heart function was tested during 2 hours in the operating theatre. It was concluded, that the native heart function was good enough to explant the LVAD with no replacement, but the inflow cannula in the left ventricular apex was left in and plugged, in case the patient would require a second LVAD later.
Nearly one year after, the patient is doing well and has no clinical signs of heart failure and the EF is about 30 % on common heart failure medication.
Conclusion: An LVAD provides the heart with a substantial afterload reduction. The question is if the present case indicates if a patient with a large established MI should be equipped with a mechanical support system during the time when remodeling is expected to occur in order to preserve normal geometry of the heart, prevent development of an aneurysm and preserve more pump power of the native heart.

P631
Intracoronary stem cell life saving infusion in a patient with chronic decompensated heart failure dependent on intra-aortic balloon pump

A Ntalianis[1]; A Repasos[1]; E Papadopoulou[1]; N Makris[1]; E Anninos[1]; I Stamoulopoulos[1]; N Zografos[1]; M Kondilis[1]; A Cohen[1]; A Koutsoukis[1]; A Mareti[1]; S Sventzouri[1]; K Tambakis[1]; I Kanakakis[1]; I Paraskevaidis[1]
[1]University of Athens Medical School, Dept of Clinical Therapeutics, Alexandra Hospital, Athens, Greece

A 57 year male old patient with idiopathic dilated cardforiomyopathy, CRT-D, atrial fibrillation on intermittent inotrope infusion for the last 3 months was implanted with an Intra-aortic balloon pump (IABP) because of decompensated biventricular heart failure. His heart echo parameters before IABP implantation are shown in table 1. After 3 months of support with IABP, weaning process failed and atrial fibrillation cardioversion plus continuation of IABP support for 2 additional months was decided. At the end of the two-month extended IABP support period, weaning process failed again and intracoronary peripheral stem cells infusion was proposed to the patient. An informed consent was obtained and after subcutaneous administration of filgastrim (a granulocyte colony stimulation factor) for 5 days, 20.000.000 CD34 cells were infused with a non-stop flow technique in the LAD, LCX and RCA. After an additional month of support with IABP, the patient was successfully weaned off and stayed alive and free of complications for 3 years when he deceased from septic shock.

LVEED (mm)	68
LVESD (mm)	58
LVEF (%)	23
MVR	1-2/4
RV (mm)	30
TDI RV (cm/s)	8

Acute Heart Failure - Pathophysiology and Mechanisms

P632
Gravity of gravetic heart failure

HS Kemal[1]; A Gunsel[1]; S Asvaroglu[2]; B Tasel[1]; L Cerit[1]; H Duygu[1]
[1]Near East University Hospital , Cardiology , Nicosia, Cyprus; *[2]Near East University Hospital, Internal Medicine, Nicosia, Cyprus*

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Introduction: We present a case of acute heart failure as the first manifestation of Graves' disease.
Description: A 49-year old woman presented with progressive dyspnoea, swelling of legs and abdominal pain for the last 5 months. She refused treatment until this time and was in NYHA class IV. She had no prior history of chronic disease. She was nervous, emotionally depressed, tachypnoeic and tachycardic. She had bilateral lower limb oedema up to the knee, lung sounds were diminished on the left side and rales were present on the right side, JVD was visible. She had an enlarged, tender liver and massive ascites.ECG showed atrial fibrillation with high ventricular rate. She was hypotensive and hypoxic.
Identification of the problem, procedures, techniques and patient management: Diuretic and dopamin infusion was started. Pleurocentesis showed serous transudate fluid. Echocardiography revealed moderate mitral regurgitation, severe tricuspid regurgitation, and biatrial dilatation. LVEF was 48% and right ventricular systolic function was slightly depressed, TAPSE 14 cm, RVSm 8 cm/s. Systolic pulmonary artery pressure was 40 mmHg. There was interventricular septal bounce movement and mitral E was 94 cm/s, mitral septal S 7cm/s, E' 77 cm/s, lateral E' 11 cm/s and there was also respiratory change in mitral and tricuspid inflow. Right heart catheterization was performed;Pulmonary artery pressure 40/20 mmHg, RV mean pressure 14 mmHg, RA P 15 mmHg, LV P 15 mmHg and PCWP was 18 mmHg, no dip and plateau was observed. Coronary angiography revealed normal coronary arteries.
Significant blood test results were: low albumin, high bilirubin levels, high GGT, decreased TSH, increased T3 and T4. Abdominal CT scan showed cirrhosis and oesophageal varices. Thyroid ultrasound showed enlarged and heterogeneous echotexture and TSH receptor antibody was positive and thyroid scintigraphy showed homogeneously increased activity.
Questions, problems or possible differential diagnosis: What is the diagnosis? Bi-ventricular heart failure? Constrictive pericarditis? Hepatic cirrhosis? Hyperthyroidism?
Conclusion and Implications: The patient was diagnosed as Graves' disease and was started on metibasol (30 mg/day) and propranolol (40 mg/day). After six months of medical therapy, and normal thyroid function for three months the patient was NYHA class I. The ECG showed sinus rhythm, reassessment by TTE showed systolic pulmonary artery pressure of 15 mmHg, normal left and right systolic functions and mild valvular dysfunction. Heart failure is generally a rare occurrence in thyrotoxicosis patients, but requires attention because it can lead to death. The RV is expected to fail in hyperthyroid states due to the pulmonary vasculature physiology. Like in our case challenging differential diagnosis could be present and Graves' disease should be kept in mind, since it is treatable and its complications may be reversible.

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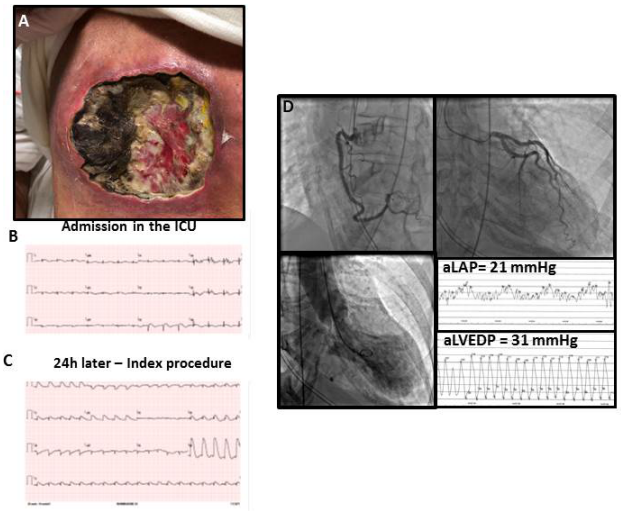
Might Imperial Caesar, dead and turned to clay, stop a hole to keep the wind away?

D Domenico D'amario[1]; A Buffon[1]; S D'arrigo[1]; F Lassandro Pepe[1]; F Crea[1]
[1]Catholic University of the Sacred Heart, Institute of Cardiology, Rome, Italy

A 73-year-old caucasian woman, with advanced breast cancer, who consistently refused surgical resection, was admitted in ER for an acute respiratory failure, associated with generalized muscle rigidity, trismus, hyperpyrexia, sweating which needed neuromuscular blocking agent and an early tracheostomy to avoid tube biting and obstruction. No previous cardiac history was reported.



Over the last four weeks, for the occurrence of secondary skin ulceration, the patient was advised to apply clay mud over the breast. Subsequently, she developed an extensive local necrosis (Figure 1A). Microbiological results from necrosectomy revealed Clostridium tetani and Clostridium sporogenes isolation. Human tetanus globulin, intravenous cephalosporin and high dosage of benzodiazepines were admistered.
ECG on admission showed a prolonged QT interval without any evidence of ST segment depression (InterTAK Score: 56) (Figure 1B). On admission, hsTroponin was 1.46, peaking 3.95 ng/mL.
The clinical course rapidly deteriorated with vegetative crisis and hemodynamic instability associated with atrial fibrillation rhythm and significant ST segment elevation (Figure 1C).
Coronary angiography was performed: no evidence of obstructive epicardial coronary atherosclerosis was observed. Following the 2017 STEMI guidelines, LV angiography was performed showing an apical type takotsubo syndrome (TTS), with high average LVEDP and left atrial pressure (Figure 1D). Sadly, the patient died less then 48h later.
To the best of our knowledge, this is the first report documenting a TTS in a patient with a diagnosis of tetanus.
Tetanus per sé may increase the systemic concentrations of catecholamines. Moreover the tetanus toxin is involved in autonomic nervous system dysregulation, suggesting that it might accelerate catecholamine release resulting in the sympathetic nervous system hyperactivity, that is the pathophysiological substrate of TTS.
As recently demonstrated, TTS may be a life-threatening condition: early cardiac catheterization is fundamental to make a correct diagnosis, even in the acute heart failure setting.

Acute Heart Failure - Diagnostic Methods

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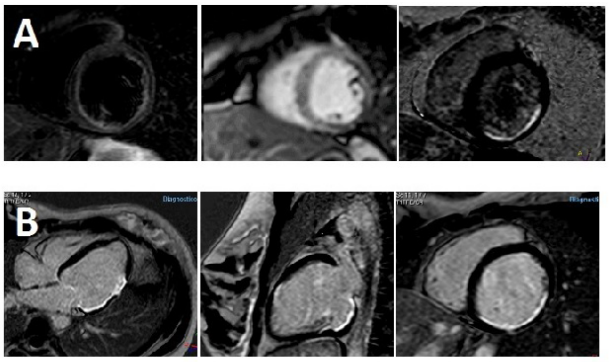
Dress syndrome and myocarditis: is the endomyocardial biopsy always necessary?

M Maria De La Cruz Mezzadra[1]; MC Carrero[1]; G Diaz Babio[1]; G Masson[1]; T Garcia Bota[1]; G Vera Janavel[1]; P Stutzbach[1]
[1]Instituto Cardiovascular de San Isidro (ICSI), Sanatorio Las Lomas, San Isidro, Argentina

Introduction: Drug Rash with Eosinophilia and Systemic Symptoms (DRESS) syndrome is a potentially life-threatening idiosyncratic drug reaction. Although liver involvement is the most common manifestation, cardiac association varies between 4 % and 21%.



CRM images. Upper panel (A) shows short axis slices during acute presentation (ischemia, edema, late gadolinium enhancement). Lower panel (B) indicates definitive myocardial involvement (late gadolinium enhancement).

Case: A 17 years old female presented in the emergency room for progressive dyspnea that started 5 days before admission. She has history of recently diagnosed minocycline-induced DRESS syndrome (severe exfoliative dermatitis, eosinophilia, liver, lung and renal involvement) with 6 months systemic steroids treatment completed 2 weeks before symptoms onset. Minocycline was given for Acne Vulgaris treatment. Physical exam at admission revealed signs of heart failure (HF). Initial electrocardiogram detected 1 mm ST-T elevation segment in DII-DIII-AVF-V5-V6 and 2 mm ST-T depression segment in V2-V3. The coronary angiography performed showed normal coronary arteries. Cardiac biomarkers were above normal range: Troponin I (TnI) 949 mg/l (normal: < 0.01 mg/L) and Pro- hormone of basic natriuretic peptide (pro-BNP) 6.388 pg/ml (normal: < 72.3 pg/ml). A transthoracic echocardiogram revealed akinesia of mid and basal segments of the inferior, inferolateral and inferoseptal walls that compromised left ventricular systolic function (LVEF: 30%) and generated a severe functional mitral regurgitation (MR). She was admitted with diagnosis of HF secondary to probable myocarditis and treatment with intravenous diuretics and vasodilators was initiated. Cardiac magnetic resonance (CMR) with gadolinium was performed to approach an etiological diagnosis. Intramyocardial edema, endocardium perfusion defect and late gadolinium endomyocardial enhancement from basal to apical segments from the inferior, inferolateral, inferoseptal walls were observed. LVEF was 25.2 %. The case was interpreted as an acute necrotizing eosinophilic myocarditis (ANEM) and immunosuppression was added to HF conventional treatment. After 2 weeks of medical treatment she was discharged with undetermined TnI and pro-BNP of 1800 pg/ml. Two months later a new CMR revealed late gadolinium endomyocardial enhancement from basal to apical segments from the inferior, inferolateral and inferoseptal walls. Some areas of transmural myocardial enhancement and mid inferolateral wall aneurism with mild MR were observed. LVEF was 46 %.
Problem: Although endomyocardial biopsy (EMB) is the gold standard for ANEM diagnosis, a sampling error due to the patchy nature of inflammation and necrosis can limit diagnosis. If we had a negative EMB, would we deny immunosuppressive treatment to this patient?
Conclusion: Unlike the rest of myocarditis, ANEM frequently involve the endomyocardium. Though not specific, CRM is very sensitive to both structural and functional changes. Considering that EMB sensitivity is not good, a CRM with late gadolinium enhancement ANEM pattern in patients with DRESS syndrome should be enough to initiate immunosuppressive treatment.

Acute Heart Failure - Treatment

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Bail out strategy: sacubitril/valsartan in de novo heart failure with reduced ejection fraction

SI James[1]; B Mcadam[1]
[1]*Beaumont Hospital, Cardiology, Dublin, Ireland*

Mr PW, 52 years old, airport baggage handler, with no prior medical history presented with progressive 4 months history of shortness of breath to the emergency department. He complained of shortness of breath at rest, sleeping on 4 pillows, and had been wakening up in the middle of the night really short of breath (NYHA IV). He has no family history of heart disease. He is an ex-smoker with 10-pack year history, does not take alcohol and lives alone. Clinical examination revealed a very dyspnoeic patient with cold extremities and raised JVP. His initial assessment showed a BP of 129/86mmHg, HR 127bpm, temperature 37.1 degree Celsius, and respiratory rate of 15 breath/minute with peripheral oxygen saturation of 93% at room air. Auscultation normal heart sounds, with reduced air entry and mild crepitation at mid-basal lung field. No sacral or pedal oedema noted. ECG was normal. Chest x-ray showed cardiomegaly with vascular congestion. His initial blood panel revealed normal full blood count, inflammatory marker, renal and liver blood tests. NT-proBNP was raised at 7097pg/ml. Fasting glucose was 8.2mmol/L with Hb1AC 44mmol/mol. TTE showed severely dilated cardiomyopathy with LVIDd of 7.2cm and LVEF of 15-20%. There was a suspicious mass in the LV suggesting thrombus. He was immediately commenced on IV furosemide and milrenone for inotropic support. He was commenced on ramipril, eplerenone and bisoprolol. Day 6 into admission, he continues to be in low output state. Ivabradine was added. He was commenced on rivaroxaban upon confirmation of LV thrombus. Despite all medical therapy, he was still having symptoms of dyspnoea at minimal exertion and severe fatigue. As a last attempt, sacubitril/valsartan 24/26mg was introduced on day 13. The milrenone and furosemide infusion was successfully weaned off by day 21. He was linked in with Heart Support Unit team prior to discharge on day 28. Diagnostic angiogram showed only minor coronary artery disease. CMR was done and cine images showed global hypokinesia with severe biventricular impairment of LVEF 12%. The EGE confirmed focal distal LV thrombus and the LGE revealed septal mid-wall fibrosis. His followup CMR showing LVEF improvement to 61% and the apical thrombus has resolved. He is currently on maximum dose of sacubutril/valsartan 103/97mg. Important differential diagnoses to consider are giant-cell myocarditis, severe infective myocarditis and infiltrative cardiomyopathy. CMR helped to establish the diagnosis of non-ishaemic DCM and rule out infiltration and myocarditis. In a low output state, maximising gold standard medical therapy can be challenging. Concomittant use of ivabradine has been shown to improve heart rate and cardiac index. The authors acknowledge that the off-label use of sacubutril/valsartan in this patient was outside of the guidelines. The implication of this early use of sacubutril/valsartan is still unknown and as such this patient's case will be closely monitored.

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An unusual cause of hypoxemia in acute heart failure

P-H Peter-Hans Tolen[1]; L El Bouazzaoui[1]; IB Van Der Bilt[1]; JWJ Vriend[1]
[1]*Haga University Hospital, cardiology, The Hague, Netherlands*

Introduction: Hypoxemia is often encountered in acute heart failure patients due to pulmonary congestion. We report a patient with an unusual cause of hypoxemia in the setting of a (semi-)acute myocardial infarction and heart failure.
Case report: This case presents a 75-year old male with a history of an ischemic cardiomyopathy and ICD-implantation due to late ventricular tachycardia. He was presented to the emergency room with feelings of becoming unwell and chest pains. Physical examination showed normal hemodynamics except a severe desaturation, a high central venous pressure and peripheral edema. His ECG showed a sinus rhythm with pathological Q-waves inferior and ST segment changes suggestive of a semi-acute inferolateral myocardial infarction. Laboratory results at admission showed an elevated troponin T (4.220 ug/l) and CK (826 U/l). His ICD readings showed no signs of rhythm disturbances. Emergency transthoracic echocardiography revealed a reasonable left ventricular systolic function and a moderate right ventricular systolic function with dilatation. He had an unexplained hypoxemia. Chest X-ray showed no pulmonary congestion. A CT-scan was performed which was unremarkable, especially no signs of pulmonary embolism. A pulmonologist was consulted, but could not explain the hypoxemia.
He was admitted to the ICU and received intravenous diuretics and Optiflow. Despite this treatment, his clinical condition deteriorated. Additional transesophageal echocardiography with agitated saline showed a dilated right ventricle with a poor systolic function and a right to left shunt due to pulmonary hypertension with high right ventricular filling pressures, and a persistent foramen ovale creating an Eisenmenger syndrome physiology. The patient was treated with iloprost inhalations to decrease his pulmonary vascular resistance, leading to a decrease in the right ventricular afterload. He was also treated with milrinone, which is a prostaglandin phosphodiesterase-3 inhibitor, creating an increase in contractility of the ventricles and vascular dilatation, which decreases the afterload and improving cardiac output. After treatment with iloprost and milrinone, he showed a steep increase in saturation and an improvement in hemodynamics. Once hemodynamically stable, patient could be transferred to the general department of cardiology. Unfortunately he had a delirium and due to his comorbidities and a late myocardial infarction it was decided to treat him conservatively. After stabilisation, he was transferred to a rehabilitation centre.
Summary: We report a 75-year old male with a semi-acute inferolateral myocardial infarction complicated by severe hypoxemia due to acute heart failure, which could not be explained by pulmonary congestion on the chest X-ray. Once pulmonary embolism is excluded, we suggest further examination for a (intra)-cardiac shunt in which a transesophageal echocardiogram is superior to a transthoracic echocardiogram.

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Successful application of extracorporeal membrane oxygenation in woman after childbirth

N S Piatrovich[1]; L G Shestakova[1]; Y P Ostrovsky[1]
[1]*Republican Scientific and Practical Centre of Cardiology, Department of extracorporeal blood circulation, Minsk, Belarus*

A 22 year-old patient(without any problems before)on ventilation with progressive cardiovascular failure,pulmonary edema in early postpartum period(cesarean section,extirpation of the uterus with fallopian tubes).Massive hemorrhage,4 episodes of ventricular fibrillation with cardiopulmonary resuscitation were observed in perioperative period.Inotropic support:dobutamine 10mcg/kg/min,epinephrine 0,3mcg/kg/min,noradrenaline 0,9mcg/kg/min). Acid-base state:pH 7,18, pO2 49,1mmHg, pCO2 31,4mmHg, SaO2 66,4%, lactate 16mmol/l, BE -15,5mmol/l.Peripheral veno-arterial extracorporeal membrane oxygenation was applied.Clinical and instrumental signs of pulmonary edema gradually increased.We carried out atrioseptotomy,intraaortic balloon pump and drainage of LV during the first day. Inotropic support was stopped on the third day but suddenly we observed neurological deterioration(lamellar dural hematoma).The patient received an adequate therapy and was extubated on the 7th day.On the 10th day ECMO was explanted because of laparotomy due to bleeding into abdominal cavity. IABP was stopped the next day.Hemodynamics remained stable, cardiac contractility significantly improved.On the 13th day the patient was transferred to the gynecological department. Problems:1)Desaturation of coronary,cerebral blood flow and aggravation myocardial insufficiency can be observed during peripheral ECMO. 2)Chronic volume LV overload can cause pulmonary edema. Discussion:1)It is important to maintain residual LV pumping function and oxygenating ability of lungs.2)ECMO management includes thorough selection of heparin dose.
Conclusions: The presented case demonstrates successful usage of extracorporeal membrane oxygenation as a component of cardiopulmonary resuscitationim catastrophic conditions.

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Optimization of pressure setting during adaptive servo ventilation support using overnight pulse-oximetry: case report

Y Yasushi Tanaka[1]
[1]*Yodogawa Christian Hospital, Osaka, Japan*

Background: Adaptive servo ventilation (ASV) therapy is a recently developed non-pharmacological therapy that has been reported to improve cardiac function and survival in patients with severe congestive heart failure (CHF).
However, a recent large randomized study suggested that ASV therapy at relatively higher pressure setting worsens some of patients prognosis compared with optimal medical therapy. On the other hand, It is well-known that overnight pulse-oximetry derived high oxygen desaturation index (ODI) predicted mortality in patients with CHF. Therefore, we examined optimal pressure settings of ASV therapy using overnight pulse-oximetry.
Case presentation
We present the case of a 80-year-old female with CHF, which was caused by right heart failure, who was admitted to our institution for dyspnea. The acute phase treatments according to the guideline-based standard medical therapy and Noninvasive positive pressure ventilation (NPPV) therapy resulted in improved congestive conditions. Then, we performed ASV therapy in terms of the default settings [peak end-expiratory pressure (PEEP) 5 cm H2O] instead of NPPV therapy. But we reperformed NPPV therpy, as CHF was worsened. We performed ASV support test, during which PEEP settings were set at levels ranging from 2 to 6 cm H2O using overnight pulse-oximetry for this patient's care. Considering the ODI of patient, PEEP of 4 cm H2O would be optimal pressure setting at least in this case.
Conclusions: Our case report was the first to use overnight pulse-oximetry to examine optimal pressure settings of ASV therapy in patients with CHF.

Coronary Artery Disease - Treatment

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Great improvement of systolic function of left ventricle in patient with chronic total occlusion of left anterior descending artery and ischaemic cardiomyopathy

MI Marta Izabela Kaluzna-Oleksy[1]; WS Skorupski[1]; ML Lesiak[1]; MJ Janus[1]; WS Skorupski[1]; ML Lesiak[1]
[1]*Poznan University of Medical Sciences, Ist Department of Cardiology , Poznan, Poland*

A 46-year-old man was admitted to our cardiology clinic with symptoms of severe chronic heart failure. The exertional dyspnea has emerged six months earlier but has been identified as associated with respiratory tract infection and treated with antibiotics without success. Over the following months, fatigue, exercise intolerance and dyspnea were increasing. On admission patient presented with NYHA class IV with tachycardia, tachypnoe and legs oedema. Blood pressure (BP) was 140/80 mmHg. In electrocardiogram sinus rhythm 150 bpm and signs of previous myocardial infarction of antero-lateral wall were observed. Laboratory tests showed elevated, but not significant for acute ischaemia, troponin level - 0,086 ng/mL, and elevated level of brain natriuretic peptide NT-proBNP - 7671,6 pg/mL. Echocardiography revealed with left ventricular end-diastolic diameter (LVEDD) enlargement - 68 mm, global hypokinesis of the left ventricle (LV) walls with left ventricular ejection fraction (LVEF) about 10%. Coronary angiography showed a chronic total occlusion (CTO) of left anterior descending coronary artery (LAD) and significant stenosis (75%) in right coronary artery (RCA). Cardiac magnetic resonance imaging (CMR) showed transmural enhancement in the apex and all apical segments, subendocardial enhancement within the medial segment of anterior wall and anterior part of intraventricular septum (IVS) > 75% of the thickness of the wall (= 3 mm viable myocardium), subendocardial enhancement within the medial segment of lateral wall and posterior part of IVS < 50% of the thickness of the wall (>5mm viable myocardium). The decision to perform in the first line the revascularization of LAD was taken. Successful PCI of CTO of LAD with bioabsorbable everolimus-eluting stent implantation was performed. Improving in the clinical symptoms was observed. Patient was discharged from hospital in stable clinical sate (NYHA II, without angina). After one month (next-step therapy) the PCI of RCA with bioabsorbable everolimus-eluting stent implantation was performed. In the following months significant reduction in the symptoms of heart failure (NYHA I/II), as well as increase of LVEF (up to 37%) were observed, what was confirmed in CMR.
Conclusion: The revascularization of CTO in the area of viable myocardium is often performed. In many patients it reduces the symptoms of ischemia. The effect on the improvement of left ventricular systolic function and survival of the patients is not objectively proven in large clinical trials. We report on the case where great clinical benefit after the full revascularization with PCI of chronic occlusion of the LAD (without clear sing of viable myocardium) was observed.

P637 Dynamics of hemodynamic indicators

	Before ECMO	During ECMO	1 day after weaning from ECMO						
2 hours	12 hours	24 hours	2 days	4 days	7 days	days			
HRper min	140	132	115	118	113	111	95	114	112
AP,mmHg	80/5	83/51	82/55	82/57	89/65	118/77	108/65	100/71	114/78
CVP,mmHg	-2	11	0	7	3	3	1	0	5
PAP,mmHg	-	26/19	17/9	21/15	22/11	21/10	12/5	12/5	34/19
PAWP,mmHg	-	13-25	5	7-10	6	-	-	2	-
LVEF,%	32	17	18	19	21	25	36	50	55
SV,ml	49	21	22	31	16	33	32	28	38
RVEF, %	52	38	40	-	-	43	49	51	51
ECMO,l/min	-	3,5	3,55	4,2	4,3	3,9	3,2	2,5	-

Myocardial Disease - Clinical

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Acute deterioration of the hypertensive heart disease in the patient with the paraganglioma of the urinary bludder

O V Olga Blagova[1]; IN Alijeva[1]; EA Bezrukov[1]; LI Ippolitov[1]; GV Polunin[1]; EA Kogan[1]; AV Nedostup[1]; EA Mershina[2]; VE Sinitsyn[2]; VV Fomin[1]
[1]*I.M.Sechenov I Moscow State Medical University, Moscow, Russian Federation*; [2]*Roszdrav Medical Rehabilitation Center, Moscow, Russian Federation*

Background: Hypertensive heart disease with acute biventricular cardiac failure is not common in clinical practice. This diagnosis requires an extensive diagnostic search aimed at excluding primary myocardial diseases.
Purpose: to describe the difficulties in diagnosis of rare causes of decompensated hypertensive heart disease and results of complex treatment of this patient.
Methods: We present the clinical case of the male patient 38 years old. He comes in the clinic with acute cardiac failure 3-4 NYHA class appeared within ten days. His mother suffered from hypertension and died at the age of 70. He had no history of heart disease, except for episodic recording of high blood pressure (up to 220 and 140 mmHg) over the past two years. The complex investigation included ECG, EchoCG, thoracic radiography and computed tomography (CT), magnetic resonance imaging (MRI), scintigraphy with 131I-MIBG and also level of anti-heart antibodies and adrenal hormones detection, cutaneous test with tuberculin antigen.
Results: EchoCG revealed symmetric hypertrophy of the left ventricle to 18 mm without its dilatation, a decrease EF to 42%, restrictive hemodynamics, overload of the right chambers, severe pulmonary hypertension (60 mm Hg). The clinical status also included persistent arterial hypertension (180-220 and 120-150 mm Hg), effusion in both pleural cavities and pericardium, ascites, renal failure (creatinine at 2.0 mg / dL), microhematuria, malignant hypertensive retinopathy. During examination (CT, MRI, scintigraphy with 131I-MIBG), bladder paraganglioma was diagnosed (urine normatenafrin 1468 μg / day). No data were obtained for pulmonary embolism, hypertrophic cardiomyopathy, sarcoidosis, amyloidosis of the heart, myocarditis, takotsubo syndrome, Fabry's disease (study of the level of anti-heart antibodies, CT, cardiac MRI, subcutaneous adipose tissue biopsy, XGAL gene study), tumors of other localization. On the background of drug therapy, resection of the tumor was performed, with ismunohistochemical research - neuroendocrine carcinoma, G1. After three months of irregular drug therapy with doxazosin, beta-blockers, furosemide, calcium antagonists, a partial regression of hypertension and cardiac failure was noted with the preservation of a high level of creatinine.
Conclusions: The paraganglioma of the urinary bludder is the very rare cause of malignant arterial hypertension, that may by the sole manifestation of tumor. The differential diagnosis of the hypertensive heart disease and the syndrome of primary myocardial hypertrophy is not easy. The complex mechanisms of myocardial damage within the pheochromocytoma can lead to acute development of biventricular heart failure. The radical resection of the tumor is the main method of the treatment, which leads to lower blood pressure, however, heart failure may be irreversible.

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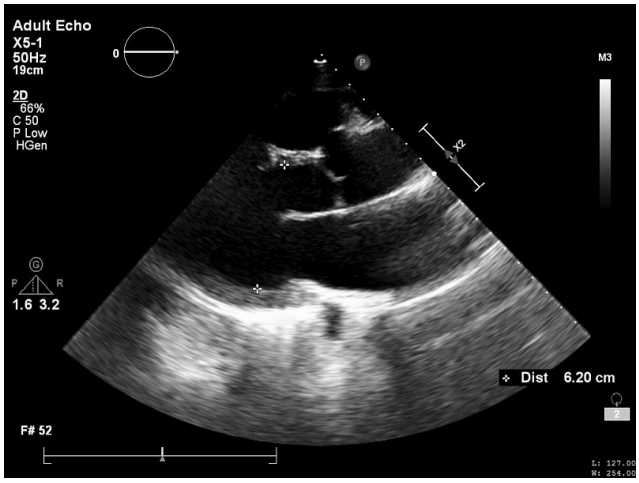
A case of late cardiac toxicity and CKD stage 4 related to chemotherapy and radiotherapy for acute leukemia treated with sacubitril/valsartan

A Alexander Valerievitch Nossikoff[1]; K Angeloff[1]; P Ilieff[1]; G Lazarova[1]; T Donova[1]
[1]*University Hospital "Lozenets", Cardiology, Sofia, Bulgaria*

A 25-year old male presented to our unit with symptoms and signs consistent with de novo NYHA III heart failure. Past medical history was remarkable for chemotherapy and total body radiation followed by allogenic bone marrow transplantation at age 16 due to T-cell leukemia. There have been no signs of disease activity since then. He was left with CKD, which is stage 4. He was followed up for cardiotoxicity until 4 years ago and his echocardiograms were normal.
The apical beat was laterally displaced, there were S3 and bibasal crackles on auscultation. Jugulars were not distended. Liver was mildly enlarged. EKG revealed NSR, QRS of 100msec, LAA, LAHB, LVH and strain.
Patient was admitted: Echocardiography revealed dilated LV with EF of 25%. The IVC was plethoric and there was small right-sided pleural effusion. The transmitral flow was restrictive. His creatinine was 320 umol/L, corresponding to eGFR of 22ml/min/1.73m2. BNP was elevated at 1165 pg/dl, hsTnI was normal, rest of labs unremarkable. We commenced torasemide with full and rapid decongestion achieved. The IVC became with normal dimensions and respiratory movement, which was against concomitant pericardial constriction. Metoprolol succinate was commenced and tolerated well. Patient was discussed on multidisciplinary meeting, diagnosis of late cardiotoxicity due to chemo- and radiotherapy was agreed. We decided to titrate very low dose ARNI under close follow up of renal function. We started with 12/13mg a day and titrated the dose every 2 weeks by another 12/13mg to our target of 2x24/26mg, which was well tolerated by the patient. We titrated the metoprolol up to 2x50mg. There was no evidence of worsening renal failure or hyperkalemia. His functional capacity improved and he is now asymptomatic during all day-to-day activities. Metoprolol will be titrated to maximum tolerated dose and LV EF will be reassessed once he has been on optimal medical therapy for 3 consecutive months. Due to high risk of contrast induced nephrotoxicity we refrained from coronary angiogram.
Conclusions: Late cardiotoxicity after chemo- and radiotherapy is a possible complication and its incidence is likely to increase with the improved survival of patients treated for malignancy. Patients with HF and concomitant severe CKD present a therapeutic challenge as the evidence on use of ACEI/ARB is unclear in this setting due to increased risk of worsening renal function and hyperkalemia. Sacubitril/valsartan is considered to have favourable cardiorenal profile compared to ACE-inhibitors, but has not been prospectively studied in eGFR < 30ml/min/1.73m2. In contrast, metoprolol succinate is safe due to its liver metabolism. EMA label allows cautious use of sacubitril/valsartan in HF patients with eGFRs of 15-30ml/min/1.73m2, which we have done in this case with a favourable clinical outcome. More data is needed on ARNI for this patient subgroup so we can be more confident in its use.



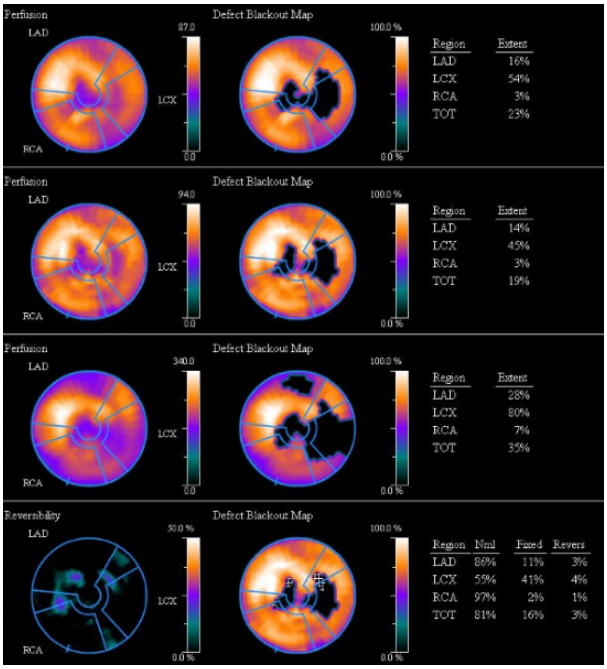
62mm LVEDD from 2D PLAX

P642

A new mutation causing arrhythmogenic right ventricular cardiomyopathy with atypical presentation

A Alberto Aimo[1]; A Barison[2]; GD Aquaro[2]; U Startari[2]; G Vergaro[2]; M Emdin[1]
[1]*Sant'Anna School of Advanced Studies, Pisa, Italy*; [2]*Gabriele Monasterio Foundation, Pisa, Italy*

A 38-years old woman with referred familiarity for myocardial infarction (MI) was admitted to an Emergency Department because of chest pain. While biomarkers of myocardial necrosis and B-type natriuretic peptide were normal, and the electrocardiogram showed only a right ventricular (RV) conduction delay, transthoracic echocardiogram revealed diffuse left ventricle (LV) wall motion abnormalities and an apical aneurism. A coronary angiography demonstrated a normal coronary tree, leading to the diagnosis of "unstable angina with normal coronary arteries, possible prior MI."



A rest and stress myocardial perfusion imaging with 99mTc-sestamibi was negative for inducible ischemia, but showed "evidence of prior myocardial infarction (MI) in the anterior and apical regions of the LV." Even the findings at cardiac magnetic resonance (CMR) were deemed "compatible with previous MI" because of late gadolinium enhancement in the apical and inferolateral LV segments, and the thinning of LV apex. The RV was overlooked.

After discharge, a re-evaluation of CMR findings at another institution raised the suspicion of arrhythmogenic right ventricular cardiomyopathy (ARVC). Gene sequencing allowed to find homozygosity for the c.428 T>A mutation in the desmoglein gene (DSG2). Although not previously reported, this was considered a pathogenic variant as it produces a stop codon, which blocks protein synthesis after inclusion of 143 amino acids instead of 1119. A definite diagnosis of ARVC was then made (two major criteria: CMR findings and a pathogenic mutation).

Considering the ventricular ectopic burden (over 6000 ectopic beats during the 24 hours, with 100 couplets), the patient underwent mapping and ablation of an arrhythmogenic focus located into the LV apex. She then repeated the CMR examination. The reader found "diffuse regional wall motion abnormalities and alterations of signal intensity within both ventricles, suggesting multiple, large areas of fibrofatty replacement." A single chamber defibrillator was eventually implanted for primary prevention. Cardiologic assessment and genetic screening of other family members is currently underway; the c.428 T>A mutation and CMR abnormalities have already been found in the patient's sister.

This is the first report of the c.428 T>A mutation as the cause of ARVC. It also demonstrates that the clinical and imaging presentation of ARVC may be misleading, so that a high index of suspicion is needed to come to the correct diagnosis.

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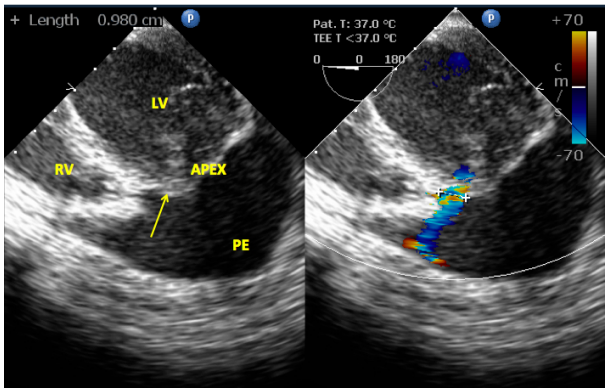
Left ventricular free wall rupture with pseudoaneurysm formation from penetrating cardiac injury

J P Rangel[1]
[1]*Philippine Heart Center, Adult Cardiology, Manila, Philippines*

Background: Left ventricular free wall rupture is a catastrophic complication of stabbing injuries and is associated with a high mortality rate due to pump failure. The majority of patients present with pericardial tamponade and subsequent exsanguination. Left ventricular pseudoaneurysms are uncommon but develop when cardiac rupture is contained by adherent pericardium and scar tissue. Diagnosis by chest radiograph and transthoracic echocardiogram are the most readily available imaging modalities in the emergency setting to diagnose these complications.



Intraoperative Transesophageal Echo

Presentation: A 27-year old male was admitted after sustaining a stab wound on his left anterior chest at the 4th anterior axillary line. He was rushed to a nearby hospital and managed as a case of hemothorax and pericardial effusion then underwent chest tube and pericardiostomy tube insertion. Despite twenty-three days since pericardiostomy tube, pericardial fluid drainage was still noted with febrile episodes accompanied by dyspnea, two to three pillow orthopnea and mild edema.

Imaging Findings: Chest radiograph showed moderate ascending pleural based density in the left hemithorax, true cardiac size could not be ascertained with minimal contralateral shift of mediastinal structures. Electrocardiogram initially showed sinus rhythm with anterolateral wall ischemia with episodes of ventricular tachycardia and ST segment elevation. Intraoperative transesophageal echocardiogram revealed penetrating anterior left ventricular wall injury with localized massive pericardial effusion, hematoma formation and possible pseudoaneurysm formation. Chest CT scan confirmed findings of contained rupture of the left ventricle with pseudoaneurysm. He underwent urgent primary repair of left ventricular injury and pseudoaneurysm with evacuation of hematoma.

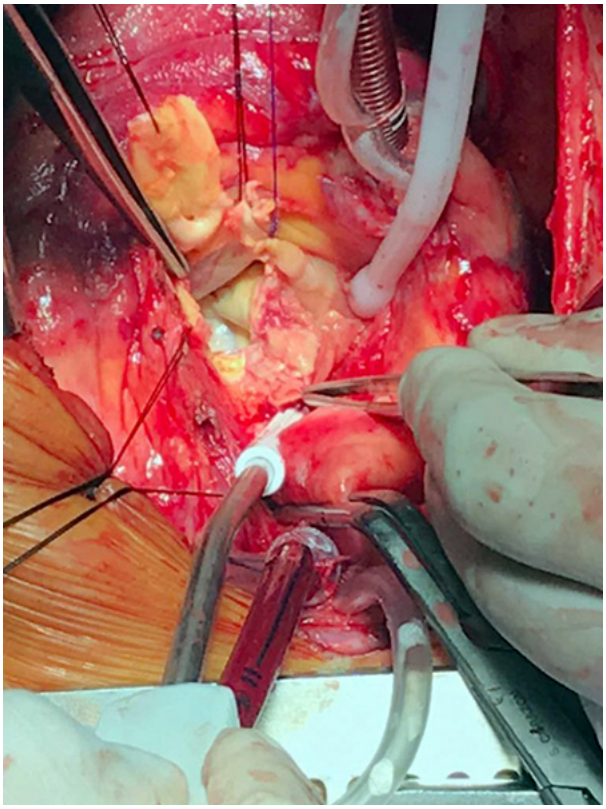
Conclusion: We presented a complicated case secondary to a stab wound injury. The patient completed antibiotics and was discharged stable. Diagnosis of left ventricular rupture and pseudoaneurysm formation is very challenging. Imaging modalities can supplement the index of suspicion and physical examination findings. The mortality rate for penetrating cardiac injuries range from 19% to 65% in several studies. Timely surgical repair therefore remains the cornerstone for management.

P644

A clinical rarity: Austrian syndrome (endocarditis, meningitis and pneumonia caused by Streptococcus pneumoniae), based on a clinical case.

CL Carlos Luis Gonzalez[1]; LN Gil[1]; MF Acosta[1]; FJ Estevez Traversi[1]; C Perea[1]; DA Pranteda[1]; LA Miserque[1]; JP Cattaneo[1]; G Di Giorno[1]; ER Catena[1]; G Vizcarra[1]; S Budelli[1]; L Saglietti[1]; CM Muzzio[1]; V Gregorietti[1]
[1]*Sanatorio Sagrado Corazón, Cardiology, Buenos Aires, Argentina*

Introduction: We present the case of a patient with endocarditis caused by Streptococcus pneumoniae. The patient also experienced meningitis and pneumonia caused by the same germ, suffering from the triad described by Robert Austrian. The syndrome generally affects the aortic valve and it is currently regarded as a clinical rarity.



Aortic annulus and abscess

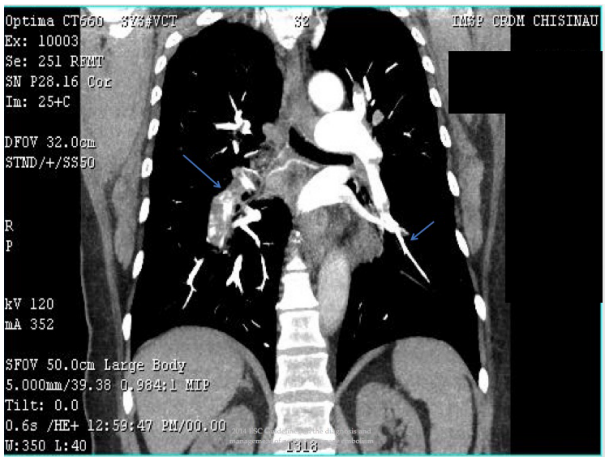
Case: 52 year old male patient, under enalapril and amlodipine treatment for hypertension. No history of cardiovascular disease. The patient was admitted to the emergency room in a state of disorientation and consciousness impairment.
The physical exam showed a blood pressure of 80/30 mmHg, heart rate of 105 bpm. Breathing rate of 20 rpm, temperature of 39.8°C. Bradypsychia, disorientated, and positive Kerning sign.
Blood test showed anemia, acid-base status reflecting metabolic acidosis with respiratory alkalosis. Blood cultures for Streptococcus pneumoniae were performed. Cerebrospinal fluid with Streptococcus pneumoniae growth was cultured. Positive latex test for the same germ.
Imaging: Chest CT showed bilateral laminar pleural effusion. Bilateral images in ground-glass, with reticular and nodular opacification. Transesophageal echocardiogram with broadly unstructured aortic valve with multiple associated masses and severe reflux. Abscess in the aortic root with discrete expansion of the left coronary sinus. Degenerative and mildly deteriorated mitral valve.
Evolution: Antibiotic treatment with ceftriaxone/vancomycin was administered. The patient evolved with signs of heart failure and subsequent tachypnea, inotropic drugs were required; poor ventilation mechanics leading to mechanical ventilation. A Swan Ganz catheter with mixed measuring pattern (distributive-cardiogenic) was placed.
The case is now diagnosed as septic shock that started in the central nervous system with lung (pneumonia) and endovascular (severely compromised aortic valve) impacts. The cardiovascular surgical team performed an emergency procedure. A No. 23 cryopreserved aortic homograft was implanted.
As a complications the patient presented cardiac tamponade that requiere surgery to remove blood clots in the mediastinum and bilateral pleural drainage due to effusion. The patient evolved favorably, was transferred to the clinical medicine service and several days later discharged from hospital.
Conclusion: Nowadays, Streptococcus pneumoniae accounts for less than 1% of endocarditis, although its mortality rate cannot be undermined. Concurrent onset of endocarditis, meningitis and pneumonia was described by Austrian proving this mortal triad in 1957. This syndrome evolution is often severe and highly aggressive, with complications such as, aortic cusps rupture and puncture and subsequent cardiac failure, myocardial abscesses, septic arthritis and glomerulonephritis. The case that we are presenting shows a clinical case with a very low incidence but increased mortality, even when fast and appropriate treatment is administered.

Autoimmune/Chronic Inflammatory Disorders and Heart Disease

P645
Upper limb vein thrombosis and pulmonary embolism in a HIV infected patient

I Irina Cabac Pogorevici[1]; V Revenco[1]
[1]*State University of Medicine and Pharmacy, Cardiology, Chisinau, Moldova Republic of*

A 32 year old caucasian male, known with congenital heart disease (i.e. biscupsid aortic valve), a positive history of HIV and drug and steroids abuse, presented to the emergency room, complaining of shortness of breath, repeated syncopes, progressive generalised oedema, oliguria for the past 2 weeks. During the 8 weeks before admission, hospitalized to a regional clinic with acute deterioration of the renal function requiring haemodyalisis. He was discharged with clinical and haemodinamical improvement, but shortly quiting the prescribed therapeutical regimen. Physical exam at admission showed hyperstenic appearance (BMI 29), audible S3 gallop, massive oedema, elavated jugular preassure, generalized cyanosis, predominantly in the upper body, multiple pulmonary crackles and abolished respiration basal bilaterally, SpO2 76 %. ECG revealed incomplete right bundle branch block, SIQIII axis, signs of right atrial and ventricular strain. The transthoracic echocardiography reported severely dilated left ventricle, with a moderately reduced ejection fraction and an apical thrombus, moderately dilated right heart with considerably elevated pulmonary artery pressure (75 mmHg). The abdominal ultrasound unveiled ascites, hepatomegaly and splenomegaly, hepatic congestion, normal looking kidneys and bilateral pleural effusion, confirmed by the chest x-ray. Doppler ultrasonographic scan of the upper limbs showed absent color flow and thrombotic masses in left basilica, subclavia and jugular veins. Thoracic CT exam found trombi in the main, segmental and sub-segmental pulmonary arteries, indicating a high probability of pulmonary embolism. Pleural liquid analysis was unremarkable.
The blood analysis showed elevated serum creatinine (147.46 mcmol/l), with a GFR 53.6 ml/min/1,73 m2, normal hepatic enzymes, positive D-dimer. General blood analysis showed anemia (hb 91 g/l), normal platelets levels and moderate lymphopenia. CD4 - 1948, ARN HIV 40 c/ml. Antiretroviral therapy with Lamivudin and Dolitegravir was initiated alongside with anticoagulation with Fondaparinux 7,5 mg od, NOAC in recommended therapeutic doses (Rivaroxaban 15mg bid). After 14 days dispneea and cyanosis subsided, and he was discharged on therapeutic doses of NOAC (Rivaroxaban 15mg bid three weeks followed by 20 mg od, indefinetely).
Conclusions: The clinicopathologic pattern related to HIV is encumbered with a spectrum of hypercoagulability states leading to thromboembolic complications.



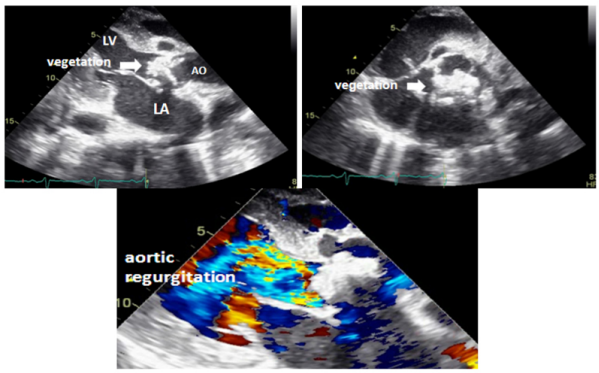
Physicians treating HIV positive patients should keep in mind that not only opportunistic infections and malignancies are following this chronic state but also less expected events such as thromboses, especially concerning younger individuals who do not meet the classical VTE risk factors. Concerning the anticoagulant treatment a special attention should be paid to potential interactions between warfarin and antiretrovirals, eventual bleeding complications could be mitigated by prescribing a NOAC regimen.

Valvular Heart Desease - Treatment

P646
Right sided heart failure in a aortic valve endocarditis caused by Campylobacter fetus

O Pachirat[1]; D Kaewkes[1]; S Pathani[1]
[1]*Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand*

Case description: A 45-year old male, poultry farmer presented with high fever, cough, chest tightness and bilateral ankle swelling for two weeks at his primary care provider with diagnosis of massive pericardial effusion impending cardiac tamponade requiring drainage and possible infective endocarditis. Pericardial fluid culture was negative. The patient had no significant medical history. He was transferred to our cardiac center for evaluation. On examination: temperature 39°C, BP 100/50 mmHg, heart rate 105 bpm. regular, a grade IV/VI diastolic blowing murmur at left lower sternal border and grade III/VI systolic ejection murmur at AVA was detected with both basal pulmonary crackles. Three sets of blood cultures were done. A transthoracic echocardiogram (TTE) revealed large vegetation on the aortic valve with severe aortic regurgitation and moderate aortic stenosis, bicuspid valve, normal left ventricular function and no evidence of pericardial effusion. Intravenous ampicillin and gentamicin were begun on admission. However, clinical of congestive heart failure worsened and the patient developed cardiogenic shock. He underwent urgent aortic valve replacement. Three sets of blood cultures were negative.



Echocardiographic features

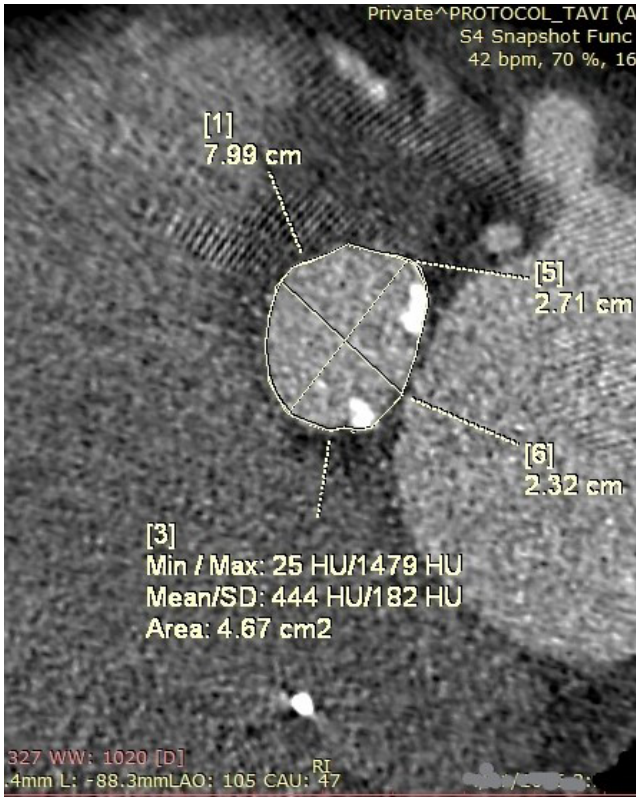
Possible differential diagnosis: In this scenario, (blood culture negative endocarditis) two main possibilities need to be differentiated: (1) the patient received antibiotics before blood was cultured (2) it was fastidious organisms such as Bartonella spp, Coxiella burnetii and Chlamydia. Campylobacter fetus was demonstrated in heart valve tissue by polymerase chain reaction(PCR). One month after surgery his cardiac condition stabilized and he was discharged from the hospital with good clinical outcome. Two years follow up he remained clinical stable.

Conclusion: C. fetus is a zoonotic and uncommon cause of human infection, mainly affect persons at higher risk and those with occupational exposure to ruminants. This case illustrates an infrequent C. fetus endocarditis associated with large pericardial effusion that might be underdiagnosed in clinical practice and emphasizes aggressive combined antibiotics treatment with early surgical intervention to prevent cardiovascular complications such as heart failure.

P647
One heart, many long-term complications of thoracic radiotherapy for Hodgkin lymphoma

S Albu[1]; A Ionescu[1]; O Mihailescu[2]; B Popescu[1]; D Deleanu[1]; C Ginghina[1]; V Iliescu[1]; O Chioncel[1]; R Jurcut[1]
[1]*Institute of Cardiovascular Diseases Prof. C.C. Iliescu, Bucharest, Romania*;
[2]*Sanador, Bucharest, Romania*

Introduction: A 60-year old patient with multiple cardiovascular risk factors complains about exertional dyspnea and angina pectoris precipitated by mild effort. At the age of 30, he was diagnosed with Hodgkin lymphoma and he received chemo- and radiotherapy, achieving remission of the neoplasia. His full history of cardiovascular events include: in 2001, persistent atrial fibrillation, which required employment of a pacemaker for antitachycardia pacing; at the age of 53, anterior myocardial infarction with angioplasty and stent implantation at the proximal segment of the left anterior descending coronary artery, at the same time his echocardiogram revealed aortic valve disease- moderate to severe stenosis.



Panel A

Patient management: The progression to severe aortic stenosis was revealed during his follow-up after a couple of years, while the patient was symptomatic by dyspnoea and angina pectoris on light exertion. Coronary angiography was repeated, but no stent restenosis or other significant atherosclerotic lesions, was revealed. His echocardiogram confirmed the aortic valve disease with severe stenosis (mean gradient 50 mmHg, indexed valve area 0.5 cm2/m2) and moderate regurgitation. The association of porcelain aorta was raised as the ascending aorta walls were thickened and calcified. Aortic valve replacement was indicated, with an EUROSCORE of 0,8%.

Questions, problems: In this case, due to the thoracic radiotherapy history and porcelain aorta, the Heart-Team decided it was best for the patient to undergo TAVR. According to angio-CT measurements (Panel A), a 26 mm Edwards Sapien XT valve was selected. He successfully underwent TAVR procedure via a left femoral artery approach.

Conclusion: Advances in radiotherapy over the past decades have improved outcomes in patients with malignancy, but increased longevity has come at the cost of late side effects - radiation-induced heart disease, which may involve any cardiac structure. The role of TAVR as an alternative to surgical aortic valve replacement (SAVR) is well established; one of the contraindications for SAVR, is the so-called hostile chest, including those with expected intrathoracic fibrosis and adhesions secondary to thoracic radiotherapy. In this setting, patients who are not ideal candidates for SAVR, TAVR is a reasonable approach, with high feasibility, acceptable risk, low mortality and high clinical effectiveness.

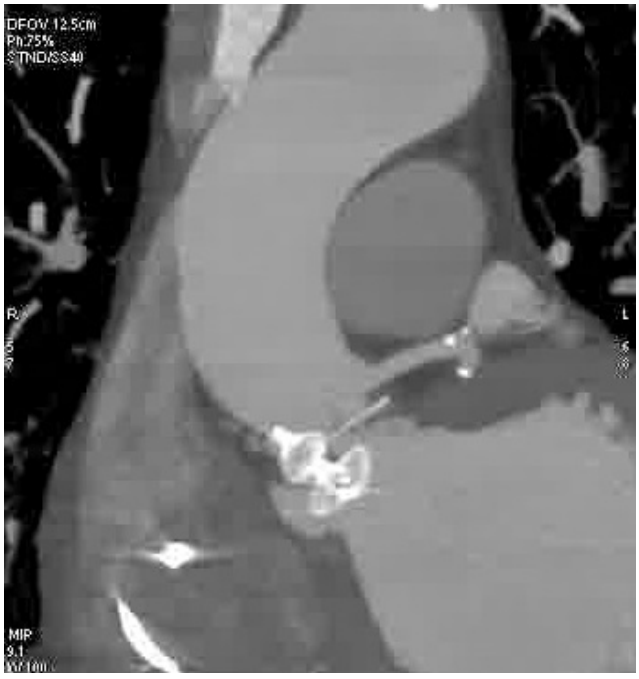
P648
Aortic valvular endocarditis masked by suspected Lime borreliosis

T Tanja Popov[1]; S Keca[1]; M Sladojevic[1]; M Stefanovic[1]; L Velicki[1]; S Susak[1]; I Srdanovic[1]
[1]*Institute of Cardiovascular Diseases Vojvodina, Novi Sad, Serbia*

Case Report: A 24-year-old female patient was sent to the urgent cardiological examination because of suspected Lime myocarditis. She was previously with good

health, had heart murmur in the childhood, but with no cardiological examination. During examination she said that the disease started about three months previous when she had got a few bites of ticks during picking strawberries. Bites were not accompanied by the local redness of the skin. A few weeks later, she noticed migratory arthritis, felt weakness and shiver. In laboratory analyzes inflamatory markers were elevated (CRP 175 mg/l and SE 100 mm/h), low hemoglobin (HgB 101 g/l). Serological analyzes for Borellia Burgdorferi were negative. She was treated with antibiotics. The infectologist suggests further examination for rheumatic diseases. The general condition of the patient was gradually worsening during a later period, with night sweats, significant weight loss, cough, ankle swelling. Two months later, she was again examined by the infectoligist and immunologist, reffered to repeat serological tests on Borellia B. (Western blot) and immunological tests. In laboratory analysis there was still high CRP 85 mg/l, worsened anemia HgB 86 g/l. She was treated with antibiotics because of bronchitis. Due to the deterioration of the dyspnea three days later, she was referred to the cardiologist because of suspected Lime myocarditis. During examination she was anxious, with dyspnoea, pale skin, an auscultatory rough systolic and diastolic murmur above the aorta, lung crackles, enlarged liver, swollen ankles. She was undergone urgent echocardiographic examination by which was registered bicuspid aortic valve, dilated ascending aorta, aortic cuspises were thickened, with suspected vegetations, and perianular pseudoaneurysms, there was severe aortic regurgitation. MSCT of the aorta shown no dissection. The patient was undergone to urgent surgery. The aortic valve was bicuspid, with tiny vegetations along both velums, which extend to the base of the frontal mitral cusp and subanular to the interventricular septum. There was several fibrotically altered abscesses subanular, and in the area of the interventricular septum. Aortic valve was replaced, with the closure of the abscesses. After surgery she was with complete atrio-ventricular block on the rithm of temporary pacemaker. Three weeks later, permanent pacemaker was implanted. She was discharged in good condition.

Conclusion: Infectious endocarditis can remain unknown for a long time, masked by associated diseases and conditions. When diagnosis and adequate treatment are made on time, serious complications and adverse events can be avoided.



P649

Fulminate endocarditis - complications and therapy

CD Botezatu[1]; D Benea[1]; G Martinelli[2]; G Lanzillo[2]; M Diena[2]; E Onorato[3]; F Armienti[4]; E Stelian[2]; A De Jong[2]; L Zamfir[1]; T Campesato[1]; G Cerin[1]
[1]San Gaudenzio Clinic, Cardiology, Novara, Italy; *[2]San Gaudenzio Clinic, Cardiac Surgery, Novara, Italy*; *[3]Clinical Institute Humanitas Gavazzeni, Bergamo, Italy*; *[4]San Gaudenzio Clinic, Radiology, Novara, Italy*

A 78 years old male patient recovered in cardiogenic shock and acute pulmonary edema is reported. One year ago the patient underwent aortic valve substitution with a biological prosthesis, and in the last 30 days presented non-investigated episodes of fever. A permanent peacemaker for complete atrioventricular block was implanted in another hospital. The patient was transferred to our center due to hemodynamic instability. Echocardiography revealed a periaortic abscess with a perimembranous interventricular septal communication, a vegetation on the aortic prosthesis (18mm length), a second vegetation on the septal cusp of the tricuspid valve (25mm length), small vegetations on the pacemaker's leads and severe mitral regurgitation due to posterior papillary muscle's rupture. Therefore an emergency surgical intervention was performed: aortic and mitral valves substitution with biological prosthesis, tricuspid valve repair, interventricular communication closure with autologous pericardial patch and pacemaker's leads removal. The patient had good outcome with empiric antibiotic therapy. Enterococcus faecalis, the bacteria incriminated for endocarditis, proved to be highly sensitive to the chosen therapy that was continued for 3 months. The patient remained asymptomatic and had normal echocardiographic exams. At six months follow up he complained of new onset dyspnea. Echocardiography revealed severe periaortic valvular leak. The optimized medical therapy didn't improve the clinical status. Blood laboratory exams showed hemolytic anemia with progressive reduction of the hemoglobin. Because of the high surgical risk, the leak was closed with a specific device implanted echo guided through a transfemural approach. The procedure was successful with an asymptomatic patient during follow-up, a well-positioned device and a mild residual leak and no hemolytic anemia. This case illustrates the management complexity of fulminate multiple endocarditis with aortic abscess and ventricular septal defect, associated with pacemaker's endocarditis and cardiogenic shock. Acute heart failure is an obvious indication for surgery performed on an emergency basis. A fulminate endocarditis with multiple valvular localization, periaortic abscess creates tissue fragility with potential devastating acute and late complications. Echocardiography proved to be an important tool in the diagnosis and the management of this case but other imaging techniques as angioCT are necessary. Use of non-surgical procedures may solve late complications in these high surgical risk patients. Results on short term follow-up are encouraging. Longer follow-up is needed to characterize the outcome of these patients.

P650

Cardiac MRI helped for decision making in a patient with ruptured tricuspid valve and severe right ventricular failure

M M Ansari-Ramandi[1]; N Naderi[2]; A Firouzi[2]; AA Ghavidel[2]; H Pouraliakbar[2]; N Rezaeian[2]
[1]Syed Mostafa Khomeini Hospital, Tabas city, Birjand University of Medical Sciences, Birjand, Iran (Islamic Republic of); *[2]Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, Iran (Islamic Republic of)*

A 62 years old man with a car accident history that leaded to a blunt chest trauma in 2002 underwent coronary angiography ten years later due to dyspnea and atypical chest pain. He had normal coronary arteries at that time and on ECG he had atrial fibrillation. He was discharged on digoxin and warfarin and was on medical therapy for the following 5 years until he was admitted in hospital due to anemia and anasarca. On admission he had severe edema and ascites. He was pale and had a systolic murmur at the left sternal border. The laboratory data showed normal renal function and thyroid function. Hemoglobin level was 9.2 mg/dl and there was low level of ferritin and serum Iron. Due to Iron deficiency anemia, stool examination was requested which showed positive occult blood. Before preparation for upper gastrointestinal (GI) endoscopy and colonoscopy, heart specialist consultation and echocardiography were done due to the murmur and edema. Echocardiography showed:
(1)moderate left ventricular systolic dysfunction, (2)severe right ventricular enlargement and dysfunction, (3)flail of anterior tricuspid valve {TV} leaflet and rupture of chordae and severe tricuspid regurgitation, (4)systolic flow reversal in hepatic veins. Systolic pulmonary artery pressure was estimated to be 25mmHG and the TV annulus was 5.5cm. Due to the severe anemia, GI endoscopy and colonoscopy were done which were reported as normal. Red blood cell scan was also done which showed bleeding from the small intestine; the gasteroenterologist believed it was due to the patient's RV failure. After treatment with furosemide, the patient underwent Cardiac MRI for clinical decision making about the need for surgery. Cardiac MRI reported the RV ejection fraction to be about 37% and the patient underwent TV replacement with a tissue valve. Treatment was continued with furosemide and the patient's condition improved over 6 months. His edema diminished and he did not have anemia any longer. This case describes the role of cardiac MRI in clinical decision making for the treatment of ruptured TV and RV failure.

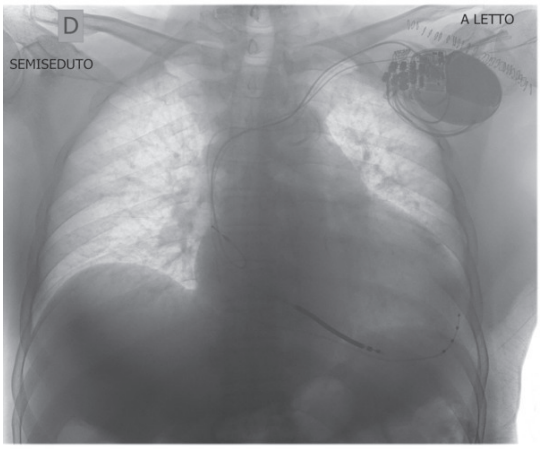
Cardiac Resynchronization Therapy

P651

Absence of the target veins during CRT-device implantation procedure: a simple approach to reduce the failures rate.

N Nikoloz Bakhtadze[1]; O Ornago[1]; C Pandini[1]; N Ashofair[1]; M Colella[1]; R Griner[1]; A Kheir[1]; M Manfredi[1]; P Peci[1]; C Piemonti[1]; S Todd[1]
[1]*San Pietro Polyclinic, Department of Cardiology, Ponte San Pietro, Italy*

CRT-device implantation is an effective and clinically proven option for some patients with HFrEF.
Optimal LV lead placement is dependent on the presence of an acceptable target vein: lateral (marginal) cardiac vein, postero-lateral cardiac vein, posterior cardiac vein. But the absence of the suitable vein/excessive venous tortuosity/unfavorable angle of the desired vein/small (atretic) vein is not a rare finding during retrograde venography.



Chest radiography AP view

A lot of studies published previously reported worse long-term outcomes in case of LV leads placed in anterior (great) cardiac vein.
The aim of our study was to verify and evaluate the possibility of the using of simple periprocedural tricks to avoid LV lead placement in anterior vein. We used the following approach in patients with no lateral vein during retrograde venography: gradual pull back displacement of delivery system with 2-3 injections of the contrast solution (to rule out the presence of postero-lateral/posterior cardiac veins) until direct cannulation of the middle cardiac vein. Using a J-tip guidewire the exploration of distal branches of the middle cardiac vein is performed in LAO (30-45°) to find anastomoses with branches of lateral/postero-lateral/posterior cardiac vein with subsequent over-the wire (OTW) LV lead placement in the target vein via distal branches connections.
Analyzing the results of CRT-device implantations (first/upgrading) performed in our centre in the period from September 2016 to October 2017 we found 5 patients (from 95 pts, 5,3%) in which above-mentioned technique was used. Mean age of these patients was 73,2 ± 4,44 yrs (range 68-79 yrs), M/F 80/20 %, ischemic vs. dilated cardiomyopathy 60/40%, 3 patients had baseline NYHA class II, 2 patients - NYHA class III. Mean EF of LV was 28% (range 25-30 %). In 4 patients (from 5 pts, 80%) our approach was successful, one patient was sent to the cardiac surgeon for epicardial LV lead placement. No major/minor complications were observed. All 4 patients were seen within 2-4 months after hospital discharges. None of them had any hospitalization for worsening of HF, 3 patients had both clinical (NYHA class, 6MWT) and echocardiographic signs of improvement (responders), one patient was sent for AV and VV intervals optimization.
Our data, even if derived from a small number of patients demonstrate simplicity, efficacy (both acute and long-term) and safety of such approach for increasing of success rate of transvenous LV lead implantation and decreasing of CRT-procedures failure.

P652

Influence of advanced age on the response and survival to cardiac resynchronization therapy

L E Camanho[1]; E B Saad[2]; C Slater[2]; LA Oliveira Jr[2]; L Carvalho Dias[2]; R Mourilhe-Rocha[1]
[1]*State University of Rio de Janeiro and Procardiaco Hospital, RIO DE JANEIRO, Brazil*; [2]*Hospital Pro Cardiaco, Electrophysiology and Pacemaker, Rio de Janeiro, Brazil*

Fundamental: cardiac resynchronization therapy (CRT) improves functional class (FC) and reduces total mortality in patients (pt) with advanced heart failure (HF) and depressed ejection fraction (EF). However, current guidelines do not suggest any upper age limit for CRT, but recommended avoidance in pt with a life expectancy less than one year.
Objective: to define the role of advanced age in the survival and response of pt undergoing CRT.
Methods: 250 pt who underwent a CRT were retrospectively evaluated. All presented in FC III/ IV (NYHA). They were divided into two groups: Group I - 92/150 pt (37%) - 75 years or older (< 75 y) and Group II - 158/250 pt (63%) - age less than 75 years. The criteria of response to CRT were: improvement of FC, increase in EF (<10%) and decrease in left ventricular end-systolic diameter (LVESD) - < 15%. The response to CRT and post-implant survival were evaluated in both groups. Statistical analysis was done through exact Fisher Test ($p < 0.05$).
Results: in group I, the mean age was 81.6 years; 73% were male; left bundle branch block (LBBB) was observed in 98% and average QRS duration was 167 ms; average EF: 28%; average LVESD and left ventricular end-diastolic diameter (LVEDD): 53 and 68 mm, respectively. BIV-ICD was observed in 72% of pt. 84% of the patients were responders to CRT and average post-implant survival was 36 months. in group II, the mean age was 61 years; 67% were male; LBBB was observed in 94% and average QRS duration was 166 ms; average EF: 26%; average LVESD and LVEDD: 58 and 72 mm, respectively. BIV-ICD was observed in 82% of pt. 85% of the patients were responders to CRT ($p = 0.13$) and average post-implant survival was 40 months.
Conclusion: despite a higher number of associated comorbidities in elderly pt, advanced age did not directly influence the response to CRT and post-implant survival, and should not be a limiting factor of this therapy.

Implantable Cardioverter / Defibrillator

P653

Possible aborted cardiac arrest in a patient with newly diagnosed non-ischemic dilated cardiomyopathy: reverse remodelling and no need for defibrillator implantation

A Alberto Aimo[1]; A Barison[2]; C Passino[1]; M Emdin[1]
[1]*Sant'Anna School of Advanced Studies, Pisa, Italy*; [2]*Gabriele Monasterio Foundation, Pisa, Italy*

A 60-year old woman with unremarkable medical history fainted while doing her housework. Her husband, a doctor, found that she did not have a carotid pulse, and did two precordial thumps. The woman regained consciousness. When the emergency medical service arrived, her electrocardiogram (ECG) showed sinus rhythm, with an heart rate of 80 beats per minute, and a left bundle branch block, not previously known. After excluding acute brain lesions, an urgent coronary angiography was performed, demonstrating normal coronary arteries. Transthoracic echocardiogram and cardiac magnetic resonance (CMR) showed severe left ventricular (LV) systolic dysfunction (LV ejection fraction - LVEF - 30%, global hypokinesis), and dilatation (LV end-diastolic volume index - LVEDVi - 128 mL/m2 at CMR, reference values 51-91 mL/m2). Non-ischemic dilated cardiomyopathy was then diagnosed. A therapy with angiotensin-converting enzyme inhibitor, beta-blocker, and aldosterone antagonist was started and uptitrated.
Since the syncopal episode was compatible with an aborted cardiac arrest, two 24-hour ECG Holter recordings were performed during the hospital stay. Only 16 ventricular ectopic beats were recorded over 48 hours, with one triplet; there were no conduction disturbances. Heart rate variability was normal, attesting a preserved autonomic balance. In addition, no area of late gadolinium enhancement (LGE) were remarked at CMR. The risk of recurrent arrhythmias was then deemed low. Moreover, a recovery from LV dysfunction and dilatation in response to treatment was expected due to a combination of established predictors of RR: female gender, non-ischemic etiology, and absence of LGE. For all these reasons, and following thorough discussion with the patient, a cardioverter defibrillator was not implanted; the patient refused even a wearable defibrillator.

After three months of clinical stability, the patient underwent a follow-up CMR examination. Her systolic function had improved (LVEF 42%), while LV dilatation persisted (LVEDVi 130 mL/m2). Four months later, her LVEF was 50%, and her LVEDVi (100 mL/m2) approached the normal range. Eight months after this last CMR, the patient feels well.

Guideline-recommended medical treatment for HF may lead to a recovery in LV geometry and function, named reverse remodelling (RR). The improvement may be substantial, as demonstrated by the 20-unit LVEF improvement over seven months in our patient. In parallel, she has been completely asymptomatic for fifteen months. Although a malignant ventricular arrhythmia may only be speculated in this case, it may be concluded that, when such arrhythmia occurs in the setting of newly diagnosed HF, defibrillator implantation may be deferred if the arrhythmic risk is low, and RR may be predicted.

Young Investigator Awards - Clinical

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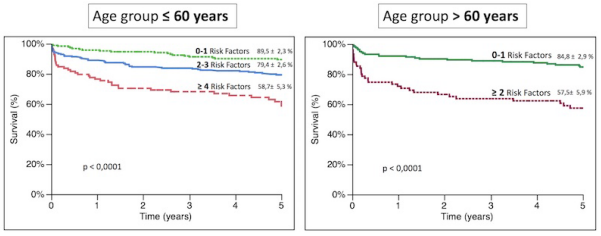
Interplay between recipient age and comorbidities in heart transplant survival: a step towards a tailored approach for advanced heart failure therapies

M Bellettini[1]; M Masetti[1]; H Luikart[2]; A Russo[1]; J Gordon[2]; N D'emilio[2]; M Gessaroli[1]; G Marinelli[1]; F Grigioni[1]; L Potena[1]; K Khush[2]
[1]University Hospital Policlinic S. Orsola-Malpighi, Heart Failure and Heart Transplant Program, Bologna, Italy; [2]Stanford University Medical Center, CV Medicine, Stanford, United States of America

Background: Heart transplantation (HT) is still the best available treatment for patients (pts) with end-stage heart failure. In context of the current donor shortage, optimal candidate selection is crucial for appropriate stewardship of this limited resource. Many risk factors are known to influence post-HT outcomes, but it remains difficult to evaluate the role of multiple comorbidities in a single patient, and their interplay with recipient age has not been adequately explored.
Purpose: We designed this study to evaluate post-transplant outcomes in recipients with multiple comorbidities, and their relevance across different recipient age strata.
Methods: Retrospective cohort study of all adult pts receiving an HT between 1999 and 2016 in two medium-large transplant centers in Europe and North America, in order to account for differences in practice between the two continents. Pts bridged to HT with an LVAD were excluded. Study population was divided into two age groups: = 60 y and > 60 y. Within each group, we examined the association between the primary endpoint (all-cause mortality at 5 years post-HT) and pre-HT clinical, laboratory and hemodynamic data. Finally, post-transplant survival was examined by the number of recipient comorbidities, stratified by age.
Results: Of the 779 pts who met inclusion criteria, 30.6% (n38) were > 60 y. There were no significant differences in 5 yr survival between the two age groups (79.3 ± 1.8 % vs 76.2 ± 2.8 % p = 0.30). Univariate analyses revealed different recipient comorbidities that are associated with survival across the two age strata: diabetes, BMI >30 kg/m2, eGFR < 60ml/min, Bilirubin > 2 mg/dl, Haemoglobin < 12 g/dl, Right atrial pressure > 8 mmHg, CHD etiology and UNOS status in those = 60 y old, and eGFR < 60ml/min, COPD, diabetes and Bilirubin > 2 mg/dl in those >60y old. Within both age groups, post-transplant survival decreased as the number of risk factors increased (Figure). Despite similar overall survival, patients >60 yrs have significantly reduced survival probability with = 2 risk factors, while the cumulative adverse effect of multiple comorbidities seems to be lower in younger patients. Similar results were obtained after adjusting for donor age.
Conclusions: Although age itself should not be considered an absolute contraindication to HT, the poor post-transplant survival seen in patients over 60 years with multiple comorbidities underscores the need to carefully select these candidates for transplantation. HT may be considered as first choice strategy in selected older pts with a low risk profile, while other treatment strategies (i.e LVAD as destination therapy) in patients with multiple comorbidities may improve allocation of a very limited resource.



5 y survival by Age and Risk Factors

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Heart failure patients with a higher protein intake live longer

K W Koen Streng[1]; JM Ter Maaten[1]; K Damman[1]; DJ Van Veldhuisen[1]; P Van Der Meer[1]; JL Hillege[1]; AA Voors[1]
[1]University Medical Center Groningen, Groningen, Netherlands

Funding Acknowledgements: CVON2014-11 RECONNECT and FP7-242209-BIOSTAT-CHF

Background: A higher protein intake has been associated with a higher muscle mass and lower mortality rates in the general population, but data about protein intake and survival in HF patients is lacking.
Methods: We studied the association between protein intake and survival in 2516 patients from the BIOlogy Study to TAilored Treatment in Chronic Heart Failure (BIOSTAT-CHF) study were included. Protein intake was calculated using a validated formula including urea excretion in spot urine, corrected for urine creatinine and body mass index (BMI) (adjusted Maroni formula; 13.9 + 0.907 * BMI (kg/m2) + 0.0305 * urinary urea level (mg/dL)). Association with mortality was assessed using multivariable Cox regression models.
Results: We included 2281 patients with available data (mean age 68 ± 12 years and 27% female). Patients in the highest quartile of protein intake were more often male, had lower NT-proBNP levels and had a higher BMI. Mortality rate in the lowest quartile was 31%, compared to 18% in the highest quartile (P < 0.001). In a multivariable model, lower protein intake was associated with a higher risk of death (Hazard ratio (HR) 1.46; 95% confidence interval (CI) 1.01-2.12, P = 0.045 for the lowest quartile and HR 1.58; 95% CI 1.19-2.28, P = 0.015 for the 2nd quartile.
Conclusions: In patients with HF we found a higher protein intake to be independently associated with a better survival. The potential benefit of a high protein diet in patients with HF warrants further study.

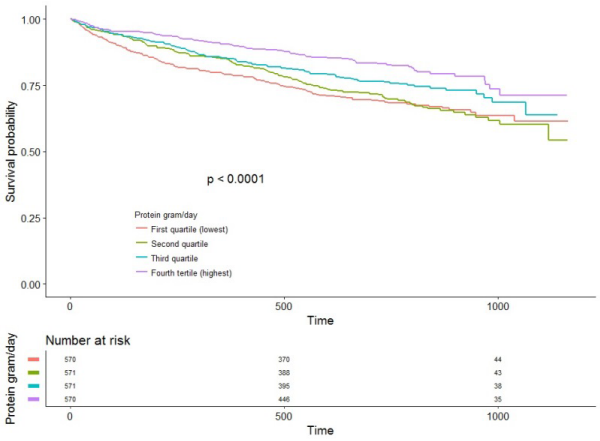

Figure 1; All-cause mortality KM

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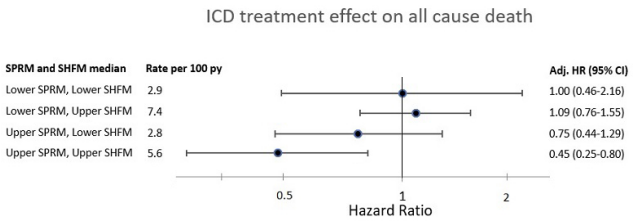
The Seattle heart failure and proportional risk model for prediction of ICD benefit in non-ischemic cardiomyopathy: A posthoc analysis of the DANISH trial

SL Kristensen[1]; WC Levy[2]; JC Nielsen[3]; J Haarbo[4]; L Videbaek[5]; E Korup[6]; NE Bruun[4]; H Eiskjaer[3]; C Hassager[1]; JH Svendsen[1]; DE Hoefsten[1]; C Torp-Pedersen[7]; S Pehrson[1]; L Koeber[1]; JJ Thune[1]
[1]Rigshospitalet - Copenhagen University Hospital, Cardiology, Copenhagen, Denmark; *[2]University of Washington, Seattle, United States of America*; *[3]Aarhus University Hospital, Department of Cardiology, Aarhus, Denmark*; *[4]Gentofte Hospital - Copenhagen University Hospital, Department of Cardiology, Hellerup, Denmark*; *[5]Odense University Hospital, Department of Cardiology, Odense, Denmark*; *[6]Aalborg University Hospital, Department of Cardiology, Aalborg, Denmark*; *[7]Aalborg University, Aalborg, Denmark*

On behalf of: DANISH investigators

Background: No single study has demonstrated benefit of an ICD for primary prevention in patients with nonischemic cardiomyopathy (NICM). A likely explanation is that ICDs are beneficial mainly in patients at high risk of sudden cardiac death (SCD). We sought to identify a subset of NICM patients at high risk of SCD and thus more likely to benefit from ICD implantation by combining two models, one predicting overall mortality and the other the likelihood of SCD among HF patients who die.
Methods: We applied the Seattle Heart Failure (SHFM) and Seattle Proportional Risk Models (SPRM) on 1116 patients from the Danish study to Assess the Efficacy of ICDs in Patients with Non-ischemic Systolic Heart Failure on mortality (DANISH). The SHFM predicts 1-year all-cause mortality while SPRM predicts the proportion of deaths due to SCD. Both models use information on age, sex, clinical and paraclinical data and pharmacotherapy. Rates of all-cause mortality and ICD treatment effect were estimated according to median SPRM and in 4 subgroups according to a combination of median SPRM and median SHFM.
Results: In DANISH, SHFM predicted a median 1-year all-cause mortality of 4.5% (Q1-Q3 2.9%-7.5%) and SPRM estimated that 54% (Q1-Q3 45%-62%) of eventual deaths would be due to SCD. Among patients with SPRM above the median, rate of death per 100 person-years (py) was 3.6, and in these patients ICD implantation reduced all-cause mortality (hazard ratio (HR) 0.63, 95% CI 0.43-0.94) whereas patients with lower SPRM had a mortality rate of 5.8 per 100 py and no apparent effect of ICD treatment (HR 1.08, 95% CI 0.78-1.49, p = 0.04 for interaction). In four subgroups further stratified by predicted 1-year all-cause mortality, rates of death varied from 2.8 up 7.4 per 100 py, with the highest rate in those with lower SPRM/upper SHFM. ICD implantation reduced all-cause death among those with upper SPRM/upper SHFM (HR 0.45, 95% CI 0.25-0.80) with no significant benefit in the other groups, p = 0.01 for interaction (Figure).
Conclusion: NICM patients with a high relative risk of SCD, as predicted by SPRM seemed to benefit from ICD implantation. Further stratification based on overall mortality risk demonstrated the strongest effect of ICD implantation in patients with both high overall risk of death and high relative risk of SCD. Patients with low relative risk of SCD did not seem to benefit from ICD implantation, regardless of absolute mortality risk.



ICD treatment effect by SPRM and SHFM

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INCIDENCE OF DYSKALEMIA IN HEART FAILURE WITH PRESERVED, MID-RANGE, AND REDUCED EJECTION FRACTION: AN ANALYSIS OF 6,401 PATIENTS FROM THE SWEDISH HEART FAILURE REGISTRY

G Savarese[1]; H Xu[2]; M Trevisan[2]; U Dahlstrom[3]; B Pitt[4]; LH Lund[1]; JJ Carrero[2]
[1]Karolinska Institute, Division of Cardiology; Department of Medicine, Stockholm, Sweden; *[2]Karolinska Institute, Department of Medical Epidemiology and Biostatistics, Stockholm, Sweden*; *[3]Linkoping University, Department of Cardiology and Department of Medical and Health Sciences, Linkoping, Sweden*; *[4]University of Michigan, Department of Medicine, Ann Arbor, United States of America*

Funding Acknowledgements: grants from Vifor Fresenius Medical Care Renal Pharma and Relypsa to Karolinska Institutet.

Background. Heart failure with preserved (HFpEF), mid-range (HFmrEF) and reduced (HFrEF) ejection fraction are characterized by demographic and clinical characteristics and treatments that may differently impact on kidney potassium (K) excretion, and thus, on the risk of developing dyskalemias (dysK). We assessed the incidence of dysK within 1 year in HFpEF vs. HFmrEF vs. HFrEF.
Methods: We included consecutive patients from Stockholm region also enrolled in the Swedish Heart Failure Registry during 2006-10. HFpEF was defined as EF = 50%, HFmrEF as EF = 40-49%, HFrEF as EF < 40%. Kaplan-Meier curves were fitted to assess the crude incidence of hyper- (hyperK) and hypokalemia (hypoK).
Results: Of 6,401 patients, 1,555 (24%) had HFpEF, 1,430 (22%) HFmrEF and 3,416 (54%) HFrEF. Mean age was 73 ± 13 years and 37% were female. In HFpEF, HFmrEF and HFrEF, baseline K levels were 4.0 ± 0.4, 4.1 ± 0.4 and 4.1 ± 0.4 mmol/l, baseline eGFR was 57.7 ± 22.8, 61.1 ± 24.1 and 62.3 ± 24.8 ml/min/1.73m2, use of ACE/ARB was 71.1%, 78.0% and 85.8%, use of MRA was 30.9%, 31.1% and 41.4% and use of diuretics was 80.1%, 69.9% and 75.8% (p < 0.001 for all the comparisons), respectively.
1-year incidence rates for any hyperK (<5.0) were 26.4% in HFpEF, 23.1% in HFmrEF and 25.4% in HFrEF (p = 0.11), for mild hyperK (K 5.1-5.5) 22.0% in HFpEF, 19.9% in HFmrEF and 22.8% in HFrEF (p = 0.07), and for moderate/severe hyperK (K>5.5) 11.5% in HFpEF, 10.9% in HFmrEF and 10.1% in HFrEF (p = 0.32). 1-year incidence rates for any hypoK (K < 3.5) were 27.3% in HFpEF, 22.0% in HFmrEF and 19.4% in HFrEF (p < 0.001), for mild hypoK (3.0-3.4) 26.8% in HFpEF, 21.8% in HFmrEF and 18.9% in HFrEF (p < 0.001), and for moderate/severe hypoK (K < 3.0) 5.0% in HFpEF, 4.6% in HFmrEF and 3.5% in HFrEF (p = 0.03).
Conclusions: Both incident hyper- and hypokalemia was common in HF, regardless of HF type. There were no differences in risk of hyperK among HF types but 1-year incidence rates for hypoK were lower in HFrEF, intermediate in HFmrEF and higher in HFpEF, reflecting the different use of treatments affecting K excretion. These data may be helpful to tailor RAASi therapy, identify patients in need of stricter K monitoring, and to design trials of e.g. RAASi and K-binder agents in HF.

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High prevalence of cancer in patients with peripartum cardiomyopathy: is there a pathophysiological connection between these two entities?

S Schlothauer[1]; T Pfeffer[1]; CS Falk[2]; M Ricke-Hoch[1]; E Stelling[1]; V Abou-Moulig[1]; M Kasten[1]; J Bauersachs[3]; D Hilfiker-Kleiner[1]
[1]Hannover Medical School, Molecular Cardiology, Hannover, Germany; *[2]Hannover Medical School, Institute of Transplant Immunology, Hannover, Germany*; *[3]Hannover Medical School, Department of Cardiology and Angiology, Hannover, Germany*

Background: Peripartum cardiomyopathy (PPCM) is a rare heart disease occurring in the last month of pregnancy or in the first 6 months after delivery. In our study we compared the risk for cancer in PPCM patients to the prevalence in age-matched women. Additionally, we evaluated the kinetics of several plasma markers potentially associated with cancer in PPCM patients.
Methods: Full medical records were available for 207 PPCM patients of the German PPCM registry. Cancer prevalence among PPCM patients was compared to the 10-year cancer prevalence in women aged 0-49 years using the German cancer registry.
Furthermore, we measured plasma levels of 61 markers at baseline (BL, n = 47), 6 months follow-up (FU, n = 44) and long-term follow-up (LTFU, 11 months to 7.5 years, n = 29) using a Luminex-based multiplex assay. Healthy age and postpartum matched women served as controls (n = 29). Depending on their outcome after 6 months we divided patients into subgroups (left ventricular ejection fraction, LVEF = 34%, LVEF: 35-49%, LVEF = 50%) and compared the data using Mann-Whitney test or Students t-test, if they were normally distributed.
Results: Our PPCM cohort shows a cancer point prevalence of 6.28% (13 out of 207), whereas the 10-year prevalence in women aged 0-49 years in Germany is only 0.59%. Since one patient presented with two different neoplasms there were 14 cancer diagnoses: 9 cases before PPCM (3 lymphoma, 2 breast carcinoma, 2 osteosarcoma, 1 melanoma, 1 prolactinoma) and 5 cases after PPCM (3 breast carcinoma, 1 colorectal carcinoma, 1 acute myeloid leukaemia).
Mean LVEF of PPCM patients included in the multiplex analysis was 23 ± 7% at BL, 48 ± 11% at FU and 52 ± 8% at LTFU. Mean LVEF of patients with cancer diagnosis was 29 ± 11% at BL. Some plasma markers potentially associated with cancer (Her2/neu, PAI-1, sIL-6Ra, Osteopontin) were significantly elevated at BL and FU (p < 0.05) in PPCM patients compared to healthy controls. Of note, these markers returned to a normal level at LTFU. Their kinetics showed no difference between PPCM patients with or without cancer. A comparison between the subgroups of PPCM patients revealed significantly elevated baseline levels of Her2/neu (p = 0.0024) and sIL-6Ra (p = 0.0435) in patients with persistently reduced cardiac function (LVEF = 34%) compared to patients with cardiac recovery (LVEF = 50%).
Conclusion: Our findings suggest that PPCM patients have a prevalence of cancer compared to age-matched woman in Germany. PPCM patients with a previous or follow-up cancer diagnosis displayed similar plasma levels of markers potentially

associated with malignancies as PPCM patients without cancer. However, Her2/neu and sIL-6Ra were elevated at baseline and follow-up in PPCM patients and high plasma levels of these two markers were associated with an adverse cardiac outcome.
Further studies are required to evaluate a possible pathophysiological connection of malignant growth and PPCM.

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Improving risk stratification for sudden cardiac death in dilated cardiomyopathy using late gadolinium enhancement cardiovascular magnetic resonance

B P Halliday[1]; AJ Baksi[1]; C Izgi[1]; M Arzanauskaite[1]; S Newsome[2]; A Gulati[1]; AS Lota[1]; SA Cook[3]; JGF Cleland[3]; DJ Pennell[1]; SK Prasad[1]
[1]Royal Brompton Hospital, Department of Cardiovascular Magnetic Resonance, London, United Kingdom; *[2]London School of Hygiene and Tropical Medicine, London, United Kingdom*; *[3]Imperial College London, London, United Kingdom*

Funding Acknowledgements: British Heart Foundation Clinical Research Training Fellowship

Background: The DANISH trial highlighted that the selection of patients with dilated cardiomyopathy (DCM) for implantable cardioverter defibrillators needs to be improved. Additional features which predict sudden cardiac death (SCD) risk are required for a more personalised approach.
Purpose: To examine the association between mid-wall late gadolinium enhancement (LGE) and SCD in DCM.
Methods: We recruited consecutive patients with DCM referred between 2000 and 2011. The presence and quantity of mid-wall LGE was determined by 2 independent experts. A blinded panel adjudicated the occurrence of the primary end-point that comprised either SCD or aborted SCD. The association between the presence, extent, pattern and location of LGE and the end-point was examined using proportional hazard modelling. The Akaike information criterion was used to compare the quality of each model in predicting the outcome.
Results: Overall, 874 patients (588 men, median left ventricular ejection fraction [LVEF 39%], median age 52 years) were followed-up for a median of 4.9 years. Mid-wall LGE was present in 300 (34.3%) cases (median extent 3.8%, IQR 2.0:6.7%; septum only: 142, left ventricular free-wall only: 42, both septum and free-wall: 116). After adjusting for prognostic variables including LVEF, the presence of LGE was associated with SCD events (HR 4.12; 95%CI 2.64:6.45; p <0.001). Estimated HRs for patients with LGE extent of 0-2.5%, 2.5-5% and >5%, compared to patients without LGE were 2.92 (95% CI 1.51-5.65), 4.28 (2.38-7.68) and 5.14 (3.01-8.79). There was a marked non-linear relationship between LGE extent and outcome such that even small amounts of LGE predicted a substantial increase in risk (Figure 1). SCD events were most strongly associated with the combined presence of septal and free-wall LGE (HR 5.82; 95% CI 3.30-10.27), followed by the presence of LGE only in the septum (HR 3.13; 95% CI 1.68-5.81) and LGE only in the free-wall (HR 2.19; 95% CI 0.76-6.31). Predictive models using LGE presence and location were superior to models based on LGE extent or pattern.
Conclusions: In DCM, the presence of mid-wall LGE is associated with a large increase in the risk of SCD events, even when the extent is small. SCD risk is greatest with concomitant septal and free wall LGE.

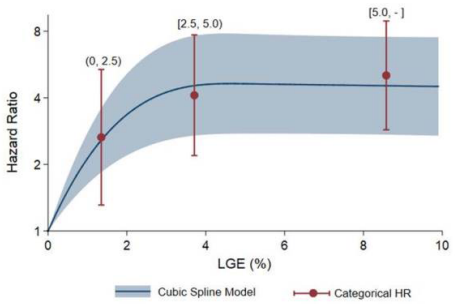

Figure 1. Estimated adjusted hazard ratios with 95% confidence intervals (red lines) for the end-point, per patient group based on increasing extent of late gadolinium enhancement (LGE) (0-2.5%, 2.5-5%, >5%). The hazard ratios are positioned at the median LGE extent within each category. A cubic spline model (blue line) has been fitted to the observed data.

Figure 1

Moderated Posters - Epidemiology

Comprehensive phenoptyping of patients with dilated cardiomyopathy and recovered ejection fraction

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B P Halliday[1]; R Wassall[1]; Z Khalique[1]; D Auger[1]; AS Lota[1]; R Wage[1]; GC Smith[1]; R Jackson[1]; T Rahneva[1]; SA Cook[2]; DJ Pennell[1]; JGF Cleland[2]; SK Prasad[1]
[1]Royal Brompton Hospital, Department of Cardiovascular Magnetic Resonance, London, United Kingdom; [2]Imperial College London, London, United Kingdom

Funding Acknowledgements: British Heart Foundation Clinical Research Training Fellowship

Background: Recovery of left ventricular ejection fraction (LVEF) is common in patients with non-ischaemic dilated cardiomyopathy (NIDCM). Whether this represents remission or cure remains unclear.
Purpose: To characterise and phenotype patients with recovered DCM.
Methods: We evaluated 54 patients with a prior diagnosis of NIDCM and LVEF = 40%, whose LV function had recovered (improvement in LVEF to = 50% with normal left ventricular size) and HF symptoms had resolved (NYHA 1), using cardiovascular magnetic resonance (CMR), cardiopulmonary exercise testing (CPET) and biomarkers.
Results: The median age of patients was 56 years, 18 were women, 7 had left bundle branch block and all were prescribed neurohormonal heart failure therapy.
CMR: The median LVEF, indexed left ventricular end-diastolic volume and indexed left atrial volume of patients with recovered DCM was 62% (IQR 55:64%; normal range 56:78%), 83ml/m2 (IQR 75:89ml/m2; normal range 50:103ml/m2) and 41.6ml/m2 (IQR 34.1:45.4 ml/m2; normal range 27:53ml/m2) respectively.
Overall, 19 (32%) patients had late gadolinium enhancement (Figure 1a). The median native T1 value of patients was 1291ms (IQR 1271:1314ms), which was not significantly different to healthy volunteers (HVOLs) (median 1284ms; IQR 1252:1316ms; p = 0.749) (Figure 1b).

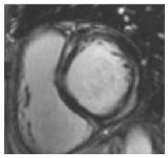

Figure 1a. Late gadolinium enhancement images of a patient with recovered dilated cardiomyopathy, demonstrating mid-wall and sub-epicardial enhancement.

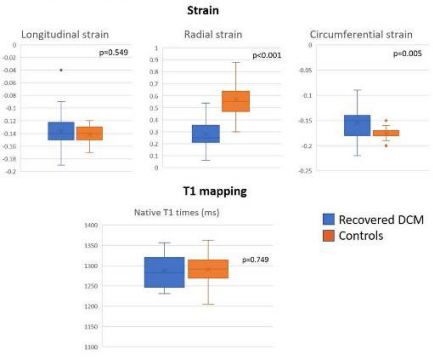

Figure 1b. Myocardial strain and native T1 times of patients with recovered dilated cardiomyopathy compared to healthy volunteers.

Figure 1

The median radial and circumferential strain of patients was 0.25 (IQR 0.21:0.35) and -0.15 (IQR -0.14:-0.18), which was significantly less than HVOLs (median radial strain 0.55, IQR 0.55:0.6, p <0.001; median circumferential strain -0.18, IQR -0.17:-0.18, p = 0.005) (Figure b). There was no difference in longitudinal strain between patients (median -0.14, IQR -0.12:-0.14) and HVOLs (median -0.14, IQR -0.14:-0.15; p = 0549).
Biomarkers: The median plasma NT-pro-BNP level was 77ng/L (IQR 43:134ng/L); 17 of 54 patients had values >125ng/L and 1 had a value >2000ng/L; 3 patients had plasma troponin I >20ng/L.
CPET: The median peak oxygen consumption of patients was 25.6ml/kg/min (IQR 22.0:31.5mlkg/min); 44 of 51(86%) patients recorded values that were >80% of the predicted peak oxygen consumption based on age, sex and height predicted normal ranges.
Conclusions: Many patients with recovered NIDCM have abnormal myocardial strain, replacement myocardial fibrosis and persistently elevated plasma NT-pro-BNP concentrations, despite normalisation of ventricular volumes and functional capacity.

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The benefits of having a nurse fully dedicated to telemonitoring heart failure patients with an implanted cardiac device: a mixed method study

M Michela Barisone[1]; A Bagnasco[1]; M Zanini[1]; G Catania[1]; G Aleo[1]; L Sasso[1]
[1]University of Genoa, Genoa, Italy

Background/Introduction: Heart failure is often the result of the clinical progression of several common diseases, such as ischaemic heart disease, arterial hypertension, and cardiomyopathy, with an incidence of 2 million cases per year in the world, 470,000 in Europe, and 66,000 in Italy.
Heart failure is the most frequent cause of hospitalization in older people.
In the last decade, there has been a rapid increase in the use of Health Technology Assessment, pacemakers, and defibrillators, which have ensure better clinical
Results: Implanted heart devices play an important role in telemonitoring heart failure. Telemonitoring systems enable to check, at any time, current and previous data produced by the implanted device, resulting in early detection of arrhythmias or incipient anomaly of the stimulation or heart defibrillating system.
Purpose: To evaluate how remote control and monitoring by nurses with arrhythmology competences reduces hospital re-admission rates, hospitalization costs and mortality.
Methods: A study with a convergent parallel mixed method design was used with two components: a descriptive qualitative study and a retrospective observational cohort study. A sample of 849 remotely monitored patients with implanted cardiac devices was recruited from January 2011 to December 2016 from electronic records. The primary endpoint of the study is to check how this activity reduces readmissions. Qualitative data were collected through semi-structured interviews with 10 dedicated nurses, to understand what type of education and practical training they had received in relation to their current practice in the field of cardiac nursing and evaluate how nursing impacts on the organization of care in terms of nursing sensitive outcomes.
Results: We found that in the centres where there was nurse dedicated to remote monitoring, hospital readmissions decreased by almost 20%, of patients who met admission appropriateness according to their diagnosis on admission. Mortality decreased in the centres with a nurse fully dedicated to remote monitoring of HF patients compared to centres where there was no dedicated nurse. A correlation between death and baseline diagnosis is highlighted. In hospitals where the seniority of cardiac nurses was higher, there was a significant reduction of readmissions and mortality.
Conclusion(s): The benefits for the patients were found to be relevant in terms of reducing social costs: reduction of transport costs for patients by 60%, reduction of working days lost by the patient and / or carers, failure to give up personal activities (patient and family members) and greater patient satisfaction and acceptance with better follow-up adherence. From the data received through the telemonitoring systems, there was a reduction of inappropriate shocks, prevention of heart failure events, reduction of the number and duration of readmissions and improved survival.

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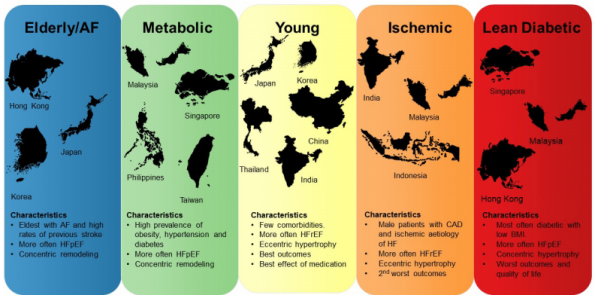
Multimorbidity in asian patients with heart failure: data from ASIAN-HF.

J Jasper Tromp[1]; WT Tay[1]; W Ouwerkerk[2]; THK Teng[1]; J Yap[1]; M Macdonald[3]; K Leineweber[4]; JJV Mcmurray[5]; MR Zile[6]; IS Anand[7]; CS Lam[1]
[1]National Heart Centre Singapore, Cardiology, Singapore, Singapore; [2]Academic Medical Center of Amsterdam, Amsterdam, Netherlands; [3]Changi General Hospital, Singapore, Singapore; [4]Bayer AG, Wuppertal, Germany; [5]University of Glasgow, Glasgow, United Kingdom; [6]Medical University of South Carolina, Charleston, United States of America; [7]Veterans affairs Medical Center, Minneapolis, United States of America

Funding Acknowledgements: Boston Scientific Investigator Sponsored Research Program, National Medical Research Council of Singapore, A*STAR Biomedical Research Council ATTRaCT

Background: Comorbidities are common in patients with heart failure (HF) and complicates their treatment and outcomes. Prior studies have focused mainly on individual comorbidities in isolation, underestimating the total burden of multimorbidity in HF.
Purpose: We sought to identify the pattern of multimorbidity in Asian patients with HF and their association with patients' quality of life, cardiac remodeling, outcomes and treatment response to HF medications.
Methods: We performed latent class analysis (LCA) using comorbidities including: atrial fibrillation (AF), CAD, stroke, CKD, obesity, hypertension, chronic obstructive pulmonary disease (COPD), peptic ulcer disease, renal artery stenosis, cancer, liver disease, dementia, anemia, depression, diabetes and peripheral arterial disease, to identify patterns of multimorbidity. Analyses were performed using 6479 prospectively enrolled patients with HF from the ASIAN-HF registry (1204 HF with a preserved ejection fraction [HFpEF]) from 11 Asian regions. Following, we investigated the associations of multimorbidity patterns with geographical distribution, patients' quality of life, cardiac structure and function, outcomes and treatment response to HF medications.
Results: We identified 5 distinct multimorbidity groups (N = 1048-1759 in each group): Elderly/atrial fibrillation (AF) (oldest, more AF), Metabolic (Obesity, diabetes, hypertension), Young (youngest, low comorbidity rates, non-ischemic etiology), Ischemic (Ischemic etiology) and Lean Diabetic (diabetic, hypertensive, low prevalence of obesity and high prevalence of chronic kidney disease). The Metabolic and Lean Diabetic groups had the highest proportions of concentric left ventricular hypertrophy (LVH) and the Young group had the highest proportion of eccentric LVH. Patients in the Lean Diabetic group had the worst quality of life, more severe signs and symptoms of HF and the worst outcomes, independent of confounders (P for all <0.001). Multimorbidity groups modified the association of guideline directed dosages of beta-blockers and mineralocorticoid receptor antagonists with outcomes (all-cause mortality and HF hospitalizations), such that patients in the Young group appeared to derive the most survival benefit with these drugs (Pinteraction <0.05 for both).



Conclusion: Among Asian patients with HF comorbidities naturally clustered in 5 distinct patterns, each associated with specific underlying patterns of cardiac remodeling, and differentially impacting patients' quality of life, outcomes and treatment response to some HF medications. These data underscore the importance of studying multimorbidity in HF and the need for more comprehensive approaches in phenotyping patients with HF and multimorbidity.

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Cognitive impairment and the level of self-care behaviors among elderly patients with heart failure

I Uchmanowicz[1]; B Prochota[2]; K Katarzyna Lomper[1]; M Lisiak[1]; A Chudiak[1]; M Wleklik[1]
[1]*Wroclaw Medical University, Department of Clinical Nursing, Wroclaw, Poland*; [2]*Health Facility , Olesno, Poland*

Introduction: Heart failure (HF) is diagnosed in 1-2% of the general population. HF is the most common cause of hospitalization among cardiovascular diseases. HF is a leading cause of hospitalizations among cardiovascular diseases. Over 80% of the HF population are patients over 65 years of age. Aging together with reduced perfusion in the cerebral blood flow in HF may be the reason for the development of cognitive impairment (CI). Cognitive impairment is one of the key barriers to achieving the satisfactory level of self-care affecting the final therapeutic effect.
Purpose: To investigate the influence of CI on the level of self-care behaviors among elderly patients with HF.Methods. The study included 100 patients (mean age of 73.78 years) with diagnosed HF hospitalized in the Public Health Care. The cognitive functions were evaluated using the Mini-Mental State Examination (MMSE) questionnaire and the level of self-care was assessed with the European Heart Failure Self-care Behavior Scale (EHBScB). In the statistical analysis, the significance level was assumed for p> 0.05.
Results: Analysis of the MMSE questionnaire showed the presence of CI without dementia in 29% of patients, CI with mild degree dementia has been reported in 24% of respondents and CI with moderate dementia in 27%. In turn, CI was not observed in the remaining group (20%). The average score in EHBScB questionnaire for the studied population was 61.78 (SD = 23.59). Post-hoc analysis showed a significant relationship between CI and the level of self-care. People with CI without dementia and without recognized CI had significantly higher levels of self-care than those with CI and moderate dementia (p = 0.001).Conclusion.Cognitive impairment significantly and negatively influences the level of self-care behaviors in elderly patients with HF.

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Increased risk of cancer death in patients with chronic heart failure with a special reference to inflammation and diabetes mellitus -A report from the CHART-2 Study-

Y Sakata[1]; T Takuya Oikawa[1]; K Nochioka[1]; M Miura[1]; R Abe[1]; S Kasahara[1]; M Sato[1]; H Aoyanagi[1]; T Shiroto[1]; K Sugimura[1]; J Takahashi[1]; S Miyata[2]; H Shimokawa[3]
[1]*Tohoku University Graduate School of Medicine, Department of Cardiovascular Medicine, Sendai, Japan*; [2]*Tohoku University Graduate School of Medicine, Department of Evidence-Based Cardiovascular Medicine, Sendai, Japan*; [3]*Tohoku University Graduate School of Medicine, Department of Cardiovascular Medicine and Department of Evidence-Based Cardiovascular Medicine, Sendai, Japan*

On behalf of: The CHART-2 Investigators
Funding Acknowledgements: This study was supported in part by the Grants-in Aid from the MHLW, MEXT and AMED (No. 17ek0210081h0001), Tokyo, Japan.

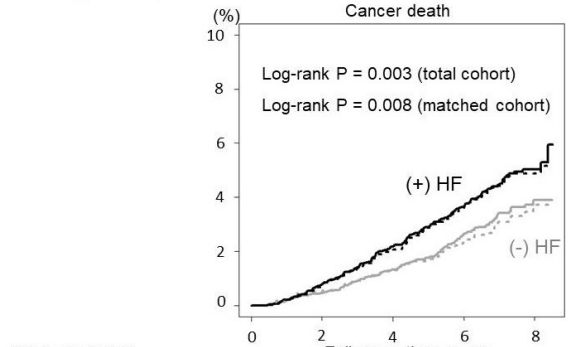
Background: It has been reported that several factors, including heart failure (HF), diabetes mellitus (DM) and inflammation, affect the incidence of cancer. However, it remains to be examined whether HF is a risk of cancer death, particularly with a reference to inflammation and DM.

Table. Impact of Temporal Changes of CRP Levels on Cancer Death in HF Patients

Changes in CRP levels from baseline to 1-year	HR	95%CI	P value
From < 2.0 mg/L to < 2.0 mg/L (N = 918)	1.00	reference	NA
From < 2.0 mg/L to ≥ 2.0 mg/L (N = 286)	1.09	0.48-2.46	0.83
From ≥ 2.0 mg/L to < 2.0 mg/L (N = 456)	1.42	0.74-2.71	0.29
From ≥ 2.0 mg/L & ≥ 2.0 mg/L (N = 569)	1.84	1.05-3.24	0.03
Variables: age, sex, heart rate, dyslipidemia, heart failure admission, NYHA Class, antiplatelet			

Purpose: To examine the relationship between HF and risk of cancer death.

Figure. Kaplan-Meier Curves for Cancer Death



Number at Risk							
Total	——	(-) HF	4,622	4,405	3,980	2,975	599
Cohort	——	(+) HF	4,221	3,817	3,242	2,474	359
Matched	– – –	(-) HF	2,895	2,793	2,495	1,888	391
Cohort	– – –	(+) HF	2,895	2,657	2,307	1,851	331

Methods: Our Chronic Heart Failure Registry and Analysis in the Tohoku district-2 (CHART-2) Study (N = 10,219) is a multicenter, prospective, observational cohort study, designed to identify the characteristics, mortality and prognostic risks of cardiovascular patients with and without HF in Japan. We examined 8,843 consecutive patients without a prior history of cancer in the CHART-2 Study (mean 68 yrs., female 30.9%).
Results: During the median 6.5-year follow-up (52,675 person-years), 282 cancer deaths occurred. HF patients had significantly higher cancer mortality than those without HF in both the overall (3.6 vs, 2.8%, hazard ratio (HR) 1.42, 95% confidence interval (CI) 1.12-1.79, P = 0.004) and the propensity score-matched cohorts (HR 1.49, 95%CI 1.08-2.05, P = 0.016) (Figure), which was confirmed in the competing risk models. Subgroup analysis showed that HF was associated with increased incidence of cancer death in patients with C-reactive protein (CRP) = 2.0mg/L (HR 2.26, 95%CI 1.34-3.79, P = 0.002) but not in those with CRP <2.0mg/L (HR 0.92, 95%CI 0.56-1.50, P = 0.728) (P for interaction = 0.014), and in patients without DM (HR 1.98, 95%CI 1.33-2.94, P <0.001) but not in those with DM (HR 1.01, 95%CI 0.64-1.59, P = 0.972) (P for interaction = 0.030). The multivariable Cox proportional hazard model showed that temporal changes in CRP levels were associated with cancer death: HF patients with CRP = 2.0mg/L at both baseline and 1-year had significantly increased mortality of cancer (Table), particularly that of lung cancer.
Conclusions: These results provide the first evidence that HF is associated with increased cancer death in the presence of prolonged inflammation, but not DM.

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Acute coronary syndrome in-hospital mortality: role of beta-blocker therapy.

M J Maria Joao Nobre De Matos Pereira Vieira[1]; D Durao[1]; A Belo[2]; K Kevin Domingues[1]; C Craveiro[1]; M Saraiva[1]; B Saldanha Santos[1]; M Alves[1]; M Leal[1]; RNSCA Investigadores Do Registo Nacional De Sindromes Coronarios Agudos[2]
[1]Hospital Santarém, Cardiology, Santarém, Portugal; *[2]Sociedade Portuguesa de Cardiologia, Lisboa, Portugal*

On behalf of: Registo Nacional dos Sindromes Coronarios Agudos da Sociedade Portuguesa de Cardiologia (RNSCA)

Background: Beta-blockers (BB) are one of the most widely used therapeutic options in the context of acute coronary syndrome (ACS). Although the long-term survival benefit from chronic BB has been proven in clinical trials, the short-term benefits of early beta-blockade in the setting of ACS are less well-established. The aim of this study was to evaluate the effects of BB therapy in early survival of patients with ACS
Methods: We performed a retrospective study including 17148 patients (age 66 ± 13 years,74,3% men), from the Portuguese Registry on Acute Coronary Syndromes (RNSCA) with the diagnosis of Acute Coronary Syndrome (STEMI n = 7284; NSTEMI n= 8670; Unstable Angina n= 1194) admitted between 01/10/2010 and 03/01/2018. The population was divided into two groups: Group A (A), with in-hospital oral BB therapy (n = 13902) and Group B (B), without in-hospital BB oral therapy (n = 3246). The primary outcome was in-hospital mortality. Demographic, clinical, electrocardiographic, echocardiographic and angiographic data were evaluated. Multivariate analysis was conducted by logistic regression.
Results: Significant differences were observed between groups regarding age, smoking habits, previous history of diabetes mellitus, chronic kidney disease, previous myocardial infarction, type of myocardial infarction at admission, left ventricular ejection fraction, use of angiotensin-converting enzyme inhibitors. Overall in-hospital mortality rate was 3,4% (n = 581), with significant differences between groups (A 1,6 % vs B 10,9 %; OR = 0,14; P < 0,001). The use of BB therapy was also associated with lower occurrence of mechanical complications (A 0,4% vs B 1,9%; OR = 0,22; P < 0,001), lower development of congestive heart failure (A 12,7% vs B 26,4%; OR = 0,4; P < 0,001), lower need for intra-aortic balloon (A 0,5% vs B 1,8%; OR = 0,25; P < 0,001) and invasive ventilation (A 1,4% vs B 4,6%; OR:0,3; P < 0,001). In the multivariate analysis, BB therapy was an independent predictor of in-hospital mortality, assuming a protective role in this setting (OR: 0,33; 95% CI: 0,24-0,46; P < 0,0001). The effect of BB therapy in in-hospital mortality was dependent of the subtype of ACS. In STEMI and NSTEMI patients the beta-blocker therapy was associated with a lower in-hospital mortality (OR = 0,30; P < 0,0001 and OR = 0,68; P = 0,039, respectively). This association was not observed in unstable angina patients with no benefits of beta-blocker therapy in early survival (P = 0,34).
Conclusions: In this study the use of BB therapy in patients with ACS decreased not only in-hospital mortality, but also the development of congestive heart failure and cardiogenic shock, mechanical complications, need for mechanical support and need for invasive ventilation. The benefits on survival were observed in both STEMI and NSTEMI patients, but in patients with unstable angina no benefits were observed.

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Care-seeking decisions in patients with heart failure: a matter of identity and previous healthcare experience

SE Serra Ivynian[1]; PJ Newton[2]; M Digiacomo[1]
[1]University of Technology, Sydney, Sydney, Australia; *[2]University of Western Sydney, Sydney, Australia*

Background: Responding to symptom exacerbation in a timely manner is paramount to effective heart failure (HF) self-management, yet, little is known about what drives patients to seek or avoid professional care for HF symptoms.
Purpose: To extend beyond what is known to impact self-management behaviours by exploring patients' perspectives of factors that influence their decisions to seek professional care for worsening HF symptoms.
Methods: Semi-structured in-depth interviews were conducted with 15 symptomatic HF patients at a teaching hospital. Transcripts were analysed using interpretative phenomenological analysis (IPA) to illuminate participants' experience of events to gain an in depth understanding of factors that led to avoidance of professional care.
Results: Participants described delayed care-seeking due to values and beliefs associated with healthcare use, and desire to avoid hospitalisation. The experience of being hospitalised represented a loss of freedom and control and served as a reminder of being ill. Perception of illness as a threat to identity led to rejection of treatment, whilst fear of being a burden to others also led to avoidance behaviours. Uncertainty about the cause and likely trajectory of symptoms often led to a 'wait and see' response, as symptoms were not perceived as serious. Professional care was often viewed as a last resort, when all alternative coping strategies were exhausted, and participants could no longer cope with the physical and emotional impact of symptoms. Patient-provider interpersonal relationships and preferences for continuity also impacted care-seeking.
Conclusion: Whilst various patient-related factors influenced care-seeking decisions, previous healthcare experiences and interactions with providers largely informed subsequent decisions to interact with health services. Positive patient-provider relationships are key in encouraging timely care-seeking in HF.

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The increased level of GRK2 correlates with preserved exercise capacity in patients with HF.

G Iaccarino[1]; G Vitulano[1]; F D'auria[1]; M Polito[1]; D Bonadies[2]; A Gigantino[2]; F Piscione[1]; M Ciccarelli[1]
[1]University of Salerno, Salerno, Italy; *[2]AOU S. Giovanni e Ruggi, Salerno, Italy*

Background: G protein-coupled receptor kinase 2 (GRK2) activates mechanisms of desensitization and downregulation of b adrenergic receptors (bAR) during chronic heart failure (HF) Previous work has proposed GRK2 as a possible biomarker for human heart failure (hHF). In this study, we evaluate the physiopathology of stress tolerance underlying the role of GRK2 levels in hHF.

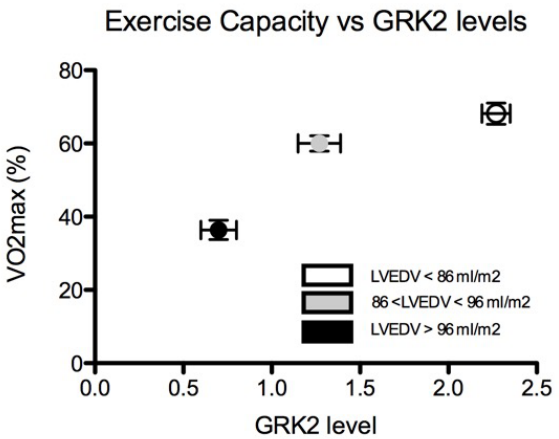

Figure 1

Methods: hHF patients (N = 31; NYHA I: 22,6%, NYHA II:58%, NYHA III:19,3%) were subjected to echocardiographic evaluation of cardiac function (Ejection Fraction, EF%; Left Ventricular End Diastolic Volume, LVEDV, ml) and cardiopulmonary test (CPET) for exercise capacity. Levels of GRK2 were evaluated in peripheral blood mononuclear cells (PBMC) by western blot (WB), on blood samples taken after CPET.
Results: As expected, LVEDV negatively correlates with %VO2 max ($R2 = 0.64$, $p < 0.01$) indicating the association of reduced exercise capacity in HF patients with dilated cardiomiopathy. GRK2 levels negatively correlate with LVEDV ($R2 = 0.53$, $p < 0.01$), but not with EF ($R2 = 0.008$, ns). Instead, GRK2 levels positively correlate with the exercise capacity, estimated as oxygen consumption (%V02 max, $R2 = 0.78$, $p < 0.01$). To confirm that level of GRK2 correlates with exercise capacity, we grouped our population by LVEDV. As shown in figure 1, patients with relatively low LVEDV and increased GRK2 level after exercise display a better exercise capacity respect to patients with increased LVEDV and reduced levels of GRK2.
Conclusions: Our data demonstrate that increased level of GRK2 correlates with exercise capacity in patients with HF.

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Prevalence and determinants of heart failure stage A and B in a population-based sample Results from the STAAB cohort study

C Morbach[1]; M Breunig[1]; G Gelbrich[2]; T Tiffe[2]; F Eichner[2]; M Wagner[2]; PU Heuschmann[2]; S Stoerk[1]
[1]University Hospital Wuerzburg, Comprehensive Heart Failure Center and Dept. of Medicine I, Wuerzburg, Germany; *[2]University of Wuerzburg, Institute of Clinical Epidemiology and Biometry and Comprehensive Heart Failure Center, Wuerzburg, Germany*

Funding Acknowledgements: German Ministry of Education and Research (BMBF 01EO1004 and 01EO1504)

Background: Heart failure (HF) is considered a progressively aggravating continuum ranging from subjects with risk factors for HF (stage A) to asymptomatic cardiac dysfunction (stage B) and symptomatic HF (stages C and D). To derive the population at risk for developing HF, we aimed to assess prevalence and characteristics of early stages of HF in a population-based cohort.
Methods: We report a planned interim analysis of the prospective Characteristics and Course of Heart Failure Stages A-B and Determinants of Progression (STAAB) cohort study investigating a representative sample of residents of the City of Würzburg, Germany, aged 30 to 79 years and reporting no previously diagnosed HF. Participants underwent detailed cardiac phenotyping and standardized echocardiography. Categorization of HF was performed according to AHA/ACC guidelines. A: = 1 risk factor for HF (hypertension, arteriosclerotic disease, diabetes mellitus, obesity, metabolic syndrome), but absence of structural heart disease (SHD); B: asymptomatic but SHD (reduced left ventricular (LV) ejection fraction, LV hypertrophy, LV dilation, stenosis or more than mild regurgitation of aortic or mitral valve, worse than mild diastolic dysfunction) or prior myocardial infarction; C: SHD and signs and symptoms of HF (Framingham criteria);
Results: We analyzed 2473 participants (54 ± 12 years, 51% female): stage A, 42% (58 ± 11 years, 42% female); stage B, 18% (58 ± 12 years, 63% female). 31% of stage B subjects had no risk factor that would qualify for A (B-not-A). Compared to individuals in stage B with present A criteria, B-not-A were significantly younger (47 ± 10 vs. 63 ± 10 years, $p < 0.001$), more often female (78% vs. 56%, $p < 0.001$), and had LV dilation as predominant B-qualifying criterion ($p < 0.001$).
Conclusion: In this population-based cohort, prevalence of both stage A and B was high and increased with advancing age. Unexpectedly, about one third of individuals in stage B showed no risk factors qualifying for stage A thus challenging the conventional conception of the HF disease continuum. Future research should aim to further characterize this pathophysiologically interesting subgroup, investigate the factors driving its natural course, and possibly adjust risk modifying strategies.

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Prevalence of early stages of heart failure in an elderly high risk population: the copenhagen heart failure risk study

F Gaborit[1]; C Kistorp[2]; T Kumler[1]; C Hassager[3]; N Toender[4]; L Kober[3]; P Hansen[5]; P Kamstrup[6]; J Faber[2]; K Iversen[1]; M Schou[1]
[1]Herlev Gentofte University Hospital , Department of Cardiology, Herlev, Denmark; *[2]Herlev Gentofte University Hospital , Department of Endocrinology, Herlev, Denmark*; *[3]Rigshospitalet - Copenhagen University Hospital, Department of Cardiology, Copenhagen, Denmark*; *[4]North Zealand Hospital , Department of Cardiology, Nephrology and Endocrinology, Hillerod, Denmark*; *[5]Herlev Gentofte University Hospital , Department of Nephrology, Herlev, Denmark*; *[6]Herlev Gentofte University Hospital , Department of Clinical Chemestry, Herlev, Denmark*

Funding Acknowledgements: The Danish Heart Foundation; Herlev Gentofte University Hospital Research Council; Toyota-Fonden, Denmark

Background: Early stages of heart failure (HF) are overlooked in the community, nevertheless, associated with increased risk of hospitalization with congestion and increased risk of death. Prevalence and clinical presentation of HF stages in an elderly high risk population is unknown.
Purpose: To describe the prevalence of HF stage B and C in a cohort of elderly patients with apparently HF stage A. Furthermore, to characterize clinical, biochemical and echocardiographic findings in each stage.
Methods: A prospective cohort study. Patients who fulfilled in- and exclusion criteria were recruited consecutively from the Department of Cardiology, the Diabetes Clinic and the Nephrology Clinic, Herlev Gentofte University Hospital, Denmark. We included 400 patients, >60 years old, with one or more risk factor of HF (diabetes, chronic kidney disease, cardiovascular disease, atrial fibrillation (AF), hypertension) and without history of HF. Patients underwent physical examination, echocardiogram, HF questionnaire and blood samples. HF stages were defined as: stage A (normal echocardiogram), stage B (abnormal echocardiogram but no symptoms of HF), stage C (abnormal echocardiogram and symptoms of HF combined with clinical signs and/or increased plasma concentrations of NT-proBNP (sinus rhythm>125pg/mL, AF>524pg/mL)). Abnormal echocardiogram was pre-defined by gender specific reference values of left ventricle systolic and diastolic function, left ventricle mass and left atrial volume, according to current guidelines.
Results: Before examination all patients were considered to be stage A (median age 72 years; 48.5% female); after thorough evaluation 45% remained in stage A, whereas 37% were stage B, 18% stage C (figure 1). In total 128 patients (32%) reported HF symptoms; 30% in stage A, 1.4% in stage B, 100% in stage C. Higher stages of HF were older; stage A median 69, stage B 74.5, stage C 74($p < 0.0001$); and more frequently had AF; stage A 22.2%, stage B 31.8%, stage C 43.1%($p = 0.0035$). Higher stages of HF had lower median estimated glomerular filtration rate (mL/min/1.73m2); stage A 76.0, stage B 65.5, Stage C 65.0($p = 0.0059$) and lower median hemoglobin (mmol/L); stage A 8.7, stage B 8.5, stage C 8.3($p = 0.0285$). Median plasma concentrations of NT-proBNP (pg/mL) increased with higher stages of HF; stage A 133.0, stage B 275.5, stage C 397.5($p < 0.0001$). Plasma concentrations of TroponinI were more frequently increased in patients with abnormal echocardiogram; 10.1% in stage A, 27.0% in stage B, 30.6% in stage C($p < 0.0001$). Minnesota Living with HF score was higher in patients with stage C, reflecting reduced quality of life; score in stage A 11, stage B 8, stage C 24($p < 0.0001$).
Conclusion: In an elderly high risk population HF stage B and C is frequent. Higher stages of HF had increased plasma concentrations of NT-proBNP and TroponinI, as well as reduced quality of life. Focus on HF symptoms and referral for an echocardiogram in this population is warranted.

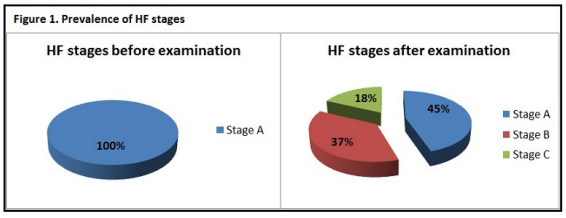

Figure 1

Clinical Case Corner 2 - Cutting edge treatment for advanced heart failure

Sixteen Hours ex-vivo perfusion for heart transplantation

Z Nurmykhametova[1]; R Kaliyev[1]; T Lesbekov[1]; S Bekbossynov[1]; M Bekbossynova[1]; T Kapyshev[1]; S Novikova[1]; A Medressova[1]; L Faizov[1]; S Dzhetybayeva[1]; M Murzagaliyev[1]; N Smagulov[1]; Y Pya[1]
[1]*National research center for cardiac surgery, Astana, Kazakhstan*

Objective: We report the successful heart transplantation following an ex-vivo allograft perfusion time of 960 minutes into a recipient with dilated cardiomyopathy and left ventricular assist device implant.
Patients: The patient was on LVAD support as a bridge to transplantation. Drive line infection influenced his clinical status necessitating heart transplantation.
Results: The patient underwent successful heart transplantation, requiring central veno-arterial ECMO support for the first 44 hours. In 13 days he was undergoing early rehabilitation with normal cardiac function.
Conclusion: We report the longest out-of-body time for a successful cardiac transplant to be added to a global learning curve of long runs using TransMedics Organ Care System.

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Regression of severe aortic regurgitation in LVAD patient

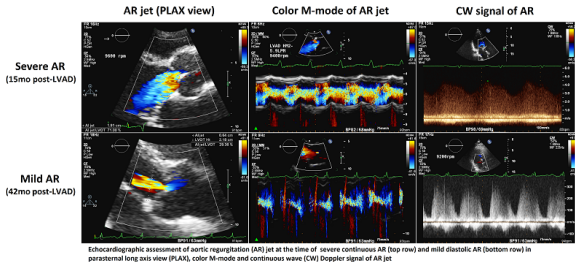
K Poopong[1]; PS Sakiyalak[2]; SJ Janwanishstaporn[3]
[1]*Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand*; [2]*Faculty of Medicine Siriraj Hospital, Mahidol University, Division of Cardiothoracic surgery, Department of Surgery, Bangkok, Thailand*; [3]*Faculty of Medicine Siriraj Hospital, Mahidol University, Division of Cardiology, Department of Medicine, Bangkok, Thailand*

Introduction: Aortic regurgitation (AR) is a significant complication in patients with continuous flow left ventricular assist device (LVAD). Severe AR can cause refractory heart failure (HF) usually requiring intervention. We present a patient with regression of severe AR associated with LVAD without aortic valve (AV) intervention.
Description: A 59-year-old Thai male with history of dilated cardiomyopathy for 10 years progressed to advanced HF with LVEF of 16%. He underwent a LVAD implantation, Heartmate II, as a bridge-to-transplantation. AR was not present in both pre- and post-operative period. After 4 months of uneventful follow-up and improved HF symptoms, TTE showed a well-decompressed left ventricle (LV) with LVEF of 42% and mild AR with intermittent AV opening.
After 1 year of implantation, his HF symptoms worsened. TTE revealed an enlarged LV with a worsening LVEF of 18% and continuous severe AR without AV opening despite optimization of pump speed by ramp study.
The patient was planned for urgent heart transplantation due to symptomatic severe AR. Unfortunately, his panel-reactive HLA antibody was extremely high, contraindicating heart transplantation. After discussing with the patient, we decided to closely observe and planned an AV intervention if his HF worsened. The heart failure medications were continued as shown in the Table. However, his HF symptoms gradually improved. Serial TTE study revealed progressive decline in AR severity to mild diastolic AR with minimal AV opening and improved LV contraction at 3 years after implantation.
Questions: What is the explanation and underlying mechanism behind the regression of severe AR in LVAD patient?
Implications: We propose the improved LV function possibly from HF medication may have contributed to AR regression in this patient. As lacking of AV opening is a key mechanism for AR in the LVAD patient. If the recovered LV can generate greater pressure to reopen the AV, this should reduce AR severity. The putative role of HF medications in LV reverse remodeling and prevention of AR in LVAD patients warrants further research.

Timeline

Timing (mo. after LVAD)	Pre-LVAD (0 mo.)	Mild AR (4 mo.)	Severe AR (15mo.)	Mild AR (42 mo.)
LVIDd (mm)	74.6	46.0	67.4	47.0
LVEF (%)	16.1	41.6	20.6	36.1
Carvedilol (mg/d)	50	12.5	12.5	25
Enalapril (mg/d)	0	40	10	15
Spironolactone (mg/d)	25	0	0	37.5

AR, Aortic regurgitation; LVIDd, Left ventricular internal diameter end-diastole;



Echocardiographic findings

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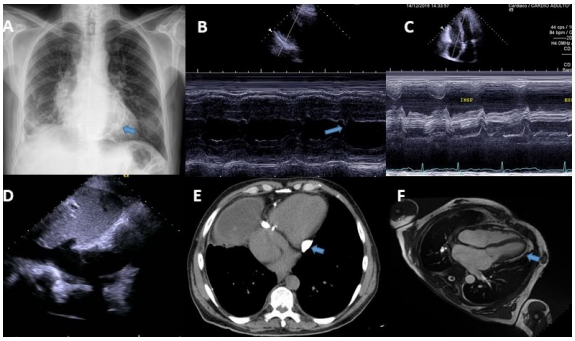
A rare cause of heart transplant

A Ainhoa Perez Guerrero[1]; C Lopez Perales[1]; A Portoles Ocampo[1]; T Blasco Peiro[1]; C Aured Guallar[1]; JM Vallejo Gil[1]; M Lasala Alastuey[1]; A Juez Jimenez[1]; P Auquilla Esteban[1]; I Caballero Jambrina[1]; A Ruiz Aranjuelo[1]; E Gambo Ruberte[1]; J Jimeno Sanchez[1]; M Sanz Julve[1]
[1]*University Hospital Miguel Servet, Zaragoza, Spain*

Introduction: Constrictive pericarditis (CP) is a potentially reversible cause of heart failure. Pericardiectomy is the treatment of choice for chronic constrictive with persistent clinical.
Case Presentation: A 57-year-old male non-immunocompromised patient with past medical history of Tuberculous pericarditis. He was readmitted due to dyspnoea, ortopnea and anasarca. Exploration revealed bilateral jugular vein dissension and hepatojugular reflux, hepatomegaly, ascites and bilateral lower leg pitting edema.
Chest X-ray revealed extensive pericardial calcifications (Figure 1A). Echocardiography showed a small left ventricle (LV) with normal systolic function. 2D and M mode demonstrated ventricular interdependence with an early diastolic notch and a dilated inferior vena cava without respiratory variability (Figures 1B, 1C, 1D). The peak early mitral annular velocities (e') assessed by pulsed wave tissue Doppler at the septal and lateral mitral annulus were 0,1 m/sg and 0,08 m/s, and the ratio of the peak early transmitral velocity (E) to e' (E/e'), was only 5 ("annulus paradoxus"). Right cardiac catheterization confirmed the presence of a constrictive physiology and assisted in discriminating between CP and restrictive cardiomyopathy (RC). Computed tomography (CT) and magnetic resonance imaging (MRI) confirmed extensive pericardial calcification and thickening mostly involving the lateral wall of LV and the atrioventricular grooves (Figures 1E, 1F).
Despite adequate diuretic therapy, the patient was readmitted with the same symptoms. Pericardiectomy was recommended to control the disease. However, due to the location of the pericardial calcification, with a high risk of perforation;

the heart team decided to perform an elective heart transplant that it resulted in a success.

Conclusion: This case illustrates an infrequent cause of CP in industrialized countries, and even more rare cause of heart transplant. Orthotopic transplantation may be considered in highly select patients with CP.



726

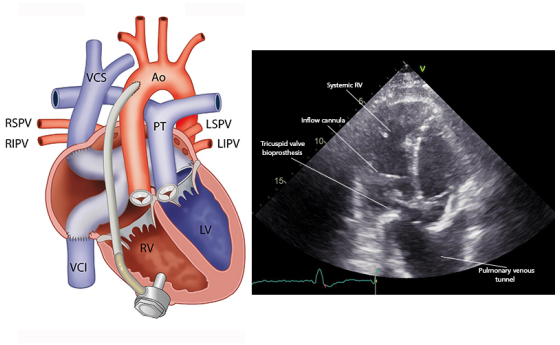
Ventricular assist device implantation in a patient after mustard correction for transposition of the great arteries

T E Zandstra[1]; M Palmen[2]; MG Hazekamp[2]; B Meyns[3]; SMLA Beeres[1]; ER Holman[1]; P Kies[1]; MRM Jongbloed[1]; HW Vliegen[1]; MJ Schalij[1]; LF Tops[1]
[1]Leiden University Medical Center, Cardiology, Leiden, Netherlands; *[2]Leiden University Medical Center, Cardiothoracic surgery, Leiden, Netherlands*; *[3]University Hospitals (UZ) Leuven, Cardiothoracic surgery, Leuven, Belgium*

We present the case of a 47-year-old man with transposition of the great arteries (TGA), for which he underwent atrial switch procedure according to Mustard at 3 years of age. He had received a pacemaker for sick sinus syndrome and later he was ablated for a supraventricular tachycardia. Because of progressive systemic right ventricular (s-RV) failure and important tricuspid valve regurgitation, he received a biological tricuspid valve prosthesis in 2016.

Because of failure of clinical improvement (NYHA class IIIb, INTERMACS level 5), he was screened for cardiac transplant and eventually accepted for ventricular assist device (VAD) implantation in his s-RV, intended as destination therapy (DT). During preoperative admission, his circulatory status was optimized with inotropic support and intravenous diuretics. Sternotomy was performed after cardiopulmonary bypass was started via the femoral vessels. Multiple trabeculations were removed from the s-RV to prevent obstruction of the inflow cannula. Because of lack of space between the sternum and the s-RV, the inflow cannula was placed mid-basally in the ventricle instead of in the apical position that is usual for VAD implantation in the left ventricle. After implantation, stable VAD inflow and outflow cannula flow patterns and normal interventricular septum position were observed with transoesophageal echocardiography. Re-operation was necessary 13 days later because of a tamponade. After that, the patient remained stable and was discharged 1 month after VAD implantation. In the outpatient setting, a ventricular tachycardia (VT) of 185 beats per minute occurred, which was hemodynamically well tolerated. Most likely it originated from the site of the inflow cannula, The VT was successfully terminated with intravenous procainamide, and treatment with sotalol was initiated to prevent recurrent VT. There have been no recurrent VTs and the patient is currently doing well 6 weeks after hospital discharge.

This case illustrates that VAD implantation as DT is a challenging but feasible treatment option for patients after atrial switch correction for TGA and failure of the s-RV.



Schematic and echocardiographic anatomy

727

Use of Therapeutic Plasma Exchange (PLEX) for Treatment of Vasodilatory Shock Post Heartmate-2 LVAD

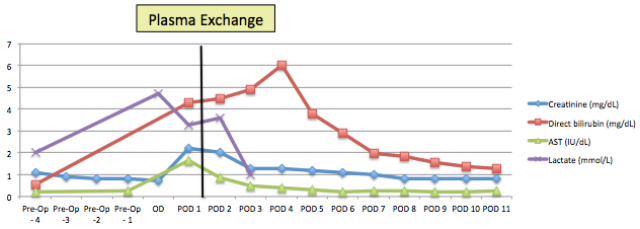
R Raymond Lee[1]; O Gilbert[1]; D Smull[1]; G Marler[1]; S Satko[1]; E Tatum[1]; P Keith[1]
[1]Novant Forsyth Medical Center, Cardiothoracic Surgery, Winston-Salem, United States of America

Objetive: Vasodilatory shock post left ventricular assist device implantation can occur in up to 50% of cases. For cases with refractory vasodilatory shock with signs of multi-system organ failure, morbidity and mortality remain high. We present a case of severe vasodilatory shock post LVAD insertion, treated with therapeutic plasma exchange.

Methods: This is a retrospective case review of a 56 year-old male with non-ischemic cardiomyopathy with New York Heart Classification Class 4 heart failure and severe mitral regurgitation. The patient underwent Heartmate 2 insertion as destination therapy and beating mitral valve repair.

Results: The patient was extubated postoperative day 1 with vasodilatory shock successfully managed by epinephrine and vasopressin pharmacotherapy. Post operative day 2, the patient began to show signs of worsening vasodilatory shock unresponsive to vasopressin, cathecholamines, methylene blue, empiric steroids, and broad spectrum antibiotics. The patient began experiencing multi-system organ failure with liver dysfunction, renal dysfunction, and lactic acidosis. We hypothesized the patient was experiencing refractory vasodilatory shock as a result of an inflammatory cytokine storm. The patient underwent two cycles of plasma exchange with 3.5 liters of FFP each. Within 24 hours, the patient was off all vasopressors with resolution of end organ ischemia and lactic acidosis. All cultures and infectious workup were negative.The patient had an uneventful post operative course and was discharged home.

Conclusions: Vasodilatory shock without an infectious source continues to be a common problem after LVAD insertion. We hypothesize this cytokine storm may be a result of reperfusion injury in a chronically hypoperfused patients and also the inflammatory mediated response to cardiopulmonary bypass. Plasma exchange can reduce TNF alpha, IL-1, IL6, and other inflammatory cytokines, which may contribute to refractory vasodilatory shock. Further studies need to be conducted to elucidate which inflammatory mediators are associated with refractory vasodilatory shock post LVAD insertion.



Laboratory Parameters with PLEX

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An unexpected cause of abrupt dyspnea and peripheral edema in heart transplantation recipient.

MN Mi-Na Kim[1]; JS Jung[1]; SM Park[1]; HS Son[1]; WJ Shim[1]
[1]*Korea university anam hospital, Seoul, Korea Republic of*

61 years old women who had underwent orthotopic heart transplantation(OHT) 32 month ago visited to emergency department due to abrupt New York Heart Association grade IV dyspnea and generalized edema. She had been diagnosed with multiple myeloma(MM, ?-type light chain) with amyloid cardiomyopathy(ACM) 5 years ago and undertaken chemotherapy. At 1 year after chemotherapy, bone marrow biopsy revealed total remission of MM but heart failure became progressively worse. Therefore she underwent OHT and did not have any symptoms and signs which were suspicious for ACM, as well as MM during follow-up. Subsequent routine endomyocardial biopsy(EMB) did not show deposition of amyloid in myocardium.
On admission, she looked puffy and her jugular vein was distended. The breathing sound was diminished in both lower lung field. Bilateral lower extremity pitting edema was observed to groin area. Chest radiography showed newly developed cardiomegaly and bilateral pleural effusion. There was no significant changes on electrocardiogram, compared with previous examinations.
Under suspicion of allograft rejection, echocardiography and EMB were conducted. Echocardiography showed thickened pericardium and increased echogenicity within pericardial space with loculated pericardial effusion(Figure1A). Left ventricular size and function were normal(LVEF = 63%) but septal bouncing motion, respiratory variation of mitral inflow and plethora of inferior vena cava were observed. Cardiac computed tomography revealed thickened pericardium(thickness = 7.8mm) with localized pericardial effusion(Figure1B). There was no evidences of allograft rejection nor amyloid deposit on EMB.
From these findings, constrictive pericarditis was diagnosed. We suspected atypical infection like tuberculosis or recurred amyloidosis as cause of constrictive pericarditis. She had heavy proteinuria (9.8 g/24h) and hypoalbuminemia(2.2g/dL). Recurrence of amyloidosis was strongly suspicious. For confirmation, minimal open pericardial biopsy was performed. Perivascular and interstitial amyloid deposits were detected on Congo-red stain(Figure1C) and polorized light microscopy(Figure1D). Electron microscopic examination showed aggregate of non-branching filaments amyloid fibrils in the interstitial tissue of pericardium(Figure1E). BM biopsy showed a 15% monoclonal plasma cell(?-type) infiltration. She began to recieve chemotherapy with lenalidomide and dexamethasone.
OTH for with cardiac amyloidosis remains controversial because of concerns about recurrent amyloid deposition in allograft heart and insufficiency of donor. Nevertheless OHT has been considered as a therapeutic option for an untreatable ACM. Recurrence of ACM in transplanted heart mostly occurs in myocardium. The amyloid involvement only in pericardium is extremely rare. To the best of our knowledge, herein we present the first case of recurred amyloidosis in pericardium without evidence of myocardial involvement in transplanted heart.

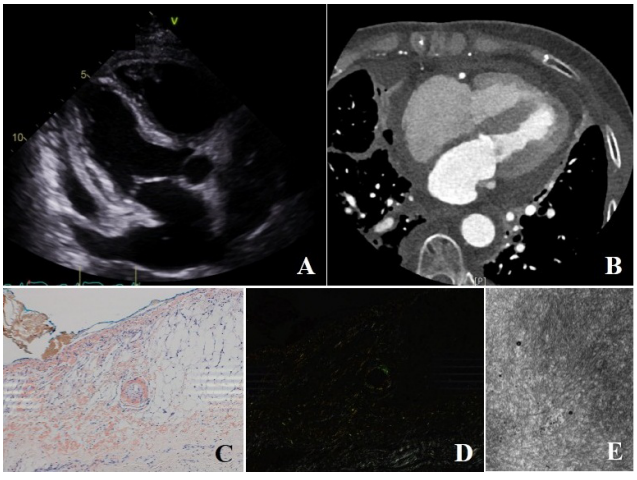

Figure 1

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Sudden death after cardiac transplantation.

I Malek[1]; M Podzimkova[1]; M Hegarova[1]; V Melenovsky[1]
[1]*Institute for Clinical and Experimental Medicine, Cardiology, Prague, Czech Republic*

Introduction: Sudden death after cardiac transplantation is relative frequent complication contributing to 10-58 % of deaths. The most frequent finding on postmorten examination is coronary vasculopathy, but in one third of deceased patients (pts) no coronary pathology has been detected. Ventricular fibrillation is suspected as a mechanism of death, but doccumented cases are rare.
Aim: Presentation of the case of the patient, who was succesfully resuscitated for sudden circulatory standstill due to electromechanical dissociation.
Case report: Male 37 years old with dilated cardiomyopathy developed terminal heart failure and in Aug. 2012 orthotopic cardiac transplantation (CTX) was performed with uncomplicated course in subsequent 16 months. Unfortunately, he interrupted immunosupressive therapy and appeared with severe graft failure due to combined cellular and antibody mediated rejection. After intensive therapy including plasmapheresis, rituximab and bortezomib graft function and clinical status improved, but donor specific antibodies (DSA) class II were present in blood (SAB Luminex method). Consecutive 3 years were uneventful, except of one episode of bradycardic syncope, solved by 2D pacemaker implantation. In 1/2017 the patientt was succesfuly resuscitated for sudden circulatory standstill and cardioverter-defibrillator (ICD) was implanted. Graft function was normal, as well as coronary angiography findings. High amounts of DSA class II were found in blood, with only partial effect of therapy including immunoadsorbtion. Three month later circulatory standstill recurred, the pt was once more resuscitaded with normal findings afterwards. No tachyarythmia or cardiac standstil was documented on ICD record. Electromechanical dissociation due to diffuse coronary spasm was suspected as the primary cause. Nowadays (11/2017) pt is in good clinical condition, medical therapy is directed on coronary artery disease prevention, including m-TOR inhibitor added to immunossuppressive prophylaxis. Unfortunately, DSA are still present, with only modest derease in spite of repeated attempts of elimination.
Conclusion: Circulatory standstill after CTX is not always sequelae of ventricular tachyarrythmia or conduction disturbance. Here we documented electromechanical dissociation, probably due to diffuse spasm of coronary vasculature. Elimination of DSA is mandatory as these antibodies contribute to the development of coronary vasculopathy.

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Ventricular assist device support for failing systemic ventricle in adult patient with congenitally corrected transposition of the great arteries and dextrocardia

S Sandra Jaksic Jurinjak[1]; M Udovicic[1]; B Starcevic[1]; M Stipcevic[1]; V Ivanovic[1]; D Susnjar[2]; H Falak[1]; J Vincelj[1]; M Planinc[2]; R Blazekovic[2]; N Bradic[3]; Z Sutlic[2]
[1]*University Hospital Dubrava, Institute of Cardiovascular Diseases, Department of Cardiology, Zagreb, Croatia*; [2]*University Hospital Dubrava, Department of Cardiac surgery, Zagreb, Croatia*; [3]*University Hospital Dubrava, Department of Cardiac Anesthesiology, Zagreb, Croatia, Zagreb, Croatia*

Patients with congenitally corrected transposition of great arteries (ccTGA) present with heart failure commonly in the fourth or fifth decade of life. Prevalence of ccTGA is < 0.5%, with dextrocardia reported among 20% of these patients. We present a 52-year old female patient with ccTGA and dextrocardia. In 2008, she was first admitted to our institution because of heart failure and diagnosed with ccTGA combined with dextrocardia. She was treated with heart failure medications for approximately ten years which improved her condition. In the January 2017, despite optimal medication, she developed congestive heart failure and required additional rehospitalization with symptoms of congestion and low cardiac output with elevated NT-pro-BNP levels up to 10752 pg/mL. Her cardiac functional status decreased to NYHA (New York Heart Association) class IV. She was treated with inotropic support and careful volume management. Echocardiography confirmed the presence of ccTGA and dextrocardia with situs solitus, with ejection fraction of dilated systemic right ventricle less than 20%. Patient also had severe tricuspid regurgitation and mild mitral regurgitation, mild pulmonic regurgitation with mild subpulmonic obstruction due to accessory fibrous tissue of basal part of interventricular septum. She was at that time evaluated for heart transplantation and placed on the cardiac transplant waiting list. Despite medication her condition deteriorated, so invasive haemodynamics measurements were repeated revealing RVP 71/6/19mmHg, PCWP 29mmHg, CI 1,39 L/min/m2, MPAP 45mmHg, PVR 6,24WU. Pulmonary hypertension may have induced right heart failure in the transplanted heart, so multidisciplinary heart transplant team decided for long term unloading with ventricular assist device (VAD) as a bridge to heart transplant candidacy. In September 2017 intrapericardial VAD (centrifugal continuous flow, fully magnetically-levitated technology) was implanted at midline position, guided by transoesophageal echocardiography for

positioning the inflow cannula in the systemic ventricle, assessment of an outflow cannula in the lateral right side of ascending aorta, in setting of dextrocardia present in our patient. Post procedural hospital course was complicated by mild subpulmonic ventricle failure managed by inotropic support and pump adjustment. Patient was discharged four weeks after implantation of VAD, taking pharmacological treatment of warfarin, acetylsalicylic acid and heart failure medication, currently in NYHA class I-II. Implantation of VAD in systemic ventricle in ccTGA has been described in small groups of patients, and to our knowledge in a single patient with ccTGA combined with dextrocardia. Accurate imaging (transthoracic echocardiography with contrast, transoesophagic echocardiography, cardiac MSCT) and multidisciplinary heart team is pivotal in successful implantation of small size intrapericardial VAD in patient with complex anatomy as ccTGA and dextrocardia.

731

Bridging a knife's edge with a percutaneous left ventricular assist device: a patient with few options to optimise, but many ways to decompensate.

J Jiliu Pan[1]; SM Ng[1]
[1]*St Thomas' Hospital, London, United Kingdom*

Case presentation: A 78 year old man presented with a one day history of chest pain and shortness of breath on a background of hypertension, previous episodes of atrial fibrillation, COPD, bipolar disorder.
The patient was peripherally shut down and a lactic acidosis suggested an element of cardiogenic shock. There was clinical and radiological evidence of pulmonary oedema. Electrocardiograms (ECG) revealed atrial flutter with ventricular rates up to 150 bpm with inferior Q-waves and lateral ST depression. A CT pulmonary angiogram (CTPA) provisionally suggested a pulmonary embolus (PE). Initial Troponin-T was 236 ng/L and peaked 2 days later at 584 ng/L.
Problems and management: It was thought that a PE drove the tachyarrhythmia which then caused the low cardiac output and subsequent coronary ischaemia. However, an effort to rate-control with beta-blocker and verapamil resulted in a bradycardic and hypotensive decompensation requiring atropine and adrenaline to resuscitate. An acute screening echo suggested severe left ventricular (LV) dysfunction, thin akinetic inferior wall and moderate mitral regurgitation. A senior radiological review of the CTPA the next day refuted the diagnosis of PE. Subsequent management involved a period of continuous positive end-expiratory pressure and diuresis. Tachycardia and hypotension was a recurrent problem but was eventually controlled on amiodarone.
Coronary angiography revealed a chronically occluded right coronary artery and severe left main stem stenosis. A multidisciplinary meeting decided that the patient was too high risk for cardiac surgery.
The patient subsequently underwent coronary intervention with the support of a percutaneous left ventricular assist device (PLVAD). Left main stem stenting achieved good angiographic result but following the procedure the patient lost intrinsic cardiac output, relying solely on the PLVAD for cardiac output and to stay awake and asymptomatic. He then improved with fluid resuscitation.
The patient later declined further treatment and discharged himself.
Discussion: This patient's cardiac output did not need much of a push to fall off the edge. Underlying it was severe coronary disease, ventricular dysfunction, tachyarrhythmia and possible PE. The cause-effect relationship between these was unclear and initial treatments were met by further compromise. A PLVAD supported him through another decompensation following coronary intervention.
Lessons learnt and future implications: This case serves as a reminder that cause and effect (especially when unclear) should not always dictate acute management while stabilisation is key. In our efforts to achieve the optimum, we must not forget the dangers of overstepping the mark with an ever-expanding therapeutic repertoire at our fingertips.
Will future technology play greater roles in mitigating our human limitations and shortcomings?

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Bortezomib-related acute cardiogenic shock in multiple myeloma patient with perivascular cardiac and renal amyloidosis. A clinical report.

A Greco[1]; C Ranieri[1]; I Raso[1]; M Wu[1]; T Spezzano[1]; B Matrone[1]; R Camporotondo[1]; R Totaro[1]; G Tavazzi[2]; E Arbustini[3]; GM De Ferrari[1]; L Oltrona Visconti[1]
[1]*Policlinic Foundation San Matteo IRCCS, Cardiology, Pavia, Italy*; [2]*Policlinic Foundation San Matteo IRCCS, General Intensive Care, Pavia, Italy*; [3]*Policlinic Foundation San Matteo IRCCS, Pathology, Pavia, Italy*

Background: Amyloidosis is a rare systemic disease in which insoluble amyloid proteins are deposited in body organs with the extent of cardiac involvement acting as the major determinant of a poor prognosis.
Case Report: A 61-year old man with kappa chain multiple myeloma complicated by perivascular cardiac and renal amyloidosis started treatment with bortezomib and dexamethasone. The day after the second cycle, he developed acute dyspnoea and was found to be in cardiogenic shock with multiple organ failure. B-type natriuretic peptide was 34308 pg/mL (nv < 210) and troponin T 3112 ng/mL (nv < 14). In comparison with recent echocardiographic evaluation (see Table 1) left ventricular ejection fraction (LVEF) dramatically dropped to 10%, with associated advanced right ventricular dysfunction. Urgent venoarterial extracorporeal membrane oxygenation (ECMO) with intra-aortic balloon pump (IABP) were required. Endomyocardial biopsy showed acute and spread myocyte damage, with some ongoing reparative processes. LVEF slowly but progressively improved allowing ECMO and IABP removal after three weeks, and discharge three weeks later. The overall behaviour was indicative of bortezomib toxicity.
Conclusions: Although proteasomes inhibition by bortezomib is known to rarely induce cardiac dysfunction, the occurrence of severe refractory cardiogenic shock has never been described. Perivascular amyloidosis has possibly contributed to the severity of the effect. Immediate advanced circulatory support and prompt diagnosis with endomyocardial biopsy have allowed a favourable outcome.

Table 1: Echocardiographic evaluation

	December 2016	February 2017 (acute onset)	November 2017
LVEF (%)	55	10	60
EDVi (ml/sqm)	63	87	75
MR	trivial	moderate	mild
TAPSE (mm)	25	10	25
PAPs (mmHg)	na	45	na

LVEF: left ventricular ejection fractionEDV: end-diastolic volumeMR: mitral regurgitationPAPs: systolic pulmonary artery pressure

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Continuous Intravenous Inotropes as a Bridge to Myocardial Recovery

O Ofer Havakuk[1]; LP Grazette[2]
[1]*Tel Aviv Sourasky Medical Center, Tel Aviv, Israel*; [2]*University of Southern California, Cardiology, Los Angeles, United States of America*

Background: Chronic inotrope therapy in advanced heart failure (HF) patients is generally considered palliative and contemporary guidelines recommend low dose and early discontinuation of inotropic therapy due to concerns for an increased arrhythmia-related mortality. However, data on the use of parental inotropes are scant and mostly predates the current treatment era in HF. Here we

732 Table 1

Age	Sex	Initial EF/EDD	Etiology	Onset of HF	Inotrope type	Inotrope duration	HF Tx	Indication	Final EF/EDD
66	F	10%/6.6cm	ChemoTx	12/2014	Milrinone	11 m	Bisoprolol 5, spironolactone 25, digoxin 0.125, ivabradine 2.5 bid	Palliation	55%/4.3cm
52	M	22%/6.7cm	CAD	07/2014	Milrinone	14 m	Carvedilol 6.25 bid, ISDN 30 tid, valsartan 80, spironolactone 25	BTT	55%/4.8cm
66	F	15%/6.9cm	Idiopathic vs ethanol	01/2014	Milrinone	12 m	Metoprolol XR 75, spironolactone 25, hydralazine 75 tid, ISDN 60 tid	BTT	60%/3.4cm

Baseline demographics, therapies and outcomes of 3 advanced HF patients on chronic milrinone therapy

present a case-series of 3 advanced HF patients for whom advanced intervention was either undesirable or not feasible, who showed remarkable myocardial recovery after a prolonged parental inotropic support combined with aggressive guideline-recommended, disease modifying therapy.

Methods and **Results:** Retrospective case review of 3 subjects presenting for evaluation of advanced HF who were discharged on IV milrinone for palliation or bridge to candidacy. Baseline demographics, therapies and outcomes are presented in table 1 and show a dramatic improvement in systolic function.

Conclusion: In select patients unsuitable or reluctant to undergo advanced interventions, extended use of inotropic therapy may facilitate application of disease modifying therapy and represent a bridge to recovery. Prospective investigations are needed.

734
The power of the kidney

P Pablo Meras Colunga[1]; V Rial Baston[1]; FJ Irazusta Cordoba[1]; O Gonzalez Fernandez[1]; A Rivas Perez[1]; A Velez Salas[1]; S Rosillo[1]; AM Iniesta Manjavacas[1]; G Veiga Fernandez[2]; V Fradejas Sastre[2]; L Gayo[3]; M Moreno Yanguela[1]; JL Lopez Sendon[1]
[1]University Hospital La Paz, Cardiology, Madrid, Spain; *[2]University Hospital Marques de Valdecilla, Santander, Spain*; *[3]University Hospital La Paz, Nephrology, Madrid, Spain*

Case description: We present the case of a 31-year-old woman with VACTERL syndrome, expressed as a severe urogenital malformation, esophageal atresia and limb abnormalities. She underwent a nephrectomy when she was 2 years old and at the age of 18 she had to start hemodialysis (HD). A few months later she received a renal transplant (Tx), with good function until 2012, when she suffered an allograft rejection and was obliged to re-start HD.
Until this moment, routine transthoracic echocardiograms (TTE) had shown no abnormalities. In 2013, she was admitted to the hospital for an acute pulmonary edema requiring urgent HD. A new TTE revealed moderate left ventricular (LV) dysfunction and secondary moderate mitral regurgitation (MR). Despite the initiation of treatment with ACEI and beta-blockers, ventricular function deteriorated. In next TTE the LV was markedly dilated, ejection fraction (EF) was 19%, with a restrictive pattern and severe MR, and there was right ventricular dysfunction and mild pericardial effusion. A cardiac magnetic resonance did not show intramyocardial edema or late gadolinium enhancement. Treatment was optimized by adding ivabradine. More important, HD sessions were intensified from three days per week to daily sessions, with strict weight and volume overload control. In addition, she was proposed for a heart-kidney Tx.
Progressively, cardiac function began to recover and one year after starting daily HD, TTE was completely normalized. LV telediastolic diameter was 39 mm with EF 63%, TAPSE 20 mm, and disappearance of MR and pericardial effusion. She was clinically better with NYHA functional class I/IV. The patient underwent a second renal Tx in 2016 and she has been stable and asymptomatic since then.
Discussion: Heart and kidney have close and bidirectional interactions, which has led to the description of cardiorenal syndrome (CRS). Traditionally, this term was used to describe a decline in renal function due to heart failure progression or to the use of therapies to relieve congestive symptoms. The mechanisms by which renal failure may lead to cardiac damage are multiple but have been worse described. Volume overload and a pro-inflammatory status have been suggested to play a role. This case represents an extreme example of CRS. The patient had a small body size (152 cm, 43 kg), so small changes in weight (for example 4 kg between HD sessions) were really important for her (10% relative gain). Volume overload with increased ventricular filling pressures could explain most of myocardial wall stress and progressive deterioration. Absence of other findings suggesting different etiologies and complete recovery with daily sessions support this explanation. Curiously, HF drugs seem to have had a minor effect in the evolution.
Conclusions: This case illustrates a pure type 4 CRS with extremely severe cardiac damage that was solved with complete recovery by means of optimal dialysis management in addition to medical treatment.

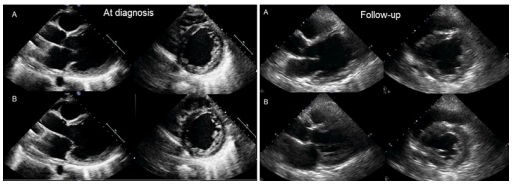

Image 1. A: end-diastole. B: end-systole

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Cardiogenic shock in an adult patient with severe haemolytic uraemic syndrome supported with veno-arterial ECMO as a bridge to recovery

M Kelham[1]; L Gleeson[1]; I Alcalde[1]; R Spiritoso[1]; J Cordingley[1]; S Woldman[2]; J Down[3]; M Scully[4]; A Proudfoot[1]
[1]Barts Health NHS Trust, Department of Perioperative Medicine, Barts Heart Centre, London, United Kingdom; *[2]Barts Health NHS Trust, Cardiology, Barts Heart Centre, London, United Kingdom*; *[3]University College Hospital, Critical Care, London, United Kingdom*; *[4]University College Hospital, Haematology, London, United Kingdom*

A 19 year old female with no past medical history presented with bloody diarrhoea. Investigations revealed acute kidney injury, thrombocytopenia and microangiopathic haemolysis. Stool sample confirmed E. coli 055 and a diagnosis of haemolytic uraemic syndrome (HUS). CT abdomen demonstrated severe pancolitis and normal sized kidneys with multiple renal infarcts. She was commenced on antibiotics, haemofiltration and daily plasma exchange. Transthoracic echocardiogram (TTE) performed on day 10, in response to a serum troponin T of >500ng/L, revealed normal biventricular function and a small pericardial effusion with no haemodynamic compromise.
On day 11 she rapidly deteriorated with tachycardia, drowsiness and a serum lactate of >8mmol/L. Bedside TTE supported a diagnosis of tamponade. Drainage of 180ml of straw-coloured pericardial fluid failed to improve her haemodynamic status. Repeat TTE (figure 1) demonstrated severe biventricular impairment with an EF of < 15%. Pulmonary artery catheter data demonstrated a cardiac index of 1.9 L/min/m2 and pulmonary capillary wedge pressure of 20mmHg. Despite moderate doses of adrenaline and milrinone her lactate remained elevated at >5mmol/L with clinical evidence of hypoperfusion. CT brain showed symmetrical changes in the basal ganglia likely secondary to microvascular thrombosis.
In view of her refractory cardiogenic shock, a multi-disciplinary conference call (SHOCK call) with heart failure cardiology, critical care and mechanical support specialists was undertaken through an app based mobile teleconference. Despite a high predicted mortality, the prognostic uncertainty merited a trial of veno-arterial extracorporeal membrane oxygenation (VA-ECMO). Plasma exchange was continued and treatment with Eculizumab, a complement inhibitor normally reserved for atypical HUS, was initiated on day 2 of ECMO in view of the evidence of significant complement over activation with likely microangiopathic injury in the coronary microvasculature, myopericarditis, and renal and central nervous system infarction. She was stabilised with an ECMO flow of 3.4L/min with pulsatility throughout. After 72 hours her physiology and cardiac imaging (TTE) supported cardiac recovery and she was decannulated from ECMO after 96 hours. She was discharged home after 13 weeks with an ejection fraction of 60%, NYHA Class I symptoms, normalisation of her renal function and resolution of the basal ganglia changes on MRI. She suffered bilateral visual loss, which is expected to persist.
We present the first adult case, to our knowledge, of HUS induced cardiogenic shock supported with VA-ECMO as a bridge to cardiac recovery. We highlight the role of the multidisciplinary team as well as the SHOCK call system to optimise decision-making and outcomes in cardiogenic shock. We also raise the potential role of Eculizumab for infection related HUS if there is evidence of complement over activation.

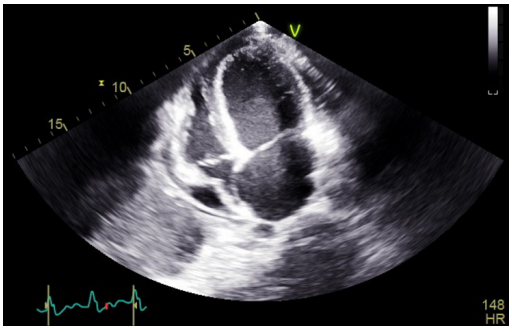

Fig1: Dilated LV & small effusion

Nursing Investigator Award

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Low socioeconomic status is associated with higher risk of readmission among patients with heart failure with reduced ejection fraction: a population-based cohort study

I Inge Schjoedt[1]; SP Johnsen[2]; A Stromberg[3]; NK Kristensen[4]; BB Loegstrup[1]
[1]Aarhus University Hospital, Department of Cardiology, Aarhus, Denmark; *[2]Aalborg University, Department of Clinical Medicine, Aalborg, Denmark*; *[3]Linkoping University, Department of Medical and Health Sciences, Linkoping, Sweden*; *[4]Aarhus University Hospital, Department of Clinical Epidemiology, Aarhus, Denmark*

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Introduction: Low socioeconomic status is associated with higher incidence of heart failure (HF) and mortality following HF diagnosis. However, the role of low socioeconomic status on risk of unplanned hospital readmission in patients with HF remains unclear.
Purpose: To investigate the association between socioeconomic status and unplanned hospital readmission following HF diagnosis.
Methods: A population-based cohort study based on data from Danish nationwide public registries. We identified patients with incident HF with reduced ejection fraction (= 40%, HFrEF) between January 2008 and October 2015 in a national heart failure registry. Socioeconomic status was assessed based on three variables; cohabiting status, highest education attained, and mean family income. Outcomes included all-cause hospital readmission, HF readmission and non-HF readmission within days 1-30, 31-90 and 91-365 following HF diagnosis. We used Cox regression to estimate hazard ratios (HR) of readmission, controlling for potential confounders.
Results: We identified 17,214 patients with HFrEF. Mean age was 70.0 ± 12.8 years, 68.6% men, 25.4 % left ventricular ejection fraction < 25% and 27.2% NYHA (New York Heart Association) functional class III-IV. A total of 8,341 patients (48%) were readmitted at least once within the first year after the HF diagnosis. Patients with a low socioeconomic status (living alone, low educational level and a low family income) had a higher risk of all-cause readmission (adjusted HR 1.42; CI 95% 1.14-1.78) and a higher risk of non-HF readmission (adjusted HR 1.35; CI 95% 1.06-1.71) within days 31-90 compared to patients with a high socioeconomic status (cohabiting, high educational level and a high family income). However, low socioeconomic status was not associated with any type of readmission within days 1-30 and days 91-365 in the adjusted analysis. Regarding the individual socioeconomic variables, neither cohabiting status nor educational level were associated with readmission within days 1-30, 31-90 and 91-365 in the adjusted analysis. However, low family income was associated with higher all-cause readmission (adjusted HR 1.20; CI 95% 1.04-1.38) and non-HF readmission risk (adjusted HR 1.31; CI 95% 1.13-1.52) within days 31-90. In addition, low family income was associated with higher risk of all-cause readmission (adjusted HR 1.27; CI 1.14-1.41, HF readmission (adjusted HR 1.26; CI 1.02-1.54) and non-HF readmission (adjusted HR 1.24; CI 1.11-1.38) within days 91-365. The same pattern was seen for medium compared to highest family income.
Conclusion: Low socioeconomic status was associated with higher risk of all-cause readmission and non-HF readmission within days 31-90 following HF diagnosis in patients with HFrEF, but not with very early or late readmissions.

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Person-centred telephone-support is effective in patients with chronic obstructive pulmonary disease and/or chronic heart failure - six-month follow-up of a randomized controlled trial

A Fors[1]; E Blanck[1]; L Ali[1]; K Swedberg[2]; I Ekman[1]
[1]University of Gothenburg, Sahlgrenska Academy, Centre for Person-Centred Care (GPCC), Institute of Health and Care Sciences, Gothenburg, Sweden; *[2]University of Gothenburg, Sahlgrenska Academy, Centre for Person-Centred Care (GPCC), Department of Molecular and Clinical Medicine, Gothenburg, Sweden*

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Background: Long term health conditions, including chronic heart failure (CHF) and chronic obstructive pulmonary disease (COPD), are one of the major challenges facing healthcare systems worldwide; and telehealth has been suggested as a safe option to promote self-management. The effectiveness of person-centred care as a tool to improve health care has been demonstrated in several conditions and contexts but there are few existing telehealth interventions that fully address person-centred care.
Purpose: To evaluate the effects of person-centred support at distance via telephone for patients with CHF and/or COPD.
Method: 221 patients = 50 years with CHF and/or COPD were randomized to usual care or a person-centred telephone-support intervention in addition to usual care and followed during six months. In the intervention group patients where phone called by a registered nurse and a person-centred health plan reflecting both perspectives was co-created, which was further discussed and evaluated during additional follow-ups by telephone. A composite score of changes that included changes in general self-efficacy = 5 units, re-hospitalization and death was used as primary outcome measure.
Results: At the six-month follow-up no difference in the composite score was found between the two study groups (57.6%, n = 68 vs. 46.6%, n = 48; OR = 1.6, 95 % CI: 0.9 - 2.7; P = 0.102). Significantly more patients in the control group decreased = 5 units in general self-efficacy (22.9%, n = 27 vs. 9.7%, n = 10; OR = 2.8, 95% CI: 1.3 - 6.0; P = 0.011). There were no differences between groups on re-hospitalization or death. In the per-protocol analysis of the composite score more patients in the control group deteriorated compared with the intervention group (57.6%, n = 68 vs. 42.9%, n = 36; OR = 1.8, 95% CI 1.0 - 3.2; P = 0.039).
Conclusion: A person-centred support at distance via telephone mitigates worsened self-efficacy without increasing the risk of clinical events in patients with CHF and/or COPD. This highlights the possibility to establish a patient-health care professional partnership, which is not dependent on face-to-face consultations, not the least in vulnerable patient groups.

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Objectively measured frailty score and mortality in elderly patients hospitalized for heart failure

K Kamiya[1]; S Tanaka[2]; N Hamazaki[2]; R Matsuzawa[3]; K Nozaki[3]; E Maekawa[4]; A Matsunaga[1]; T Masuda[1]; J Ako[4]
[1]Department of Rehabilitation, School of Allied Health Sciences, Sagamihara, Japan; *[2]Department of Cardiovascular Medicine, Kitasato University Graduate School of Medical Sciences, Sagamihara, Japan*; *[3]Kitasato University Hospital, Sagamihara, Japan*; *[4]Department of Cardiovascular Medicine, Kitasato University School of Medicine, Sagamihara, Japan*

Background: Frailty in geriatric patients is defined as a syndrome of decreased physiological reserve and vulnerability to stressors, broadly classified as acute or chronic illnesses. Due to a lack of a simple and objective tool for its assessment, the impact of frailty on the prognosis of elderly patients hospitalized for heart failure (HF) remains unclear.
Objectives: This study was performed to examine the prognostic utility of frailty score in elderly patients hospitalized for HF.
Methods: A retrospective cohort study was performed in 603 consecutive HF patients with a mean age of 75 ± 6 years (378 men). Frailty was measured by a composite of four markers combined into a frailty score (possible range 0 - 12): gait speed, handgrip strength, serum albumin, and activities of daily living status (Green et al.JACC Cardiovasc Interv 2012). The Meta-Analysis Global Group in Chronic Heart Failure (MAGGIC) risk score was calculated for each participant to assess prognosis on the basis of clinical parameters. The endpoint was all cause mortality. Survival was evaluated using the Kaplan–Meier method and compared by the log-rank test. The relations between each component of the frailty score and mortality were evaluated by Cox regression analyses. The prognostic ability of frailty score was also examined by Cox regression analysis constructing two predictive models as follows: Model 1: MAGGIC risk score, Model 2: Model 1 + comorbidity score + BNP.
We calculated the incremental information added by frailty score over MAGGIC risk score using the continuous net reclassification improvement and integrated discrimination improvement, developed as more sensitive statistical methods to quantify model improvement with the addition of a new variable to an existing clinical model.

Results: Over a mean follow-up period of 1.7 ± 0.5 years, 89 patients died. Following adjustment for several preexisting factors associated with prognosis, i.e., MAGGIC risk score and comorbidities, the frailty score (hazard ratio [HR]: 1.11; P = 0.014) and frailty (HR: 1.75; P = 0.036) were independently associated with all-cause mortality. Including frailty score in the MAGGIC risk score significantly increased continuous net reclassification improvement (0.396; P < 0.001) and integrated discrimination improvement (0.017; P = 0.030) for all-cause mortality.
Conclusions: Frailty score provides accurate prognostic information in elderly patients hospitalized for HF.

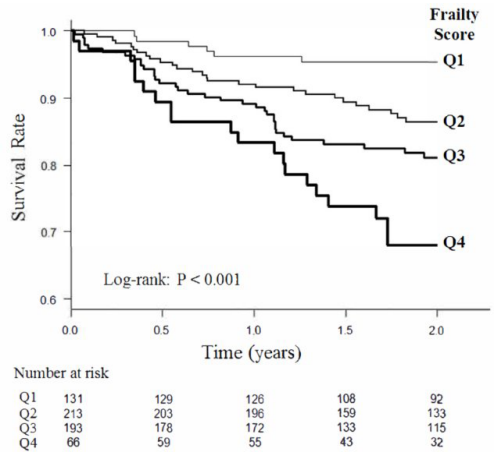

Fig. Frailty Score and Mortality

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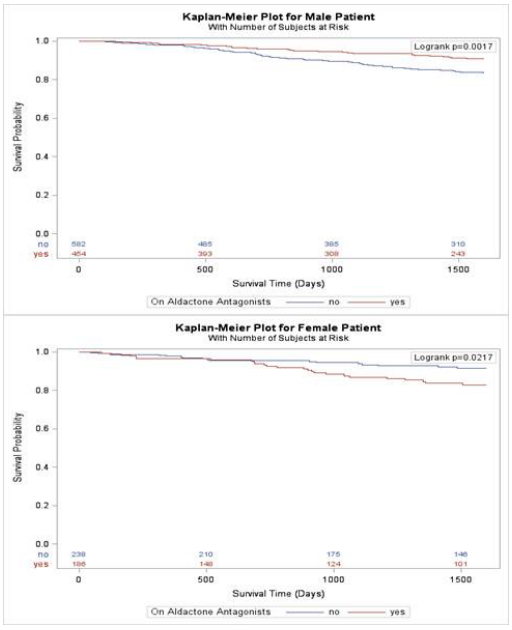
gender differences in the response to spironolactone in patients with chronic heart failure : a propensity matched analysis

M May Khateeb[1]; R Odeh[2]; HA Ardah[2]; AM Ahmed[2]; AA Alanazi[2]; MH Al-Mallah[2]
[1]King Abdulaziz Medical City, Riyadh, Saudi Arabia; [2]King Abdulaziz Medical City, King Abdulaziz Cardiac Center, Riyadh, Saudi Arabia

Background: The current ACC guidelines recommend using spironolactone in patients with advanced heart failure reduced left ventricular systolic function (HFrEF). The aim of this analysis is to determine whether gender differences exist in the response to spironolactone use in a contemporary HFrEF cohort.



Methods: We included 2,805 (Mean age of 57.8, 28.34 % females) consecutive HFrEF patients treated in dedicated heart failure clinic. Patients were divided into 2 groups depending on whether they received spironolactone. Propensity matching was used to match the groups in a 1:1-2 fashion. The primary outcome was all-cause mortality (ACM)
Results: Of the initial 2,805 patients, 692 spironolactone users were matched with 917 non users. The matched cohort did not have differences among demographics and clinical variables. Overall, the prevalence of the use of guideline suggested therapies was 96%. After a median follow-up duration of 4.4 years, 231 patients died. Overall, spironolactone use was associated with decreased ACM (14.2% vs. 19.7%; P = 0.006). In multivariate adjusted analysis, there was a significant interaction between gender, spironolactone use and ACM. A significant reduction in ACM was observed among male patients (HR 0.700; 95% CI 0.493t o 0.993), while there was a trend towards increased mortality among females (HR 1.311; 95% CI 0.804to 2.139).Result
Conclusion: In this analysis of well treated HFrEF patients, spironolactone was associated with improved survival, primarily in male patients.

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App based remote monitoring of cardiac implantable device:patients' expectation

A Zanni[1]; C Sticozzi[1]; M Pessina[1]; A Villani[1]; MF Piepoli[1]; GQ Villani[1]
[1]Guglielmo da Saliceto Hospital, Cardiology, Piacenza, Italy

Background: Remote monitoring (RM) of cardiac implantable electronic devices (CIEDs) is an established technology integrated into clinical practice, which allows data exchange, doctor–doctor and doctor–patient communication, and remote vital sign monitoring. Recent developments in smartphone technology and the introduction of smartphone-compatible devices that can measure various health parameters and able to automatic transferring of generated data, have increased the possibilities for remote monitoring and the interest in Mobile health (mHealth).
Objective: The patients' interests in the possibility of receiving directly RM data from their CIED, clinical and health advices on their smartphones were investigated.

Which data related to device mode of operation are you interested to receive on your smartphone?	
1	Device function alert
2	Heart rate changes
3	Device battery life
4	Lead integrity
5	Stimulation percentage
Which clinical data are you interested to know?	
6	ECG tracing
7	Physical activity level
8	Heart failure severity
9	R-R interval variability
10	Atrial fibrillation occurrence
11	Severe arrhythmias occurrence
12	Silent device intervention
Which healthy lifestyle promotion alerts are you interested to receive?	
13	Have you performed at least 30' physical activity daily?
14	Did you check your weight?
15	Did you check your daily liquid intake?
16	Did you take your pills?
17	Have you been careful in your diet?
18	Have you reduced your salt intake?
19	Stop smoking alert
In addition are you interested in	
20	Regular remind for your pill intake
21	The possibility to have direct contact with your GP and/or medical center

Figure 1

Methods: A questionnaire entitled "Expectations for future possibility of self-management of device data" (Figure 1) (Likert scale scored) was submitted to 300 consecutive patients attending the outpatient clinic. The questionnaire was focused to collect patients' expectations in receiving direct information regarding their CIED status (item 1, five questions), their own clinical status (item 2, seven questions) and advices on healthy lifestyle promotion (item 3, nine questions). Individual patient characteristics associated with higher interest were also investigated.
Results: Complete questionnaires were available from 268 patients (221 males, 69 ± 14years). The Cronbach test reported an alpha value of 0.98 for the item 1, 0.94 for the item 2 and 0.97 for the item 3. Patients declared to be mainly interested in the device interventions (62%) and in the severe arrhythmias occurrence (61%), followed by data on heart failure severity (54%) and their performed physical activity (48%). Patients showed very little interest on ECG tracing (37%). The lowest interest was expressed towards healthy lifestyle promotion advices (< 40%). An high educational degree and the presence of caregiver positively affected the interest in receiving RM information (p < 0.001).

Conclusions: The patients' interests were mainly directed in receiving information related to technical data of the CIED and not to the overall management of the disease, underlying the need to increase patients' awareness on the importance of self-control health status.

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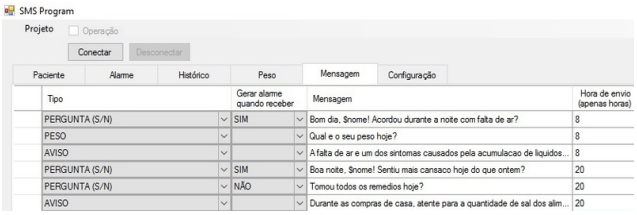
Healthcare professionals and engineers can work together? development and testing of a text messaging monitoring software for patients with acute decompensated heart failure

L Lopez Pedraza[1]; JR Wagner De Moraes[2]; E R Eneida Rejane Rabelo-Silva[1]
[1]*Federal University of Rio Grande do Sul, Heart Failure Clinic and Transplant Group at Hospital de Clinicas de Program at the Nursing School, , Porto Alegre, Brazil*;
[2]*Federal University of Rio Grande do Sul, Porto Alegre, Brazil*

Introduction: Strategies and new approaches are necessary in the current scenario and worldwide panorama of HF epidemiology, in order to prevent both hospital readmissions and morbidities caused by this clinical syndrome. In this perspective, there is an opportunity to boost the increasing accessibility of mobile technologies to enable patients to monitor their own health outside the hospital especially in developing countries. Short Message Service (SMS), which has high utilization rates among less favored socioeconomic groups, is a promising platform for the management of chronic diseases in low-income populations.
Purpose: To develop and test of a text messaging monitoring software for patients with acute decompensated heart failure (ADHF).
Methods: The elaboration of the prototype was developed in three stages: definition of all the expected functionalities, codification of the program modules and tests. The program sends two types of messages: questions that should be answered by the patients, and educational reinforcements that don't require answers. In addition, the system generates alarms in case of no response or according to a flow chart to detect congestion in the patient previously created by the team. For the test we included 10 patients admitted to the hospital for ADHF. After discharge, the system asked about weight, shortness of breath, fatigue and medications so as to detect congestion. Messages that required responses were sent for one week (two in the morning and two in the evening). Educational SMS was sent once every two days.
Results: All the functionalities were defined in several meetings with the researchers of the study, software modules were encoded and several tests were performed. Ten patients participated in the prototype test. The mean age was 67 ± 13 years old. The patients were predominantly males and lived with relatives. The ejection fraction was $35 \pm 7\%$. Of the 264 SMS sent, 247 were answered. The alarm was triggered seven times: three patients woke up with shortness of breath for two consecutive nights and four patients felt more fatigued for two consecutive days. All patients took the prescribed medications during follow-up. The study nurse guided the patients who generated alarm in the system.
Conclusions: SMS software was successfully developed and during the test was possible to visualize some limitations that were corrected. We observed a high response rate and preliminary evidence of improvements in self-management of HF.



Software interface

Young Investigator Awards - Basic Science and Translational Science

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Generation and validation of a mouse model of the phospholamban p.Arg14del mutation

T R Eijgenraam[1]; HHW Sillje[1]; RA De Boer[1]
[1]*University Medical Center Groningen, Experimental Cardiology, Groningen, Netherlands*

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Background: The phospholamban p.Arg14del (PLN-R14del) mutation is the most frequently identified mutation in cardiomyopathy patients in the Netherlands. Human carriers of the PLN-R14del mutation have a high risk of developing heart failure with a phenotype of arrhythmogenic cardiomyopathy (ACM) or dilated cardiomyopathy (DCM). Cardiomyopathy patients with the PLN-R14del mutation show more appropriate implantable cardioverter-defibrillator (ICD) discharges and greater family history of sudden cardiac death (SCD). So far, no established therapeutic treatment exists for these patients.
Purpose: In order to investigate the underlying pathology of this disease, we aimed to develop a mouse model that exactly resembles the situation of human PLN-R14del carriers.
Methods: The PLN-R14del mutation was introduced into the genome of C57BL/6N mice and backcrossed into C57BL/6J mice. Presence of the mutation was confirmed by genomic sequencing and RNA expression of the mutant form was confirmed by cDNA sequencing. We performed cardiac phenotyping on these mice including cardiac MRI, ECG and histological analysis (n = 3-8).
Results: Homozygous PLN-R14del mice showed increased left ventricular (LV) volume in diastole (42.91 ± 0.20µl vs. 58.31 ± 4.68µl, $p < 0.05$) and systole (16.40 ± 1.23µl vs. 39.93 ± 4.83µl, $p < 0.001$) with a decreased LVEF ($61.85 \pm 1.92\%$ vs. $31.96 \pm 2.89\%$, $p < 0.001$) and limited life span as compared to control mice. We also demonstrated other findings compatible with DCM, including decreased wall thickness in diastole (0.70 ± 0.01mm vs. 0.64 ± 0.01mm, $p < 0.05$) and systole (1.07 ± 0.07mm vs. 0.86 ± 0.04mm, $p < 0.05$). Furthermore, decreased QRS-complex voltage (1.18 ± 0.13mV vs. 0.55 ± 0.06 mV, $p < 0.01$) was observed. Finally, histological analysis demonstrated a strong increase in cardiac fibrosis ($1.07 \pm 0.11\%$ vs. $14.31 \pm 2.42\%$, $p < 0.05$).
Conclusions: We have generated a representative mouse model of PLN-R14del-induced cardiomyopathy that develops a similar cardiac phenotype as seen in human mutation carriers and thus properly mimics the human situation. This model will be useful in better understanding of cardiomyopathies that are primarily caused by PLN mutations or with secondary PLN abnormalities. At a later stage, we will study potential therapeutic treatment strategies.

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HDAC inhibitors repress cardiac hypertrophy through hyperacetylation of 14-3-3 chaperones and nuclear accumulation of class II HDACs

D Daniel Finke[1]; LH Lehmann[1]; L Frischbier[1]; S Wieber[1]; HA Katus[1]; J Backs[1]
[1]*University Hospital of Heidelberg, Heidelberg, Germany*

Histone deacetylase inhibitors (HDACi) are new anti cancer drugs. It has also been suggested that HDACi inhibit cardiac hypertrophy, but the critical downstream targets remained unclear.
Here we show that superoylanilide hydroxamic acid (SAHA) treatment reduced the activity of the transcription factor myosin enhancer factor 2 (MEF2) in neonatal rat ventricular cardiomyocytes (NRVMs). Additionally, the prohypertrophic effects of endothelin (ET-1), phenylephrine (PE) or serum (FCS) on NRVMs were blunted. (FCS: 177% vs. 115%**; PE: 163% vs. 106%**, ET-1: 164% vs. 115%**; ** = $p < 0.05$). Gene silencing of HDAC1 to HDAC11 by siRNA unmasked that HDAC4 and HDAC5 act as the main repressors of MEF2. Likewise, HDAC4/HDAC5 double knockout mice displayed reduced fractional shortening and cardiac hypertrophy at an age of 18 weeks, whereas single HDAC deletion did not lead to an obvious cardiac phenotype, pointing to redundant roles of HDAC4 and HDAC5 in the regulation of cardiac function and hypertrophy. Treatment with SAHA led to hyperacetylation of the chaperone 14-3-3, which resulted in a lower binding affinity of 14-3-3 to HDAC4 and HDAC5. Accordingly, mimicking 14-3-3 acetylation by replacing specific lysines with glutamines at the predicted acetylation sites led to reduced HDAC-14-3-3 binding. SAHA also inhibited nuclear export of class IIa HDACs upon ET-1, FCS or PE treatment. The critical histone deacetylases that act enzymatically on 14-3-3 were further identified by the siRNA approach, leading to the identification of distinct HDACs that do not inhibit but promote MEF2 activity.
We conclude that HDACis might act as antihypertrophic agents by promoting nuclear accumulation of the class IIa HDACs HDAC4 and HDAC5 with subsequent MEF2 inhibition. This effect might be explained by a loss of binding of HDAC4 and HDAC5 to the hyperacetylated chaperone 14-3-3.

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Changes in titin phosphorylation and PKG activity underlie diastolic dysfunction at the cross-bridge level in the early stages of type 2 diabetes

MT Waddingham[1]; N Hamdani[2]; AJ Edgley[3]; H Tsuchimochi[4]; T Sonobe[4]; DJ Kelly[3]; N Yagi[5]; WJ Paulus[1]; M Shirai[4]; JT Pearson[4]
[1]*VU University Medical Center, Amsterdam, Netherlands*; [2]*Ruhr University Bochum (RUB), Bochum, Germany*; [3]*University of Melbourne, Melbourne, Australia*; [4]*National Cerebral and Cardiovascular Center, Osaka, Japan*; [5]*Japan Synchrotron Radiation Research Institute , Harima, Japan*

Background: Patients with insulin resistance (IR) and type-2 diabetes mellitus (T2DM) are at a significantly increased risk of developing heart failure with preserved ejection fraction (HFpEF). The pathological changes to the myocardium that drive the evolution of diabetic cardiomyopathy (DCM) and eventually HFpEF, are still largely unknown. Using synchrotron radiation as a source for small angle x-ray scattering (SAXS) in the in situ beating heart and simultaneous left ventricular (LV) pressure-volumetry, we have shown a clear correlation between diastolic myosin head displacement and declining LV function in a rat model of early type-1 diabetes (T1DM). These data suggest that the actin-myosin cross-bridges and the myofilament/sarcomeric regulatory proteins play a role in the development of DCM in early T1DM.
Purpose: To examine if pathological changes at the level of the cross-bridge and the myofilament/sarcomeric regulatory proteins contribute to myocardial dysfunction in the early stages of T2DM.
Methods: Male Goto-Kakizaki (GK) rats, a non-obese model of IR and T2DM (10-12 weeks old, n = 7) and age-matched Wistar control rats (n = 9) were surgically anaesthetised, thoracotomised and cardiac catheterisation was performed. Myocardial SAXS patterns showing myosin mass transfer within in situ cardiomyocytes were then digitally recorded in different layers of the LV free-wall. Western blotting and SDS-PAGE were used to determine total and phosphoprotein levels of sarcomeric proteins and protein kinase activity in the myocardium.
Results: In comparison to the Wistar rats, GK rats exhibited mild hyperglycaemia ($P < 0.05$) and greater cardiomyocyte cross-sectional area ($P < 0.01$). Early diastolic dysfunction was demonstrated in GK rats as evidenced by a significantly prolonged Tau relaxation constant (12 ± 1 vs. 9 ± 1msec, $P < 0.05$) and a slight elevation in LV end diastolic pressure (11.9 ± 2.2 vs. 8.3 ± 1.2 mm Hg, NS). Myosin head displacement from actin in the subendocardium was increased ($P < 0.05$) in GK rats compared to Wistar rats. No differences in the relative phosphorylation of the small myofilament proteins cMyBP-C, cTnI or MLC-2 were found between the two groups, however titin phosphorylation was significantly lower in GK rats ($P < 0.05$) when compared to Wistar. Importantly, site-specific titin phosphorylation was significantly lower at the PKG site S4080, which was associated with reduced myocardial PKG activity in GK rats (both $P < 0.05$ vs. Wistar rats). These changes occurred largely independent of indices of oxidative stress.
Conclusion: Early diastolic dysfunction may be attributed to myosin head displacement from actin in sarcomeres of the subendocardium in young IR GK rats. Given that the phosphorylation state of titin is an important regulator of myocardial relaxation and cross-bridge kinetics, a reduction in myocardial PKG activity may be an underlying cause of early DCM and its progression to HFpEF.

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Myocyte BDNF generation prevents chronic post-ischemic decompensation via cardiac reinnervation: the role of beta-AR and GRK2 signals.

A Cannavo[1]; G Rengo[2]; ML D'amico[2]; A Elia[2]; J Agrimi[3]; G Gambino[2]; D Liccardo[2]; N Ferrara[2]; WJ Koch[1]; N Paolocci[4]
[1]Temple University School of Medicine, Center for Translational Medicine, Philadelphia, United States of America; *[2]Federico II University of Naples, Translational Medical Sciences, Naples, Italy*; *[3]Sant'Anna School of Advanced Studies, Pisa, Italy*; *[4]Johns Hopkins University of Baltimore, Baltimore, United States of America*

Introduction: In the heart, Brain-derived neurotrophic factor (BDNF) sustains contraction and relaxation and confers protection against ischemia. However, the mechanisms of such protective actions remain elusive. Moreover, neuronal but not myocardial BDNF has been deemed important in preventing post-myocardial infarction (MI) heart failure (HF). Yet deleting myocardial bdnf enlarges the heart at baseline, suggesting a role for autologous BDNF. In the brain, adrenergic signaling promotes BDNF production in the target cell but whether, and under which conditions, szligßAR stimulation accounts for BDNF genesis in the heart is currently unknown.
Purpose: In post-ischemic HF mice, we tested the effect of ßAR dysfunction induced by the up-regulation of G protein-coupled receptor (GPCR) kinase 2 (GRK2) on myocyte-borne BDNF. We also determined if limiting GRK2 activity (thus enhancing myocardial BDNF signal) promotes cardiac re-innervation that is a major protective mechanism.
Methods: Isolated neonatal rat ventricular myocytes (NRVMs) were used to directly measure myocardial BDNF production while modifying myocyte GRK2 levels. Wild-type (WT, male C57BL/6J) and cardiac GRK2 over-expressing (BK12) mice were employed to correlate BDNF levels with LV function and extent of cardiac innervation after MI in vivo.
Results: Stimulating NRVMs with the ß1/2AR agonist, isoproterenol (ISO), augmented myocyte BDNF content. This effect was prevented in NRVMs infected with an Adenovirus (Ad) encoding for GRK2 to induce chronic ßAR desensitization. In vivo, we observed that WT mice exhibited a marked rise in cardiac BDNF levels immediately after MI (up to 24 hrs) when GRK2 expression was still unchanged. Whereas, with ensuing HF (i.e., 4 weeks after MI) and in presence of significantly augmented cardiac GRK2 content, cardiac BDNF protein abundance declined below values found under control (non-ischemic) conditions. Of relevance, the latter change was accompanied by a marked impairment of cardiac sympathetic innervation measured via tyrosine hydroxylase (TH) staining. To establish a direct in vivo link between GRK2/BDNF levels with the extent of post-MI cardiac innervation, we subjected GRK2 (BK12) cardiac over-expressing and non-transgenic control (NLC) mice to MI. We found that when HF is overt (i.e, 4 weeks after MI), BK12 mice had more severe LV dysfunction and remodeling than infarcted NLC mice, and exhibited markedly reduced cardiac BNDF content. Consistently, the amount of cardiac TH positive fibers was substantially reduced in infarcted BK12 mice as compared to the NLC counterpart.
Conclusion: ßAR dysfunction due to GRK2 up-regulation contributes to chronic post-MI HF, at least in part, by reducing myocardial BDNF generation. Preserving or enhancing this autologous production could represent a new avenue to arrest HF progression. Our data suggests that the communication between the heart and the autonomic nervous system is bidirectional.

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Desmosomal integrity is challenged by exercise-induced strain in iPSC-derived cardiomyocytes with a novel desmoplakin mutation

M Vermeer[1]; MC Bolling[2]; YM Hoedemaekers[3]; JDH Jongbloed[3]; MP Van Den Berg[1]; RA De Boer[1]; P Van Der Meer[1]
[1]University Medical Center Groningen, Department of Cardiology, Groningen, Netherlands; *[2]University Medical Center Groningen, Department of Dermatology, Groningen, Netherlands*; *[3]University Medical Center Groningen, Department of Genetics, Groningen, Netherlands*

Funding Acknowledgements: HFSP-Young Investigator's grant

Background: Desmosomes are transmembrane cell-cell connecting organelles providing resilience against tissue strain, mostly in the heart and skin. Patients with desmosomal mutations are prone to develop arrhythmogenic cardiomyopathy and skin fragility. Exercise is believed to accelerate disease progression, however this is mostly based on epidemiological data. It is unknown whether strain (as a proxy for exercise) accelerates the loss of desmosomal integrity.
Purpose: Investigate the direct effect of strain on the integrity of desmosomes from cells compromised by a pathogenic desmosomal mutation.
Methods: Four patients from one family, presenting with mild and severe forms of cardiomyopathy, and a control were included in the present study. We identified the genetic cause and evaluated desmosomal integrity on ex vivo explanted heart and skin material. Induced pluripotent stem cells (iPSC) were generated, and differentiated into cardiomyocytes (CMs), these were investigated under static and low intensity strain conditions (15% cyclic strain induced at 60 strains/minute).
Results: Two compound heterozygous patients, carrying a splice mutation (c.273+5G>A) and a novel truncating mutation (c.6687delA; p.(Arg2229Serfs*32) in desmoplakin (DSP), had end-stage HF due to fat deposition in the right and a non-compacted left ventricle (LV). In addition, palmoplantar keratoderma (PPK) and woolly hair were observed. In one of them, the explanted heart showed reduced and aberrant desmosomes in the RV, but not in the LV. Heterozygous patients, only carrying the truncating mutation, had LV non-compaction and PPK. Skin biopsy staining of compound heterozygous and heterozygous patients showed no desmosomal aberrations under non-stressed conditions.
In vitro iPSC-CMs from compound heterozygous and heterozygous carriers showed a two-fold reduction in DSP mRNA compared to control($P < 0.005$). The truncating product undergoes nonsense mediated RNA decay (NMD), because NMD inhibition resulted in a truncated protein product not otherwise observed(Fig.1B). Furthermore, static CMs from compound heterozygous carriers had significantly lower DSP levels compared to heterozygous carriers and control($P < 0.05$)(Fig.1A). Low intensity strain did not reduce already low DSP levels in CMs derived from compound heterozygous carriers, but did significantly reduce DSP levels in heterozygous carriers($P < 0.05$), something not observed in control CMs (Fig.1C).
Conclusion: We show that in vitro iPSC culture provides the platform to investigate the plastic nature of desmosomal integrity under static and strained conditions. Our study demonstrates that the integrity of desmosomes from control CMs are not challenged by low intensity strain. When desmosomes are compromised due to a DSP mutation, their integrity is challenged, supporting the concept that exercise indeed may lead to disease progression.

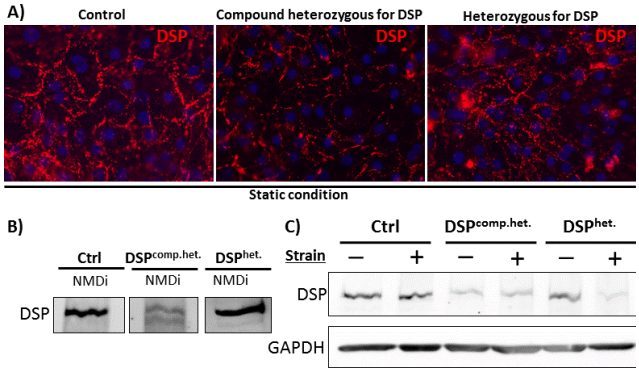

Figure 1

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The myocardial infarction context dictates the phenotypic polarisation of antigen-specific CD4+T-cells and favours pro-healing responses in the wounded myocardium

M Max Rieckmann[1]; P Steinau[1]; B Ludewig[2]; K Heinze[3]; G Alber[4]; S Frantz[5]; U Hofmann[5]; GC Ramos[5]
[1]University Clinic Halle (Saale), Mid-German Heart Center, Department of Internal Medicine III, University Hospital Halle, 06120 Halle, Halle, Germany; *[2]Kantonhospital, Institute of Immunobiology, St Gallen, Switzerland*; *[3]University of Würzburg, Rudolf Virchow Center for Experimental Biomedicine, Würzburg, Germany*; *[4]University of Leipzig, Institute of Immunology, Centre of Infectious Diseases, Leipzig, Germany*; *[5]University Hospital Würzburg, Comprehensive Heart Failure Center, Würzburg, Germany*

On behalf of: Mid-German Heart Center
Funding Acknowledgements: Deutsche Forschungsgemeinschaft, Deutsche Gesellschaft für Kardiologie, Dr.-Marija-Orlovic-Stiftung

Recent studies revealed that myocardial infarction (MI) triggers the activation of CD4+T-cells in mice, which in turn modulate myocardial inflammation, healing, and remodeling. In the present study, we sought to assess whether antigen specificity is crucially involved in these circumstances, and how T-cell responses are fine-tuned in the injured myocardium milieu. Thus, cardiac-myosin-specific Thy1.1+ CD4+ T-cells (TCR-M) were adoptively transferred into Thy1.2+ WT recipients prior to MI induction. Flow cytometry and light-sheet microscopy analyses showed that TCR-M cells accumulate in the heart and mediastinal lymph nodes of infarcted, but not of sham-operated animals, at the peak of healing process (day 7), whereas no TCR-M accumulation was observed in other irrelevant sites (spleen, subiliacal

lymph node). Notably, these cells vanished at later chronic remodeling phase, indicating that post-MI T-cell auto-reactivity is self-limiting. Most strikingly, TCR-M cells, which are pathogenic and drive lethal myocarditis in their donors, differentiate into Foxp3+ cells, acquire a unique pro-healing gene expression profile and promote cardioprotection when transferred into MI-recipients, leading to preserved functional parametres. Our results provide definitive evidence that post-MI T-cell responses are largely driven by heart-specific antigens. Furthermore, beyond specificity, our data reveal that the unique MI-milieu dictates the phenotypic polarization of specific CD4+ T-cells favoring the development of autoimmune responses that benefit self-maintenance.

Moderated Posters - Novel treatment

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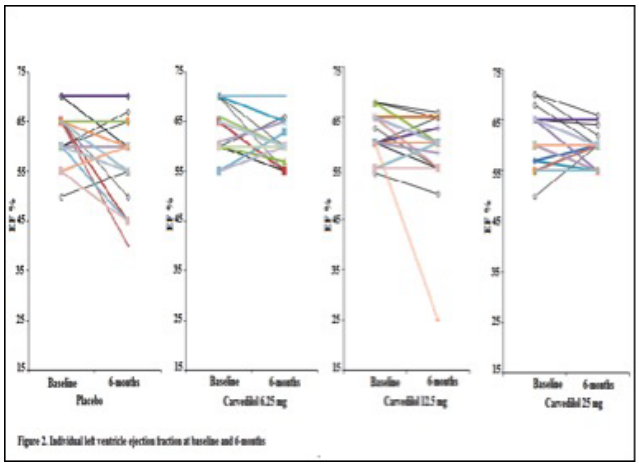
Prophylactic use of carvedilol to prevent ventricular dysfunction in patients with cancer treated with doxorubicin

A J Abuosa[1]; A J Elshaikh[1]; A J Kinsara[1]
[1]*King Saud bin Abdulaziz University for Health Sciences, COM-J. King Abdul Aziz Medical City -WR, King Faisal cardiac center , Jeddah, Saudi Arabia*

Objective: Deterioration in ventricular function is often observed in patients treated with anthracyclines for cancer. There is a paucity of evidence on interventions that might provide cardio-protection. We investigated whether carvedilol can prevent doxorubicin-induced cardiotoxicity and whether any observed effect is dose related.
Methods: A prospective, randomized, double-blind study in patients treated with doxorubicin, comparing placebo (n = 38) with different doses of carvedilol [6.25 mg/day (n = 41), 12.5 mg/day (n = 38) or 25 mg/day (n = 37)].
Results: The primary endpoint was the measured change in left ventricular ejection fraction (LVEF) from baseline to 6 months. LVEF decreased from 62% ± 5% at baseline to 58% ± 7% at 6-months (p = 0.002) in patients assigned to placebo but no statistically significant changes were observed in any of the 3 carvedilol groups. At 6 months, only one of 116 patients (1%) assigned to carvedilol had an LVEF < 50% compared to four of the 38 assigned to placebo (11%), (p = 0.013). No significant differences were noted between carvedilol and placebo in terms of the development of diastolic dysfunction, clinically overt heart failure or death.
Conclusions: Carvedilol might prevent deterioration in LVEF in cancer patients treated with doxorubicin. This effect may not be dose related within the studied range.



LVEF between placebo and carvedilol

		Placebo	P value	Car (6.25 mg)	p value	Car (12.5 mg)	P value	Car (25 mg)	p value
LVSd	Baseline	28.0±4.4	0.002	29.3±4.4	0.059	29.2±4.2	0.178	30.2±5.7	0.458
6 months	30.7±5.7	30.4±3.0	30.3±4.3	30.9±4.1					
LVDd	Baseline	45.3±5.3	0.566	46.0±5.1	0.166	44.8±4.3	0.011	44.6±6.3	0.368
6 months	45.9±7.5	46.8±4.0	46.0±3.7	45.5±5.3					
EF	Baseline	62.0±4.6	0.002	61.4±3.9	0.059	60.0±4.1	0.100	60.4±4.2	0.073
6 months	58.2±6.6	60.0±2.9	58.2±6.6	59.2±2.8					
E'	Baseline	11.3±3.0	0.365	11.9±3.2	0.067	13.2±5.0	0.001	11.8±3.4	.015
6 months	10.9±3.8	10.9±3.4	11.8±4.9	10.8±3.0					
E/A	Baseline	1.22±0.4	0.533	1.20±0.5	0.359	1.26±0.5	0.949	1.17±0.3	0.251
6 months	1.20±0.4	1.14±0.4	1.27±0.6	1.13±0.3					
DT	Baseline	190.7±33.9	0.188	200.8±28.2	0.637	203.6±38.7	0.228	199.5±38.8	0.139
6 months	199.7±39.8	197.1±30.0	213.3±45.1	209.3±40.9					
E/E'	Baseline	7.2±2.6	0.413	7.4±3.0	0.730	7.0±3.3	0.033	6.9±2.6	0.788
6 months	7.6±3.3	7.6±3.6	8.0±4.0	7.0±2.2					

Comparison of echocardiography and tissue Doppler variables at baseline and 6 month of follow-up

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What proportion of patients with HFrEF might be candidates for Sacubitril-Valsartan?

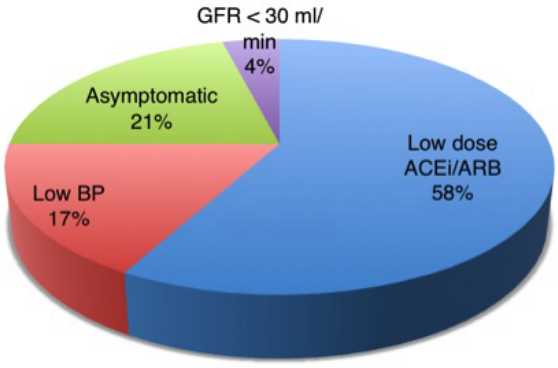
M Montoro Lopez[1]; T O'connor[1]; T Ibrahim[1]; E Sweeney[1]; F Bakcsi[1]; M Islam[1]; N Stakelum[1]; N Carter[1]; C Gray[1]; C Halley[1]; P Keelan[1]; NF Murphy[1]
[1]*Our Lady of Lourdes Hospital, Cardiology, Drogheda, Ireland*

Background: After the landmark PARADIGM-HF trial, the 2016 ESC HF guidelines included Sacubitril-Valsartan (SV) in the HFrEF management algorithm. Nevertheless, unlike the inclusion criteria of the PARADIGM trial, ESC guidelines recommend mineralocorticoid receptor antagonists (MRA) as a previous step before considering SV (Table). This difference may cause that a lower number of patients than expected are eligible for SV and, thus, benefit from it. The aim of our study was to retrospectively determine what proportion of patients would meet the criteria for SV according to the ESC algorithm in a chronic HF outpatient clinic.

Criteria to be eligible for SV

	PARADIGM-Trial	ESC HFrEF algorithm
Echocardiography	EF ≤ 35%	
Optimal medical treatment	ACEi or ARB equivalent to Enalapril 10 mg BID + Beta-blocker	ACEi or ARB equivalent to Enalapril 10 mg BID + Beta-blocker + MR antagonist
Laboratory	BNP ≥ 150 or NT-proBNP≥ 600 pg/mL BNP ≥ 100 or NT-proBNP ≥ 400 pg/mL if recent hospitalization (<12m) GFR > 30 ml per minute per 1.73 m2 of body-surface Potassium < 5.4 mmol per liter	
Clinical status	NYHA II,III or IV	
Blood pressure	SBP < 95 mmHg	

Methods: We conducted an observational and retrospective study in the specialized HF clinic of our institution (Ireland). From January 2015 to December 2016, all patients referred to the clinic were included in the analysis. Clinical, echocardiographic and analytic variables were collected from medical records in order to select the population eligible for SV.
Results: Over a 2 year period, 434 new patients were referred to the HF clinic. Out of them, 116 patients had EF = 35%. From this group, 51 patients (44%) were eventually prescribed a MRA in addition to ACEi/ARB and betablockers. From this group, after taking into account NYHA class, blood pressure, ACEi/ARB dose and GFR, 27 patients would have been eligible for SV (23% of all referrals with HFrEF). The main cause to be excluded for SV was intolerance to high dose of ACEi/ARB (figure).
Conclusion: In our HF clinic, less than a quarter of patients with HFrEF met the criteria for SV according to the ESC-HFrEF algorithm. More flexibility in these criteria may increase the potential number of eligible patients for this life-saving drug.



Causes for not being eligible for SV

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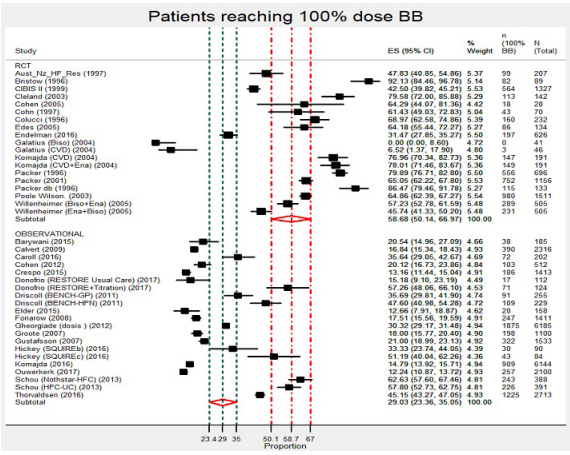
Heart failure patients with reduced left ventricular ejection fraction, who reached 100% target dose of beta-blockers in randomized and observational studies

M J Maria Juana Oyanguren Artola[1]; P Latorre[1]; LL Garcia Garrido[2]; M Nebot[3]; I Lekuona[4]; J Torcal Laguna[1]; A Lopez Rodriguez[1]; T Soria[5]; M Moure[6]; Y Sanchez Paule[7]; J M Pinilla[7]; R Lopez Vilella[8]; I Gomez Otero[6]; A Giraldez[9]; A Esteban[10]
[1]*Osakidetza- Basque Health Service, Bilbao, Spain*; [2]*University Hospital de Girona Dr. Josep Trueta, Girona, Spain*; [3]*Bellvitge University Hospital, Barcelona, Spain*; [4]*Hospital Galdacano, Galdacano, Spain*; [5]*University Hospital Puerta de Hierro Majadahonda, Madrid, Spain*; [6]*University Hospital of Santiago de Compostela, Santiago de Compostela, Spain*; [7]*University Hospital Virgen de la Victoria, Malaga, Spain*; [8]*Hospital Universitario y Politécnico La Fe, Valencia, Spain*; [9]*Hospital General Jerez de la Frontera, Jerez de la Frontera, Spain*; [10]*Hospital Clinic San Carlos, Madrid, Spain*

On behalf of: ETIFIC Research Team
Funding Acknowledgements: Carlos III Health Institute FIS PI 14/01208,European Regional Development Fund,Basque Country Government Exp 2014111143

Introduction: It is recommended to take beta-blockers (BB) for patients with heart failure (HF) and reduced left ventricular ejection fraction (LVEF) to decrease hospitalizations, mortality and improve symptoms. To achieve maximum clinical benefit 100% target dose (ESC Guidelines) or maximum tolerated dose are advised. The n (%) patients who reached target dose in randomized trials (RCT) and observational studies (OS) has not been studied enough. Its evaluation can guide quality indicators in clinical practice
Objective: To evaluate n (%) of patients with HF and reduced LVEF, who reached 100% target dose of BB in RCT and OS
Methods: Systematic review of bibliography (PUBMED, EMBASE, CINHAL, COCHRANE Library) and manual search in relevant journals. 2 independent reviewers. Inclusion criteria: RCT, drug vs. placebo or drug vs. drug, (1994-2017) and multi-center OS (2007-2017) of BB, carvedilol, bisoprolol and nevibolol, which evaluated n (%) of patients in target dose. Categorical variable described as n%. (95% CI). We performed a random-effects meta-analysis with the Stata metaprop program (Stata v10). For the extraction of RCT results the Analysis by intention to treat has been considered.
Results: 242 articles were reviewed and 16 RCTs were selected (7,830 patients) 3 of them with 2 intervention arms, not considering data from the placebo arm and 18 OS (27,645 patients), 3 of them with 2 arms. Subtotal RCT 58.68% (95% CI: 50.1-66.97) Subtotal OS: 29.03 % (95% CI: 23.36-35.05) (Figure).
Conclusions: Significant RCT / OS differences were observed in the proportion of patients achieving BB target doses. New studies are needed on the possible conditions associated, clinical and sociodemographic characteristics of the patients and the organization of the intervention, in order to establish improvement programs.



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Metabolic response to exercise training in heart failure with preserved ejection fraction

M Bahls[1]; N Friedrich[1]; M Pietzner[1]; F Edelmann[2]; G Hasenfuss[3]; R Wachter[4]; M Nauck[1]; SB Felix[1]; S Schwarz[5]; M Halle[5]; M Dorr[1]
[1]University Medicine of Greifswald, Greifswald, Germany; *[2]Charite - Campus Virchow-Klinikum (CVK), Berlin, Germany*; *[3]Ernst Moritz Arndt University of Greifswald, Department of Internal Medicine B, Greifswald, Germany*; *[4]Heart Center of Leipzig, Leipzig, Germany*; *[5]Technical University of Munich, Munich, Germany*

On behalf of: DZHK (German Centre for Cardiovascular Research), partner sites Greifswald, Munich, Göttingen and Berlin, Germany

Background: Heart failure (HF) with preserved ejection fraction (HFpEF) accounts for more than 50% of all HF cases with rising prevalence. No evidence-based pharmacological treatment options exist to reduce disease burden. Exercise training (ET) has been shown to partly reverse diastolic dysfunction and improve exercise capacity. However, the biological mechanisms underlying these observations are not completely understood.
Purpose: We aimed to improve our understanding of exercise induced cardiac and cardiopulmonary improvements in HFpEF by analyzing metabolic changes related to a 12-week ET utilizing a targeted plasma metabolomics approach in patients of the EX-DHF-P trial.
Methods: The EX-DHF-P trial was a multi-center, prospective, randomized, controlled parallel group study exploring the impact of structured ET on cardiac function and exercise capacity in patients with HFpEF. We used the Biocrates AbsoluteIDQ® p180 Kit to quantitatively measure the concentration of 188 endogenous plasma metabolites in 44 patients who participated in ET (EX) and 20 controls (CON). Generalized estimating equation and linear regression models were used to assess differences in changes in metabolite concentrations over time between responder and non-responder as well as the relation between alterations in cardiac outcomes and metabolites, respectively. Further, responders to ET were defined based on whether the change in outcome of interest (i.e. VO2peak, E/e', LAVI, VE/VCO2 slope) was above the median.
Results: Overall, 70 metabolites significantly changed from baseline to follow-up in both groups. In EX a total of 51 metabolites were reduced and only one was increased. In the CON, 11 metabolites were decreased and 10 were increased. There was an overlap between the groups of 12 metabolites with decreased concentrations. Ten metabolites showed a significant time*group interaction. Specifically, in EX glutamine concentration increased while three sphingolipids (i.e. SM(OH) C16:1, SM C18:0 and SM C24:0) decreased. In CON circulating carnitine as well as four phosphotidycholines (i.e. PC aa C28:1, PC aa C34:2, PC ae C44:4 and PC aa C36:2) increased while acetylornithine decreased. A total of 39, 12, 6, and 36 metabolites were related to changes in VO2peak, E/e', LAVI and VE/VCO2 slope, respectively. The abundance of 14, 15, and 15 metabolites were different between VO2peak, E/e' and LAVI, respectively, when responders and non-responders were compared.
Conclusions: Twelve weeks of exercise training in HFpEF patients resulted in a large number of metabolites being decreased compared to control. Interestingly, metabolic changes vary vastly according to the investigated outcome parameter. Overall, plasma metabolomics may be a useful technology to identify biomarkers and mechanisms of metabolic changes in HFpEF and response to therapy. Further, this method allows monitoring metabolic changes that have previously been reported only by invasive skeletal muscle.

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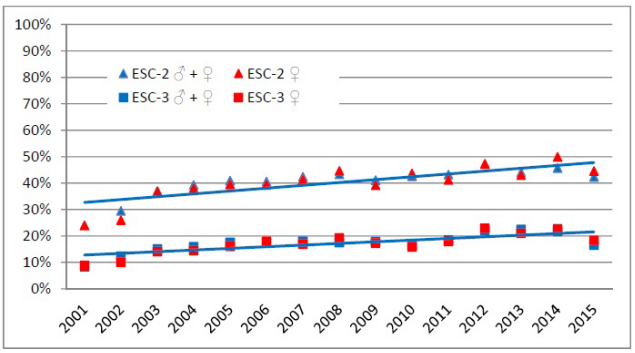
Adherence to ESC guidelines after hospital admission for heart failure in 22500 Dutch patients: 2001-2015

WJ Kruik-Kolloffel[1]; HJ Kruik[2]; KLL Movig[3]; GCM Linssen[2]; J Van Der Palen[3]
[1]Röpcke-Zweers Hospital, Clinical Pharmacy, Hardenberg, Netherlands; *[2]Hospital Group Twente, Cardiology, Hengelo, Netherlands*; *[3]Medical Spectrum Twente, Clinical Pharmacy, Enschede, Netherlands*

Introduction: Adherence to guideline-recommended medication in patients with chronic heart failure (HF) improves clinical outcomes. In the past two decades, specific disease-modifying HF drugs have been incorporated into the European (ESC) practice guidelines. However, use of advocated medication in real-world clinical practice is still suboptimal.
Purpose: To analyse how evolving guideline-directed recommendations influenced the medication profile at discharge after a first hospital admission for HF. We focussed on diuretics, angiotensin-converting-enzyme inhibitors (ACEI)/angiotensin-receptor blockers (ARB), beta-blockers (BB) and mineralocorticoid-receptor antagonists (MRA).
Methods: We extracted from the PHARMO Database Network 22500 patients in the Hospitalisation Database with a diagnosis of HF or hypertensive heart disease with (congestive) HF at hospital discharge, in the Netherlands, between 2001 and 2015. Patients were unselected. Drug dispensings from primary and secondary care prescriptions were extracted from the Out-Patient Pharmacy Database.
Results: The prescription of ACEI/ARB and diuretics was stable at about 63% and 82%, respectively. The proportion of ARB increased, without foundation in the guidelines. The percentage of patients on combined ACEI and ARB was less than 3% and declined till less than 1% after the formal warning of the regulatory authorities. Despite the substantially enhanced recommendation in ESC guideline 2012 of MRA to NYHA class II, the percentage of patients in which MRA was prescribed remained approximately 40%. A rise in the prescription rate of BB was a result of the distinct recommendation since the guideline of 2001, mostly BB with a market authorisation for HF. Subsequently, the percentage of patients prescribed ACEI/ARB and beta-blocker almost doubled to about 50%; the percentage of patients prescribed ACEI/ARB, BB and MRA reached almost 20%. See the Figure. There were no differences between males and females. Each year of higher age was associated with 2% decrease in dual therapy (ACEI/ARB and beta-blocker) and 1.5% of triple therapy (ACEI/ARB and BB and an MRA).
Conclusion: The adherence with the European (ESC) HF guidelines influenced prescription behaviour at discharge after a first hospitalisation for HF. However, adherence with the guidelines varied for the individual recommendations. At the same time some developments were demonstrated, which were not covered by the guidelines. Although the exact HF classification of the patients was unknown, our large and representative database provided insights in real-world HF medical therapy from 2001 till 2015.



ESC-2: Beta-blocker + (angiotensin-converting-enzyme inhibitor or angiotensin-receptor blocker)
ESC-3: Beta-blocker + (angiotensin-converting-enzyme inhibitor or angiotensin-receptor blocker) + mineralocorticoid-receptor antagonist

Prescribed medications in HF: 2001-2015

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Cardiovascular outcomes with the incretin-based therapies GLP-1 agonists and DPP-4 inhibitors in type 2 diabetes participants with and without heart failure

SL Zheng[1]; P Collins[1]
[1]Royal Brompton Hospital, London, United Kingdom

Background: Incretin-based therapies (GLP-1 agonists and DPP-4 inhibitors) are frequently used in patients with type 2 diabetes. Incident heart failure is associated with poor outcomes in these patients. The overall effect of incretin-based therapies from pooled cardiovascular outcome trials in patients with and without heart failure has not been tested.
Aim: To investigate the effect of GLP-1 agonists and DPP-4 inhibitors on the primary outcome in cardiovascular outcome trials in patients stratified by baseline heart failure status.
Methods: Meta-analysis was used to pool primary endpoint data for GLP-1 agonist and DPP-4 inhibitor cardiovascular (CV) outcome trials. The primary outcome in these trials was pooled CV mortality, non-fatal stroke and non-fatal myocardial infarction (MI). Effects were analysed in participants with and without heart failure. Required data was available from study publications in all cases except for EMPA-REG OUTCOME, where data was provided by the study sponsor. Results were analysed as pooled HR format, with 95% CI. Random-effects meta-analysis model was used. Statistical analysis done on Review Manager 5.3.
Results: There were five CV outcome trials enrolling a total of 58,551 participants (Drug: 29,283, Placebo: 29,268). Three trials enrolling 27,388 participants tested GLP-1 agonists: EXSCEL (Exenatide), LEADER (Liraglutide), and SUSTAIN-6 (Semaglutide). Two trials enrolling 31,163 participants tested DPP-4 inhibitors:

SAVOR-TIMI 53 (Saxagliptin) and TECOS (Sitagliptin). There were 9015 participants with heart failure (15.4% of participants). GLP-1 agonists reduced the primary outcome in participants without heart failure (HR 0.84, 95% CI 0.73 to 0.95, P = 0.007), but had no effect in those with heart failure (HR 0.97, 95% CI 0.84 to 1.11, P = 0.62). DPP-4 inhibitors had no effect, regardless of baseline heart failure status. Incretin-based therapies combined reduced the outcome in participants without heart failure (HR 0.90, 95% CI 0.82 to 0.99, P = 0.03) but not in those with heart failure (HR 1.00, 95% CI 0.90 to 1.10, P = 0.93).

Post-hoc inclusion of studies enrolling post-MI participants (ELIXA and EXAMINE) did not affect the Results: GLP-1 agonist (without heart failure: HR 0.88, 95% CI 0.77 to 1.00, P = 0.04; and with heart failure: HR 0.96, 95% CI 0.85 to 1.08, P = 0.50), DPP-4 inhibitor (without heart failure: HR 0.99, 95% CI 0.91 to 1.06, P = 0.72; and with heart failure: HR 0.98, 95% CI 0.84 to 1.15, P = 0.82).

Conclusion: Incretin-based therapies reduce the CV endpoint in patients without heart failure, but not in those with heart failure. This was effect was driven by the differential effect of GLP-1 agonists by baseline heart failure. While there was no reduction in the primary endpoint in patients with heart failure, there was no evidence of harm. Incretin-based therapies may be used in patients with heart failure for glycaemic control, but did not reduce the CV outcome.

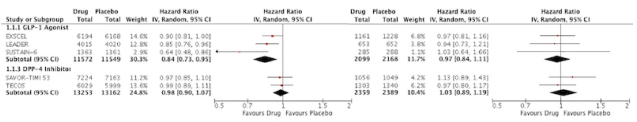

Figure: Forest plot of CV outcomes

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Functional and anatomical pulmonary arterial disease in patients with persistent pulmonary hypertension after left valve replacement according to the hemodynamic phenotype

E Domingo[1]; J Grignola Rial[2]; P Trujillo[3]; B Janssen[3]; R Aguilar[4]; A Roman[5]
[1]University Hospital Vall d'Hebron, Cardiology, Barcelona, Spain; *[2]Hospital de Clinicas Dr. Manuel Quintela, Pathophysiology, Montevideo, Uruguay*; *[3]Hospital de Clinicas Dr. Manuel Quintela, Cardiology, Centro Cardiovascular Universitario, Montevideo, Uruguay*; *[4]University Hospital De La Princesa, Cardiology, Madrid, Spain*; *[5]University Hospital Vall d'Hebron, Clinic de Pneumologia, Barcelona, Spain*

Background: The prediction of pulmonary vasculopathy severity in patients (p) with pulmonary hypertension associated with left heart disease (PH-LHD) based on hemodynamic phenotype is a matter of debate.

Purpose: To assess pulmonary arterial stiffness (PAS) and area wall thickness (AWT) and their role on the right ventricular-arterial coupling (RVAC) according to the hemodynamic phenotype in p with persistent-PH after mitral (MVR) and aortic (AVR) valve replacement.

Methods: 15 p (72 ± 7 y, 13 F) underwent successful MVR (6 with concomitant AVR) at least one year ago presenting PH by echo (<50 mmHg). Prosthesis-p mismatch and LV dysfunction were discarded. All p were submitted to RHC and intravascular ultrasound in medium-sized PAs at rest and during iNO (20 ppm). We assessed mean PA pressure (mPAP), PA wedge pressure (PAWP), cardiac index (CI), peripheral and total pulmonary vascular resistance (PVR, TPR), PA capacitance (PAC), PAS (elastic modulus -EM-), and the relative AWT. We obtained the ratio TAPSE/sPAP. Data were compared with a historical cohort of control subjects.

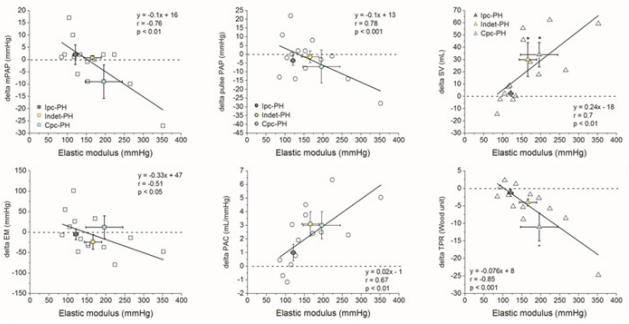
Results: 5 p had combined post and pre-capillary PH (Cpc-PH, diastolic pressure gradient-DPG- = 7 mmHg and PVR > 3WU), 5 p had isolated post-capillary PH (Ipc-PH, DPG < 7 mmHg and PVR = 3 WU) and 5 p presented indeterminate phenotype (Indet-PH, DPG = 7 mmHg or PVR >3 WU). All p showed significant pulmonary vasculopathy (Table). Transpulmonary gradient, DPG, PVR, and PAC were correlated with EM (r>0.6, p < 0.05). RVAC was significantly correlated with PAC (r = 0.63) and EM (r=-0.59), which is worst in Cpc-PH p (0.16 ± 0.02, p < 0.05). During iNO, p with the highest rest EM showed the most significant change in TPR, mPAP, pulse PAP, EM, stroke volume (SV), and PAC (Figure).

Conclusions: Persistent-PH after MVR/AVR shows different hemodynamic phenotypes which cannot be identified by echo-doppler. The worse pulmonary vasculopathy, the worse RVAC, and the higher vasoreactivity response to iNO.

Hemodynamic data

	Ipc-PH (5)	Indet-PH (5)	Cpc-PH (5)	Control (10)
mPAP, mmHg	32±2*	34±2*	52±5	15±1.3§‡*
CI, L/min/m^2	2.3±0.2	2.1±0.1	1.9±0.2	2.6±0.03‡*
PVR, WU	2.4±0.3*	4.1±0.2*§	12.2±3.1	2.9±0.4‡*
PAC, mL/mmHg	2.2±0.2*	1.6±0.1*§	1.3±0.4	6.2±0.4§‡*
PAWP, mmHg	19±0.6	19±0.7	23±0.2	8.8±0.6§‡*
DPG, mmHg	-2.6±1.5*	0.2±1.1*	14±0.2	2.7±1.3*
EM, mmHg	121±6	166±23	196±49	21±2§‡*
AWT, %	20.4±2.1	23.2±2.2	22.5±1.1	1.4±0.4§‡*

mean ± SE. §p < 0.05 vs Ipc-PH; ‡p < 0.05 vs Indet-PH; *p < 0.05 vs Cpc-PH



Acute hemodynamic effects of iNO

Clinical Case Corner 3 - Untold stories about arrhythmias and devices

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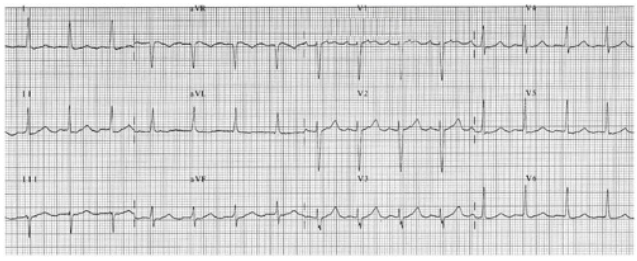
Effective catheter treatment of atrial tachyarrhythmias in non-responder to cardiac resynchronization therapy

S Garkina[1]; R Tatarsky[1]; D Lebedev[1]; V Lebedeva[1]; T Lubimtzeva[1]; V Orshanskaya[1]; A Kamenev[1]; YU Miller[1]; E Mikhaylov[1]; S Gureev[1]
[1]*Almazov National Medical Research Centre, Saint-Petersburg, Russian Federation*

Background: Candidates for cardiac resynchronization therapy (CRT) often experience atrial tachyarrhythmias that may reduce the probability of positive response after resynchronization due to different reasons, including rapid and irregular ventricular rhythm inconsistent with a permanent LV capture when compared to patients in sinus rhythm.



ECG with atypical atrial flutter

Case presentation: We report a clinical case of a 46-year-old male who was a candidate for cardiac resynchronization due to congestive heart failure symptoms including dyspnea and massive edema and also demonstrated LBBB pattern (QRS duration of 182 msec) on ECG. He experienced frequent hemodynamically significant atrial fibrillation episodes with rapid ventricular response and maximum ventricular rate up to 170 bpm. Physical examination and instrumental data confirmed diagnosis of dilated cardiomyopathy with significant impairment of left ventricle systolic function (ejection fraction level (EF) of 28 %). Coronary angiography didn't reveal any abnormalities. The patient was implanted CRT-D system for primary prevention. However, he didn't respond well to cardiac resynchronization therapy and decompensated during 2 years due to heart failure progression. Control echocardiography revealed severe systolic disfunction (EF level of 20%). Considering longstanding atrial fibrillation patient was planned to catheter treatment and underwent three subsequent radiofrequency ablation procedures. During endocardial electrophysiological study different types of arrhythmias were demonstrated: typical atrial flutter, atrial fibrillation and right atrial tachycardia. Three months later the patient developed atypical left-side atrial flutter with rapid ventricular response (Figure 1). Repeated radiofrequency ablation procedure with sinus rhythm restoration contributed to clinical improvement. Persistent conduction block was shown on the mitral isthmus, and the patient remained free of atrial tachyarrhythmia during 16 months of follow-up using device telemetry. Now patient is stable and demonstrates good physical tolerance along with improvement in the global systolic function of the LV (EF level of 48%).

Answers and discussion: Sinus rhythm restoration is especially important in CRT candidates because failure of biventricular capture may contribute to the lack of benefit of resynchronization in patients with persistent or permanent atrial fibrillation. This clinical case illustrates role of effective catheter treatment of atrial arrhythmias in patients with implanted CRT devices.

Conclusions: and implications for clinical practice. All patients who meet the current criteria for CRT, despite their atrial arrhythmias burden, should be recommended to receive this therapy. Early catheter ablation is indicated with continuous monitoring of cardiac arrhythmias and clinical re-evaluation of current treatment to optimize rhythm or rate control in CRT patients.

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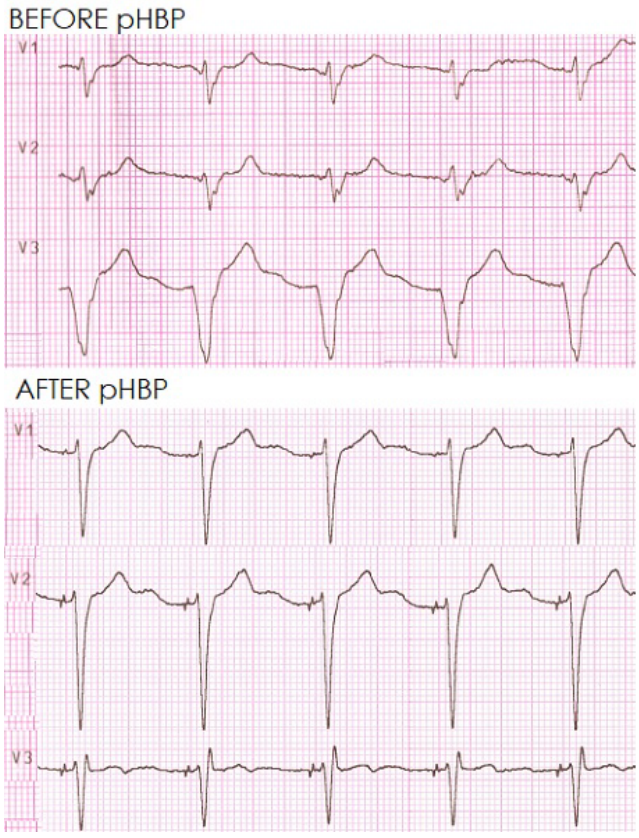
Permanent his-bundle pacing for cardiac resynchronization therapy in a patient with an imlantable cardioverter-defibrillator.

B Skonieczny[1]; A Gajek[1]; J Adamowicz[1]; J Gajek[1]; A Slawuta[2]
[1]*Wroclaw Medical University, Department of Clinical Nursing, Wroclaw, Poland*;
[2]*Klodzko County Hospital, Department of Cardiology, Klodzko, Poland*

69 years old male with ischemic cardiomyopathy, diabetes mellitus type 2 [DMT2] and permanent atrial fibrillation [pAF] had a sudden cardiac arrest [SCA] in 2007 due to ventricular fibrillation [VF]. As prevention of subsequent episodes of the arrhythmia an implantable cardioverter-defibrillator [ICD] was implemented. Unfortunately a disease course was further complicated by an adequate as well as inadequate ICD therapies treated successfully with increased dose of beta blocker. This medication resulted in slowing of atrioventricular conduction. Since that time the dominant ventricular rhythm was right ventricular pacing. The obvious effect of this was prolonged QRS duration (200 ms). Echocardiography revealed left ventricular ejection fraction (LVEF) decrease and the patient developed symptoms of heart failure New York Heart Association [NYHA] functional class III with seriously impaired quality of life. Upgrade from conventional ICD to cardiac resynchronization therapy [CRT] was implemented – patient underwent an implantation of pacing lead in His bundle area with selective capture and satisfactory pacing threshold. Procedure resulted in restoring of native QRS complexes which were narrow (118 ms), increase in LVEF (+7%) and improvement in NYHA class (for now on functional class I).



Biventricular pacing [BiV] is a well established method for CRT, although permanent His bundle pacing (pHBP) seems to be more physiologic way of pacing and as such it is promising alternative for BiV, either as a rescue strategy or as a first line treatment. Case of our patient shows that pHBP could be successfully used as primary strategy for CRT in patients with high percentage of ventricular pacing with both echocardiographic and clinical improvement. However, there is still a strong need for high quality randomized clinical trials to legitimate efficiency of pHBP in particular indications for CRT and establish its position.

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A case of reversible dilated cardiomyopathy caused by atrial fibrillation

G Gulnoza Dussekeyeva[1]; AB Isakhanova[1]; GS Bimagambetova[1]
[1]*Scientific Research Institute of Cardiology and Internal Diseases, Almaty, Kazakhstan*

On behalf of: Issakhanova Ainur, Bimagambetova Gulnaz

37-year-old male was consulted to the cardiology because of clinics of heart failure (edema, dyspnea). Heart failure symptoms firstly appeared 2 years ago. He had no history of hypertension or recently infectious process. Electrocardiography (ECG) finding was atrial fibrillation with average ventricular rate of 150-178 per minute. Transthoracic echocardiography showed all heart cameras dilated, reduced ejection fraction: left atrium-5,1 centimeters (cm), right ventricular 4,6 cm, end diastolic size-7,2cm, end systolic size -6,5?m, end diastolic volume -274 milliliters (ml), end systolic volume -209ml, impact volume -65 ml , ejection fraction by Simpson - 35%, ?S-11%, intraventricular wall thickness-1,0 ?m, left ventricular posterior wall thickness -1,0 ?m. Coronary angiography showed no significant stenosis of coronary artery. 24-hour Holter Monitoring showed atrial fibrillation with average ventricular rate of 148-170 per minute, one episode of wide-complex tachycardia longing 30 seconds. The short wide-complex tachycardia episode was then registered on ECG and identified as ventricular tachycardia. He was admitted optimal heart failure therapy (beta-blockers, angiotensin-converting enzyme (ACE)-inhibitors, diuretics) and anticoagulant therapy. Transesophageal echocardiography showed no thrombosis signs in heart cameras. Heart team diagnosed Dilative Cardiomyopathy and made a decision to implant this patient Implantable Cardioverter Defibrillator (ICD) for the prevention of sudden cardiac death. By the end of hospitalization, clinical signs of heart failure had regressed. Patient adhered prescribed treatment strictly 6 months, on time he sensed ICD shock. ICD checking confirmed one ICD shock because of ventricular tachycardia. On control clinical examination patient had no signs of heart failure. On ECG is sinus rhythm 67 beats per minute. After 6 months, follow-up echocardiography showed that LV function markedly improved with decreased LV size.
Transthoracic echocardiography showed: left atrium-3,1 cm, right ventricular 3,6 cm, end diastolic size-4,7 cm, end systolic size -3,4?m, end diastolic volume -103 ml, end systolic volume -48 ml, impact volume -55 ml , ejection fraction by Simpson - 54%, ?S-28%, intraventricular wall thickness-1,1 ?m, left ventricular posterior wall thickness -1,2 ?m.

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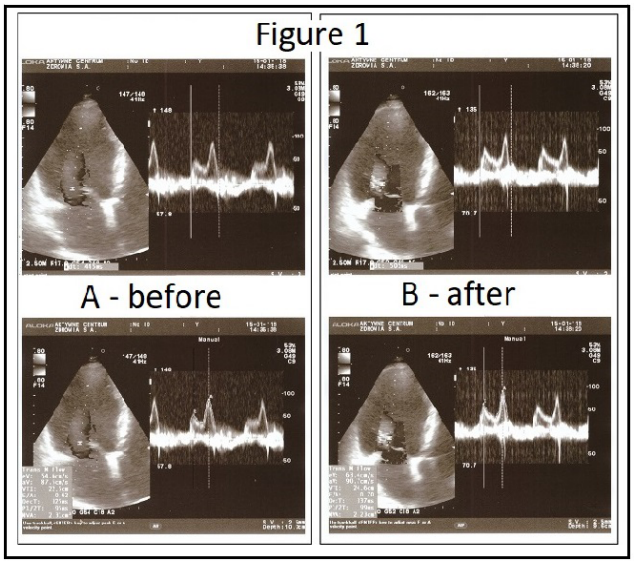
Left ventricle filling improvement by permanent his bundle pacing treatment in patient with atrial fibrillation, first-degree atrioventricular block and impaired left ventricle systolic function.

P Piotr Strozik[1]; J Zawadzki[1]; A Gajek[1]; J Adamowicz[2]; J Gajek[2]; A Slawuta[3]
[1]*Wroclaw Medical University, Students Scientific Association, Wroclaw, Poland*;
[2]*Wroclaw Medical University, Department of Clinical Nursing, Wroclaw, Poland*;
[3]*Klodzko County Hospital, Department of Cardiology, Klodzko, Poland*

Introduction: A 72-year-old male presented with ischemic cardiomyopathy. The LV ejection fraction decrease to 42% was the cause of coronary angiography, which revealed satisfactory effect of previous angioplasty of Cx. The sinus bradycardia resulted in a low dose of metoprolol. In 2015 the first atrial fibrillation (AF) episode was confirmed with the heart rate 100 bpm and spontaneous sinus rhythm return was observed. The next year one more oligosymptomatic incident of arrhythmia was diagnosed. In 2017 during several hospitalizations, because of non-cardiac reasons, observed AF was considered to be permanent. Several months later in the cardiology ward the echocardiography showed enlargement of the left ventricle with significant deterioration of its function (LVEDD 70mm, EF 33%). The patient was qualified for ICD (Implantable Cardioverter Defibrillator) with possible upgrade to the CRT-D system due to the slow AF. After 2 weeks, the patient came again due to symptomatic dizziness. ECG revealed sinus bradycardia (44 bpm) with first degree atrioventricular block (PQ 240ms). The patient was consulted by a specialist who, recognizing the risk of pacing-induced deterioration after implantation of dual chamber ICD, qualified the patient for implantation of the CRT-D system with direct His bundle pacing (DHBP).
Procedures, techniques
The patient underwent CRT-D device implantation with the use of LV-channel electrode for permanent His-bundle pacing. Selective DHBP was achieved with satisfactory pacing threshold. The atrial lead was placed in the Bachmann's bundle. The basic rate was set to 65 bpm, with rate response up to 80 bpm. The av and vv delay programming (A-LVonly) of the device resulted in PR interval of 170 ms.
First-degree atrioventricular block (AV block) is a disorder of the electrical conduction system of the heart. The prolongation of PR interval is a known reason of increased mortality and the risk of atrial fibrillation. The first-degree AV block is usually a result of proximal disorder in atrioventricular node conduction. The possible shortening of the conduction by ablation is more speculative than clinical. Another approach to reduce the PR interval is the DHBP procedure. This method of treating first-degree AV block seems to be very promising, yet frequently ignored.
Conclusions: This case illustrates the potential of improving EF by integrating electrical and mechanical function of atrium by mean of DHBP and by preserving narrow QRS with A-V interval shortening. The P-R interval with DHBP and delay programming was reduced from 240ms to 170ms. Those settings gave benefit of the increase in mitral filling time by 60 ms and mitral VTI increase by 2 cm (Figure 1). The rough estimation of the cardiac output change indicates the increase of approximately 300 ml/min. The use of existing CRT device not only makes this approach widely available but also makes it possible to treat patients with already implemented pacemakers.



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Recurrent syncopes in a patient on androgen deprivation therapy for prostate cancer: a clinical case presentation

I Ilir Sharka[1]; S Myftiu[1]; B Dita[1]; J Rustemaj[1]; D Malaveci[1]
[1]*University Hospital Center Mother Theresa, Department of Cardiology & Cardiac Surgery, Tirana, Albania*

Introduction: Androgen deprivation therapy (ADT) is considered an important treatment in patients (pts) with prostate cancer. Concerns about adverse cardiovascular effects have been raised, although no reports on its potential proarrhythmic effects in previously healthy pts. This is a case of a prostate cancer patient with recurrent syncopes due to very frequent Torsades de Pointes (TdP) under ADT.
Case presentation: A 70 years old prostate cancer male treated surgically 6 month before with a recent history of syncope was admitted to ICCU due to a wide QRS tachycardia associated loss of conscience. Resting ECG showed mild bradycardia, a borderline QTc, inverted U wave & good hemodynamic conditions. He was on Bicalutamide 50 mg/d for 3 months and Goserelin injection a month to referral. He had no chest angina history. Several patterns of extrasystoles, atrial and junctional tachycardia were seen and lab tests revealed blood electrolytes abnormalities (low K, Ca, Mg), normal cardiac echo, troponin & other tests. The 1° day of admission, besides the correcting doses of electrolytes the patient experienced two self-limited episodes of TdP, which were treated with 1 gr iv Mg. QTc interval kept increasing, despite normalizing blood electrolyte levels from the preliminary clinical workup. We didn't find any other relevant causes of this phenomenon and concluded

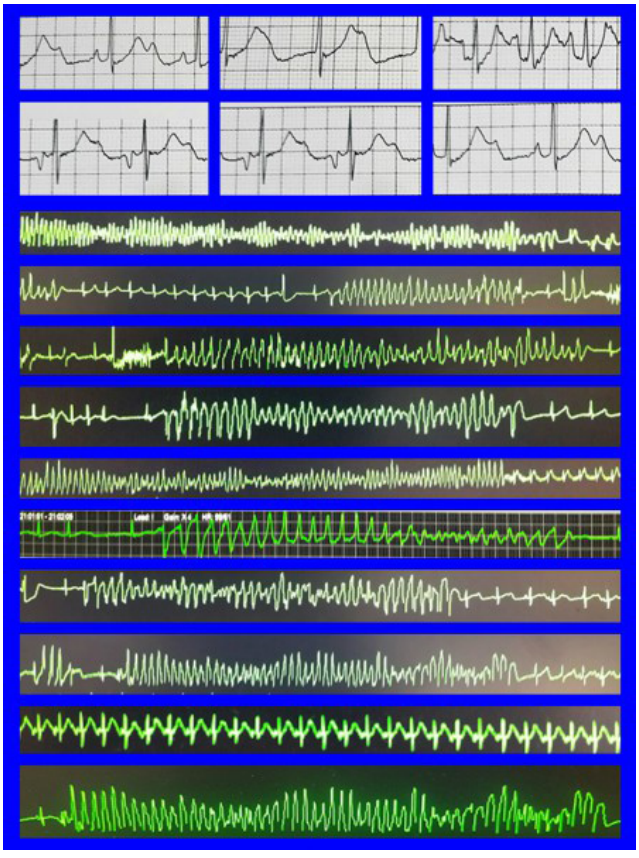
that a potential complication of ADT should be considered. We decided to stop Bicalutamide. The 2° day appeared with worse clinical scenario; nausea, vertigo, agitation and ECG parameters (Tab 1). Continuous Mg infusion & Dobutamine to maintain a heart rate round 90bpm improved clinical symptomatology, a stable heart rhythm and normalization of QTc, without complex arrhythmias. The patient was referred to oncology follow up.

Conclusion: ADT may lead to severe electrolyte imbalances and life-threatening cardiac arrhythmias. It should be considered an important cause of QT prolongation. Further studies are necessary to investigate its effects in several cardiac populations.

Tab 1

Day	1	2	3	7	14
K*	3.3	3.9	4.1	4	3.9
Ca*	0.79	0.74	0.98	1.1	1.15
Mg*	0.68	0.8	0.87	0.91	0.85
QTc**	447	581	569	442	435
PR interval**	160	210	160	150	150
U wave	Inverted	Positive	Prominent	Small	Absent
TdP episodes	2	18	2	0	0

* - mmol/l** - ms



ECG patterns of rhythm disturbances

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Disease development of arrhythmogenic cardiomyopathy: a case report.

E Eszter Fodi[1]; R Faludi[1]; T Simor[1]
[1]*University of Pecs, Heart Institute, Pecs, Hungary*

The diagnostics of arrhythmogenic cardiomyopathy (AC) has been facilitated by a complex criteria system that is continuously improving to increase sensitivity. Due to the great differences in the clinical picture, decision making is challenging even with the use of recently available imaging techniques.

We report a case of a 29-year-old male patient, whose cardiac evaluation started 10 years ago because of pre-syncopal episodes during driving. Based on the initial echocardiographic and cardiac MRI examinations in NYHA I, a primary dilated cardiomyopathy (DCM) was diagnosed (36 % EF, slightly dilated left and right ventricle with diffuse hypokinesis). His treatment and follow-up were set up according to DCM. But recently, based on the appearance of an epsilon wave in lead V1 on a follow-up 12 lead surface ECG, cardiac MRI was repeated with the indication of AC. The cardiac MRI confirmed AC, as it showed the previously known reduced left (41%) and novel low right ventricular EF (35%) and proved both right ventricular and left ventricular delayed enhancement (Figure 1). According to the analysis of the 20 ECGs collected during the 10 years, we found only minor ECG criteria for AC. The epsilon wave appeared only recently for the first time. Therefore, the risk of sudden cardiac death was re-evaluated and based on the heart failure, the documented novel non-sustained right ventricular outflow tract ventricular tachycardias and still present pre-syncopal episodes, implantable defibrillator therapy was suggested. Unfortunately, the patient declined the intervention.

Our case draws attention to the diverse presentation of AC (both right and left ventricular involvement). Furthermore, our case shows the progressive nature of the AC disease development. We emphasize the fact that besides the regular clinical follow-up visits the disease progression should be estimated paying close attention to the changes both on the surface ECG and cardiac MRI.

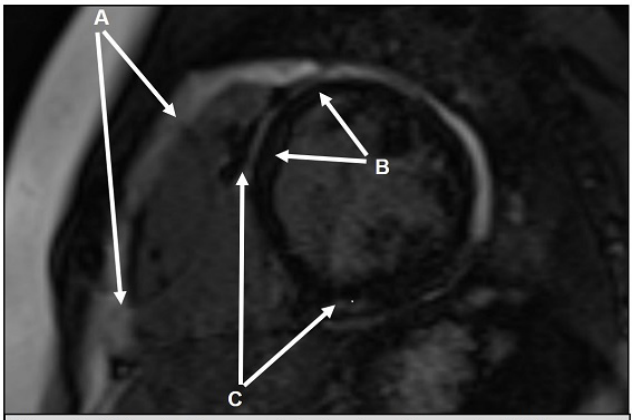

Figure 1. Delayed-enhancement short axis cardiovascular MRI image of the patient showing delayed enhancement in the right ventricular free wall (A), mid-myocardial (dilated cardiomyopathy pattern) (B) and subepicardial delayed enhancement (myocarditis pattern) (C) in the left ventricular wall.

Figure 1. Short axis cardiac MRI image

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Iatrogenic cardiac arrest and cardiogenic shock

M Carrington[1]; AR Santos[1]; J Pais[1]; B Picarra[1]; D Bras[1]; R Azevedo-Guerreiro[1]; K Hyde-Congo[1]; J Carvalho[1]; J Aguiar[1]
[1]*Hospital Espirito Santo de Evora, Cardiology, Evora, Portugal*

A 61-year-old woman with previous history of severe hypertension presented with a rapid deterioration of mental state and was assisted by a pre-hospital emergency team. An extreme bradycardia was detected, with no response to atropine, and a transcutaneous pacemaker stimulation was applied. During hospital transport, she had a cardiac arrest in asystole, with return to spontaneous circulation after five cardiopulmonary resuscitation cycles. She was intubated and mechanically ventilated and carried to our emergency department. On examination, she was hemodynamically instable with hypotension and a deficient external pacemaker stimulation causing an extreme bradycardia of 20 bpm, and had discrete inferior limbs oedema. The electrocardiogram showed sinus arrest with escape beats. A cardiogenic shock secondary to extreme bradycardia was assumed and she was immediately admitted at the coronary intensive care unit for urgent stabilization.

She had previous history of a severe hypertension and dyslipidaemia. She was being treated with diltiazem 300mg od, carvedilol 25mg twice a day, rilmenidine, spirono-lactone, torasemide and simvastatin. She was being treated for her hypertension by her general practitioner and two different specialists.

A transvenous pacemaker was immediately implanted and vasopressor support was initiated with need for noradrenaline dose titration. On echocardiogram, she had a non-dilated left ventricle (LV), with concentric hypertrophy and a moderately

depressed global LV ejection fraction (EF). Right ventricle was normal and both mitral and tricuspid moderate insufficiencies were present. Biochemical and hematologic investigations revealed renal dysfunction with severe hyperkalaemia (7,5mmol/L), hepatic dysfunction and normal c-reactive protein and troponin I.
She had a rapid recovery and in the thirty-six hours following admission, she was extubated and vasopressor support was gradually weaned. The electrocardiogram revealed sinusal rhythm at 80 bpm, with normal AV and interventricular conduction and no ST-T segment changes. Coronary angiography showed no angiographic significant lesions and echocardiographic re-evaluation showed a preserved global LVEF and no significant functional valvular alterations.
Beta-blockers therapy is the most common cause of drug-induced bradycardia. The addition of non-dihydropyridine calcium channel blockers augments the effects of beta-blockade, as both drugs depress cardiac electrical and mechanical activity. They interfere with slow action potential generation and atrioventricular conduction and both have negative chronotropic and inotropic effects. Non-coordinated treatment of severe hypertension by different doctors is potentially fatal, as demonstrated by this clinical case. All patients should be advised to carry a personal medication and dosage chart, which should be revised for potential drug-interactions by treating doctors each visit.

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Reversal of systolic dysfunction in a male adolescent with left ventricular hypertrabeculation/noncompaction and Wolff-Parkinson-White syndrome after accessory pathway ablation

K Rezkalla[1]; E Gatterer[1]; JO Huber[1]; C Neuhold[1]; C Claudia Stoellberger[1]
[1]*Rudolfstiftung Hospital, Department of Internal Medicine II, Vienna, Austria*

Introduction: Recurrent or incessant tachycardia may occur in symptomatic Wolff-Parkinson-White (WPW) syndrome, leading to ventricular dysfunction, tachycardia-induced cardiomyopathy (TIC). Asymptomatic WPW syndrome-induced TIC has rarely been reported, with incidence rates higher in pediatric patients than in adults. Left ventricular hypertrabeculation/noncompaction (LVHT) is a cardiac abnormality of unknown etiology and is found in normally sized, well contracting left ventricles as well as in dilated ventricles with systolic dysfunction. LVHT associated with WPW has been reported several times, however reversal of systolic dysfunction after ablation has not been described so far.
Description of the patient: A previously healthy 17-years old male underwent the first electrocardiogram (ECG) of his life at the conscription for military service. ECG showed WPW-syndrome with overt pre-excitation, and he was referred for cardiological investigation. He reported no cardiac symptoms and was an active soccer player. Clinical investigation was normal. Echocardiography revealed an enlarged left ventricle (enddiastolic diameter 59mm), a reduced ejection fraction (14%) and LVHT of the apex and lateral wall. Resting ECG and 24-hour Holter monitoring disclosed multiple episodes of atrial tachycardias with a heart rate of 110/min. After repeated inquiries the patient admitted that he felt frequently "rapid heart beats", but this was so normal that it did not bother him.
Patient management: Cardiac magnetic resonance (CMRI) imaging was planned but could not be carried out because of atrial arrhythmias. Electrophysiological examination disclosed an epicardial left posteroseptal accessory pathway with ante- and retrograde conduction. Radiofrequency ablation was carried out in October 2017. After 16 radiofrequency deliveries in the left atrium and in the coronary sinus, the retrograde conduction was completely blocked and the anterograde conduction was blocked intermittently. The postinterventional ECG did not show Delta waves any more. Two months later, in December 2017, echocardiography showed a normally sized left ventricle (enddiastolic diameter 56 mm) with normal systolic function (EF 60%) and unchanged LVHT. The patient did not receive any pharmacotherapy except acetylsalicylic acid 100 mg/d for 4 weeks after ablation. The patient is continuously in NYHA I class of heart failure and reports that he feels no "rapid heart beats" any more. CMRI is scheduled for February 2018. Genetic testing is under way.
Conclusions: and implications for clinical practice: WPW-induced TIC may even occur in asymptomatic patients, who are so adapted to their arrhythmias that they do not recognize them. Ablation of the accessory pathway leads to reversal of systolic dysfunction without necessity for neurohumoral therapy. Since the further course of the cardiac situation including LVHT is uncertain, the patient remains under cardiologic observation.

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Cardiac thromboembolic stroke due to inappropriate implantable cardioverter defibrillator shock

D Zizek[1]; B Antolic[1]; M Jan[2]; L Notar[3]
[1]*University Medical Centre Ljubljana, Department of Cardiology, Ljubljana, Slovenia*; [2]*University Medical Centre Ljubljana, Department of Cardiovascular Surgery, Ljubljana, Slovenia*; [3]*University Medical Centre of Ljubljana, Department of Neurology, Ljubljana, Slovenia*

Introduction: Device detected atrial tachyarrhythmias, especially subclinical atrial fibrillation (AF) episodes, are associated with an increased risk of stroke. However, the precise threshold of AF episode duration and daily burden that justifies initiation of oral anticoagulation is still controversial. Additionally, in spite of tachyarrhythmia discrimination advances implemented in implantable defibrillators devices the incidence of inappropriate therapy remains relatively high.
Case report: A 57-year-old male with recently implanted cardiac resynchronization therapy device with a defibrillator (CRT-D) due to nonischaemic heart failure (HF), no history of AF and receiving contemporary HF medication was admitted to the Neurology department due to symptoms of stroke and impaired consciousness. Computed tomography angiography scan, performed 2 hours after the onset of stroke symptoms, demonstrated an occlusion of the left middle cerebral artery (MCA) (Figure 1A - arrow) and the treatment with intravenous tissue plasminogen activator (tPA) was initiated according to the guidelines. In addition, before stroke symptoms, the patient reported a defibrillator shock. CRT-D device interrogation revealed an inappropriate device-related shock due to short AF episode (< 3 minutes) with rapid ventricular response (Figure 1B) approximately 1 hour before the onset of stroke symptoms. There were no additional atrial tachyarrhythmia episodes registered since the device was implanted. As cardiogenic thromboembolism was suspected transoesophageal echocardiography was performed which revealed a thrombus in the left atrial appendage (Figure 1C - arrow).
Clinical question: Could abrupt device-related sinus restoration in an inadequately anticoagulated patient present an additional thromboembolic risk irrespective of subclinical AF duration?
Conclusion: In HF patients with implantable CRT-D or defibrillator devices detection of new subclinical AF requires appropriate clinical management and decisions (oral anticoagulant treatment, antiarrhythmics, device programming etc.) not only because device-detected AF is a determinant of stroke but also due to possible risk of inappropriate shock related thromboembolism.

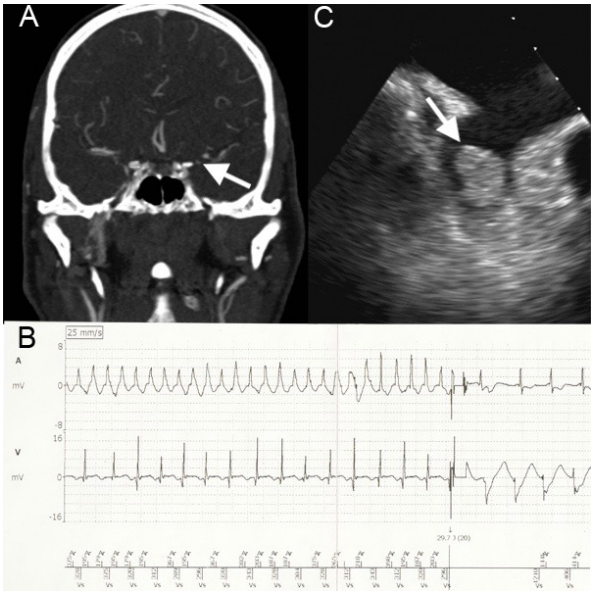

Figure 1.

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Catecholaminergic polymorphic ventricular tachycardia with ventricular dysfunction: a new reality?

T Tatiana Duarte[1]; S Goncalves[1]; C Sa[1]; R Marinheiro[1]; M Fonseca[1]; J Farinha[1]; F Seixo[1]; L Parreira[1]; R Caria[1]
[1]*Hospital Center of Setubal, Cardiology, Setubal, Portugal*

Introduction: Catecholaminergic polymorphic ventricular tachycardia (CPVT) is a highly malignant inheritable cardiac channelopathy, the most common genetic mutations responsible for CPVT occur in the gene that encodes the cardiac ryanodine receptor (RyR2).
CPVT is characterized by episodic syncope occurring during exercise or acute emotion in individuals without structural cardiac abnormalities. In the literature has been reported the association with takotsubo cardiomyopathy in scarce cases.

Considering all cardiac events (syncope, aborted cardiac arrest, sudden death), the rate of occurrence is 54-58% in untreated individuals, according some data 33-38% of patients presented with cardiac arrest.
Case report: An 52 year-old female patients was admitted in emergent department (ED) by episodic syncope without prodromes and no previous history similar. Patient with history of intermittent left bundle branch block (LBBB), arterial hypertension and profound venous thrombosis and family history of sudden death.
In ED, hemodynamically stable without precordial pain. ECG with intermittent LBBB and negative troponin. She realized CT angiography that excluded pulmonary thromboembolism but CT cranioencephalic with subarachnoid hemorrhage without need for invasive therapy.
Coronary angiography excluded coronary disease and echocardiography transthoracic with evidence of moderate-severe left ventricular dysfunction. The cardiac NMR showed moderate left ventricular dysfunction (LVEF 40%) by diffuse hypokinesia without ventricular dilation and no ischemia pattern. The electrophysiological study was normal.
During hospitalization without evidence of dysrhythmic episodes and evolution in NYHA class II. At the 25th day, there was discharge after implantation of cardioverter-defibrillator.
After one year, she is followed in a Heart failure (HF) outpatient clinic, actually in NYHA class I and recovered ventricular function and no dysrhythmic events. The genetic study evidenced a new variant of mutations in gene of RyR2 (Ala4860 Val), potentially pathogenic, however without record any other case in the literature.
Conclusion: The association between CPVT and takotsubo syndrome has been a reality, although the cases described are scarce and the mechanics not yet cleared as well as the prognostic impact.
In our case, the segmental alterations are not compatible with takotsubo, but eventually the transient dysfunction may be explained by similar mechanisms: effect of catecholamines, effect of intracellular calcium and its role in HF.
Our knowledge about CPVT continues to grow and new genetic mutations are found, more studies are important to help shape newer diagnostic and treatment strategies.

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A rare combination of two genetic cardiomyopathy (arrhythmogenic right ventricular dysplasia and left ventricular noncompaction) and the role of myocarditis in disease progression

O V Olga Blagova[1]; AV Nedostup[1]; EA Kogan[1]; YA Lutochina[1]; NV Varionchik[1]; EV Pavlenko[1]; SA Alexandrova[2]; AG Shestak[3]; EV Zaklyazminskaya[3]
[1]*I.M.Sechenov I Moscow State Medical University, Moscow, Russian Federation*; [2]*Bakoulev Center for Cardiovascular Surgery RAMS, Moscow, Russian Federation*; [3]*Russian Research Center of Surgery, Moscow, Russian Federation*

Background: First identified the phenotype of dilated cardiomyopathy (DCM) should be considered as a syndrome that requires expanded nosological diagnosis. Simultaneous presence of sustained ventricular tachycardia (SVT) increases the probability of the genetic nature of the disease.
Purpose: to evaluate the features of the clinical picture, laboratory and instrumental diagnostics and the effectiveness of complex treatment in a patient with a high risk of sudden cardiac death.
Methods: There was a female patient 34 years. From 23 years (after a respiratory infection) - chest pains, shortness of breath. Coronary arteries are intact. In 2013 she survived syncope, in Holter-ECG she had 2048 PVBs / day, episode of SVT (1 minute). MRI was performed, and a cardioverter-defibrillator (ISD) was implanted. Follow up is 50 months.
Results: ECG showed the low QRS voltage and negative T waves in leads V2-V6. EchoCG revealed LV EDD 6.2 cm, RV EDD 4.0 cm, LVEF 35%, LV myocardial noncompaction (NCM). Late ventricular potentials were detected. MRI sowed NCM of LV, thickening of the epicardial fat on the anterior wall of the right ventricle (RV), RV EDV 133 ml/m2, EF 41%, LV EDV 115 ml/m2, EF 25%, hypo / dyskinesia of the anterior wall, subepicardial gadolinium enhancement in the early and late phase in the LV, intraventricular septum and the free walls of the RV. The level of all anti-heart antibodies was high (1:160-1:320). The reasons for statement of a possible diagnosis of myocarditis in this case were the connection the onset of symptoms with viral infection, high titers of anti-heart antibodies, early and late subepicardial gadolinium enhancement by MRI. The endomyocardial biopsy of RV was performed: subendocardial lipomatosis (about 10%), separation of myocardium by fibrous septa, lymphocytic infiltrates (more than 14 cells), vasculitis without viral genome. DNA diagnosis revealed a splicing mutation in the gene desmoplakin (DSP). Arrithmogenic right ventricular dysplasia (ARVD), LV NCM and myocarditis were diagnosed. Immunosuppressive therapy (hydroxychloroquine, prednisone, azathioprine) was prescribed, LV EF stabilized at 40%. The appropriate shock of the ICD for VT (HR of 210 / min.) with transformation in ventricular fibrillation was recorded twice. For this reason, sotalol was replaced with amiodarone.
Conclusion: In a young patient with arrhythmogenic syncope and DCM syndrome was diagnosed combination of ARVD (3 major and 2 minor criteria, definite diagnosis) and NCM with the biopsy proved virus-negative chronic myocarditis. The DCM as a syndrome can have multiple causes, and the combination of myocarditis and primary cardiomyopathy is not rare. NCM can be observed in patients with typical desmosome proteins mutations. The use of immunosuppressive therapy led to the stabilization of heart failure, however, recurrent ventricular arrhythmias a greater degree determined by the presence of primary cardiomyopathy.

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A comparison between strain echocardiography and quantitative gated myocardial perfusion scintigraphy in patients with low ejection fraction of left ventricle prior to implantation of CRT-D

A Alexander Kazakov[1]
[1]*Saint Petersburg Pavlov State Medical University, Hospital surgery ? 2, Saint Petersburg, Russian Federation*

Objective: The objective of this study is to compare the strain echocardiographic and scintigraphic parameters for evaluating of the left ventricular (LV) functions in patients prior to implantation of CRT-D.
Methods: Fifteen our patients (male/female: 10/5) were included in this study. All patients underwent gated myocardial perfusion scintigraphy gated single-photon emission computed tomography (GSPECT) and echocardiography (EC). LV was divided into 17 segments. The echocardiographic strain (S) and strain rate (SR) values were calculated by using speckle tracking method. The results obtained by these techniques were compared to each other. Also global strain of LV were measured using speckle tracking echocardiography (STE) and ejection fraction of LV using GSPECT.
Results: A total of 255 (17x15) segments of LV wall were evaluated. In all patients, 94 segments were scored as normokinetic, 65 as hypokinetic, 96 as akinetic or dyskinetic using echocardiographic strain method; and 89 as normal thickening, 105 as decrease thickening and 61 as no thickening using GSPECT. All patients had decreased global strain (<12%) and low ejection fraction (<35%).
Conclusion: GSPECT and STE allow to evaluate regional and global myocardial contractility in patients prior to implantation of CRT-D. We showed that GSPECT and STE were in agreement with each other. Also, STE method could be used in order to choose optimal localization of LV electrode as a non-invasive alternative of other methods.

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Right-sided subcutaneous ICD in a patient with congenitally corrected transposition of the great arteries with situs inversus and dextrocardia

I Igor Zupan[1]; K Prokselj[1]; M Kozelj[1]; J Tasic[1]; D Zizek[1]; J Winter[2]
[1]*University Medical Centre of Ljubljana, Department of Cardiology, Ljubljana, Slovenia*; [2]*University of Dusseldorf, Division of Cardiac Surgery, Dusseldorf, Germany*

Introduction: Subcutaneous implantable defibrillator (S-ICD) may require nonstandard placement because of anatomic abnormalities in patients with complex congenital heart disease. We describe the placement of an S-ICD on the right side of the thorax in a patient with congenitally corrected transposition of the great arteries with situs inversus and dextrocardia.
56 years old woman with complex congenital heart disease presented with presyncope and dizzines. Holter monitoring revealed episodes of non-sustained ventricular tachycardia. Treatment with amiodarone was contraindicated due to Wegener disease and thyroid dysfunction. Implantation of a conventional ICD in a subpulmonary ventricle was questionable because of the presence of a small atrial septal defect and further need for an anticoagulation treatment. Besides, she had a hystory of bleeding from an aneurism of left segmental pulmonary artery, probably caused by endocarditis of the pulmonary valve seven years ago.
Echocardiography revealed slightly dilated subpulmonary ventricle with 50% ejection fraction, enlarged both atria, small atrial septal defect, moderate pulmonary hypertension and moderate pulmonary stenosis.
She received a S-ICD (Boston Scientific, Model SQRX) implanted intermuscularly between the anterior surface of serratus anterior and the posterior surface of latissimus dorsi on the right side. The pulse generator pocket incision overlied the fifth to sixth intercostal space 3-4 cm lateral to the mid-clavicular line towards the mid-axillary line. The distal tip of the electrode was tunnelled from the pocket above the fascial layer and fixed at the xyphoid with the suture sleeve. We opted for a third incision, so that the distal tip could be visualized and fixed.
A 50-Hz burst induced VF with adequate sensing and termination of VF with restoration of sinus rhythm after 17 seconds from a single 65-J shock. After a few seconds atrial fibrilation appeard which used to be her basic rhythm over past years. At 2 months follow-up, the patient has presented no complications and no significant events have been recorded.

The S-ICD system can be used effectively in the right thorax in patients with complex heart disease and dextrocardia. We are not aware of any case of particular congenital disease with right-sided S-ICD implantation.

880

His-bundle-pacing-based ICD as an innovative approach in decompensated chronic heart failure and concomittant permanent atrial fibrillation.

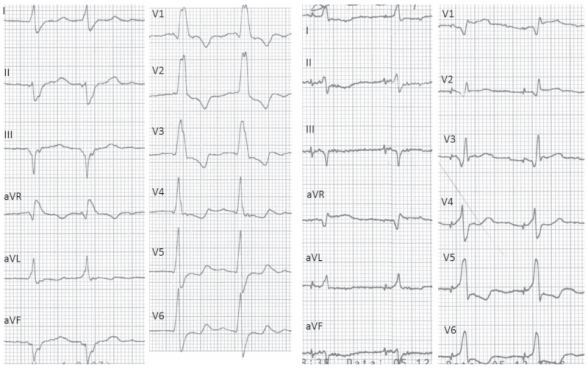
J Adamowicz[1]; A Slawuta[1]; M Sokolowska[2]; J Adamowicz[2]; J Moszczynska-Stulin[3]; J Gajek[4]; D Zysko[5]

[1]Klodzko County Hospital, Department of Cardiology, Klodzko, Poland; *[2]Wroclaw Medical University, Students' Scientific Association, Department of Cardiology, University Hospital, Wroclaw, Poland*; *[3]Wroclaw Medical University, Department of Cardiology, University Hospital,, Wroclaw, Poland*; *[4]Wroclaw Medical University, Department of Clinical Nursing, Wroclaw, Poland*; *[5]Wroclaw Medical University, Department of Emergency Medicine, Wroclaw, Poland*

Introduction: Patients with atrial fibrillation and congestive heart failure decompensation prove to be a troublesome population. AF often recurs after an electric cardioversion, requiring a strict rhythm control approach. According to recent reports index population may not benefit from ß-blocker therapy, due to insufficient blockage of adrenergic stimulation, limited by impaired AV conduction and depletion of cardiac output. Ambiguous reports about intravenous digoxin were noted. Inotropic agents may be useful as heart failure symptoms aggravate, however sympathetic activation promotes higher ventricular response in AF, impeding haemodynamic benefit.

Case description: 68-year male with a history of chronic heart failure with permanent AF after inferior myocardial infarction with partially ischaemic mitral regurgitation was admitted with a consecutive episode of decompensation. Patient presented with dyspnoea, ortopnoea, peripheral oedema and right sided pleural effusion. Echocardiography revealed enlarged LVEDD (72mm) with EF = 28%. A severe MR with jet area estimated at 11 cm^2 was a significant finding was as well. Carefully dosed catecholamines caused tachycardia with exacerbation of heart failure. Digoxin administered intravenously resulted in only moderate negative chronotropic effect. As a detrimental influence of atrial fibrillation proceeded, we decided to regularize the rhythm with pacing. Because of ECG pattern of RBBB patient was not a target candidate for conventional resynchronization. In these circumstances the direct His bundle pacing (DHBP) seemed to be a more appropriate alternative. We achieved a broad zone of selective His Bundle pacing with additional RBBB abolition. The His bundle electrode was connected with atrial port of the dual ICD and ICD electrode was placed in RV apex. The heart rate regularization enabled to stop i.v. drugs administration, up-titrate digoxin and start beta-blocker. The oral loop diuretic doses were gradually reduced. The initial pacing rate of 80 bpm was lowered to 70 bpm. After the procedure echocardiography showed immediate LVEDD reduction to 69mm and EF increase to 35%. During 12-month follow up the patient required few modifications of pharmacotherapy according to renal status, blood pressure and AV conduction, but there was no episode of heart failure decompensation.

Conclusions: 1. Standard pharmacological treatment of decompensated heart failure with AF may lead to a detrimental effect on patient's haemodynamics. 2. Direct His-bundle pacing in patients with non-LBBB QRS morphology is an attractive treatment option to regularize the heart rate without harmful right ventricular pacing. 3. In presented case the innovative His-ICD implantation during episode of acute heart failure enabled better patient's treatment with immediate and subsequent clinical and echocardiographic improvement.



12-lead ECG; pre- and postprocedural.

Clinical Case Session 1

909

Multifocal ectopic Purkinje-related premature contractions caused by mutation in SCN5A gene may result in arrhythmia induced cardiomyopathy

T Tereza Nedvedova[1]; M Kubanek[1]; A Krebsova[1]; L Piherova[2]; M Blaha[1]; J Vrbska[1]; V Melenovsky[1]; P Peichl[1]; S Kmoch[2]; J Kautzner[1]
[1]Institute for Clinical and Experimental Medicine (IKEM), Prague, Czech Republic; *[2]First Faculty of Medicine and General Teaching Hospital, Institute of inherited metabolic diseases, Prague, Czech Republic*

Funding Acknowledgements: research grant of the Ministry of Health, Czech Republic [MZ 15-27682A]

Background: The SCN5A gene encodes the subunit of voltage-gated sodium channel which is responsible for rapid electrical transmission through cardiac conduction system and for myocardial excitability. Mutations of SCN5A have been associated with a broad spectrum of hereditary arrhythmias and/or cardiomyopathies. Multifocal ectopic Purkinje-related premature contractions (MEPPC) have been recognized as a cause of arrhythmia induced reversible systolic dysfunction which can be sometimes reversed by class I antiarrhythmic drugs. These drugs are known to decrease the rapid depolarizing sodium influx, thereby slowing depolarization and reducing the amplitude of the action potential. This results in slower conduction and reduced automaticity.
Methods: We present a patient with non-ischemic, severe left ventricular systolic dysfunction due to frequent multifocal ectopy originating from the conduction system with a verified - likely pathogenic - mutation in SCN5A gene. Molecular diagnostics were performed by whole exome sequencing.
Clinical case: A 38-year-old female was examined due to palpitations and dyspnea at mild exertion. Her ECG showed junctional rhythm with MEPPC, which constituted 44% of the 24h ECG recording. Echocardiography revealed severe systolic dysfunction of non-enlarged left ventricle (LVEF 20-25%), while MRI did not show late gadolinium enhancement. Quinidine sulfate 800 mg daily suppressed MEPPC and resulted in rapid improvement of LVEF to 35-40% during the initial hospitalization. At 12 months of follow-up, MEPPC were reduced to 3% of beats and LVEF normalized (60%). An attempt to replace quinidine with flecainide 100 mg daily resulted in reappearance of MEPPC. After re-administration of quinidine sulfate 600 mg daily, the patient remains clinically stable with preserved LVEF and significant suppression of MEPPC. Genetic testing confirmed a pathogenic SCN5A gene mutation (c.68635 C>T, p. R814W). Cascade screening in the family revealed the same mutation in the patient's father, which was characterized by very frequent MEPPC and normal LV function.
Conclusions: Frequent MEPPC due to mutations in SCN5A gene may cause arrhythmia-induced cardiomyopathy. Targeted antiarrhythmic therapy may lead to normalization of LV systolic function. However, there is an uncertainty about the optimal prevention of sudden cardiac death of patients with this condition.

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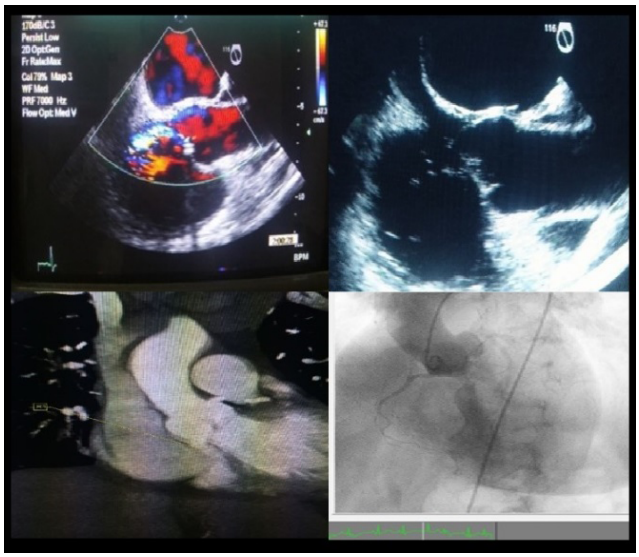
Acute right heart failure presented as acute abdomen

I Ina Refatllari[1]; A Banushi[1]; V Beqiraj[2]; H Gjergo[1]; A Demiraj[1]; A Goda[1]
[1]University Hospital Center Mother Theresa, Cardiology, Tirana, Albania; *[2]Polyclinic Ambulatory Service, Cardiology, Tirana, Albania*

Introduction: Acute heart failure has a poor prognosis. Early identification and correction of its cause is crucial in order to increase the chances of survival. Spontaneous rupture of a Sinus of Valsalva may lead to serious hemodynamic instability and death if left untreated.Case report: A 67 y.o female patient presented in the ER as acute cholecystitis complaining of strong epigastric pain irradiating in the right hypochondrium and shortness of breath. The pain started a week ago spontaneously and at first it was succeeded by a syncope. Moreover, she had an isolated fever episode of 38.5 °C and persistent diarrhea. Otherwise than hypertension and blood pressure lowering therapy, her past medical history was unremarkable. She underwent a transthoracic echocardiography examination three years earlier with no significant findings.An abdominal ultrasound was performed and it showed dilated suprahepatic veins, vena porta of 14 mm, gallbladder with thickened walls, sludge and pericholecystic fluid. On initial assessment the patient was pale, diaphoretic, tachycardic (115/min) and orthopneic. She had irregular heartbeats, an ejection systolic murmur (5/6 in intensity) all over the precordium, diminished breathing sounds at the lung bases and dilated jugular veins. BP was 140/80 mmHg. She was admitted for further evaluation. Transthoracic echocardiography revealed a possible aorta to right atrium fistula in a tricuspid aortic valve with right chambers dilation, mild tricuspid regurgitation, severe pulmonary hypertension (PAP 79 mmHg) and normal left ventricular function. Subsequently, a transesophageal echocardiography and an aortic angio CT confirmed the diagnosis and showed a communication between the noncoronary cusp and right atrium. She was immediately started on diuretics i/v and referred to the angiography cath lab to confirm the fistula and exclude the presence of coronary artery disease considering the patient's age and risk factors. The patient was transferred to the cardiac surgery department and underwent reconstructive surgery of the aorta. Endocarditis was excluded as a possible cause. The patient was discharged in good condition a week later.Discussion: Aorto-atrial fistulas (AAF) are rare but important pathophysiologic conditions of the aorta and have varied presentations such as acute pulmonary edema, chronic heart failure and incidental detection. A variety of mechanisms such as aortic dissection, endocarditis with pseudoaneurysm formation, post surgical scenarios or trauma may precipitate the fistula formation. Prompt surgical repair is usually helpful in relieving symptoms and decreasing mortality.
Conclusion: Spontaneous rupture of a nondilated Sinus of Valsalva is rare. Was angiography really necessary to confirm the fistula presence considering the patient's condition and imminent cardiac surgery? Non-invasive imaging techniques play an important role for making the correct diagnosis without needing further invasive examination.



Aorto-Atrial fistula images

911

Fecal microbiota transplantation in a heart transplant recipient

Z Zoltan Tarjanyi[1]; G Prinz[2]; A Kiraly[1]; A Assabiny[1]; N Parazs[1]; ZS Szakal-Toth[1]; T Teszak[1]; B Sax[1]; B Merkely[1]
[1]Semmelweis University Heart Center, Budapest, Hungary; *[2]Szent Laszlo Hospital, Budapest, Hungary*

We report a case of a 64 years old patient who received heart (HTX) in March 2016 due to end stage ischemic cardiomyopathy. Postoperative period was uneventful. One month after HTX repeated Weber tests were positive for occult blood in stool. A

colonoscopy was performed, which showed sessile polyps in the colon confirmed as high grade dysplasia with histopathological examination.
As removal with endoscope was not feasible, we decided to closely follow the lesion, because surgical removal would have carried high infectious risk because of the high immunosuppression (IS) level due to the very early stage after HTX. The controls showed no progression. At the one year checkup a PET-CT was performed showing fluorodeoxyglucose uptake in the dysplastic region. Oncology multidisciplinary team recommended right hemicolectomy, which was performed in May 2017.
In the next three months after the surgery patient was admitted to hospital several times due to Gram negative sepsis, gastrointestinal (GI) infections and weight loss. Despite to various antimicrobial therapy we were not able to stop the recurrence of the GI infections caused by Clostridium difficile and multi-resistant Gram negative bacterium species. Reducing IS was not an option due to a constant low-to-mid grade allograft rejection. With the failure of conventional treatments we decided to perform fecal transplantation. The procedure was performed in August 2017 for the first time in Hungary for a HTX recipient. The donor was the healthy daughter of the patient.
In the 5 months after the fecal transplantation the patient was free of GI infections and gained 12 kilograms. With this case we would like to draw attention to an effective treatment option for immunosuppressed patients with recurrent gastrointestinal infections.

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Cardiomyopathy due to severe malnutrition reversed after total parentral nutrition

M Noshi[1]; AT Mahdi[1]
[1]*Sheikh Khalifa Medical City, Abu Dhabi, United Arab Emirates*

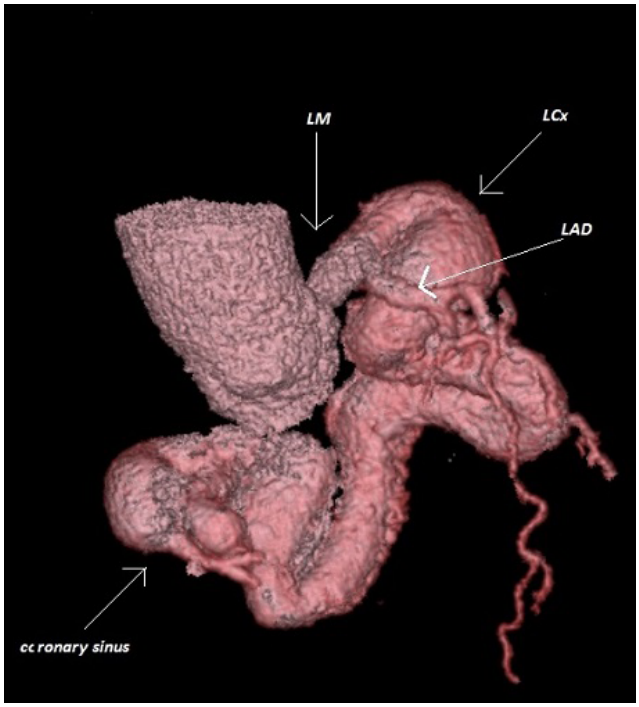
Background: Cardiomyopathy has been linked to nutritional status in conditions such as Beriberi, kwashiorkor, and Keshan disease. Micronutrients deficiency such as selenium has been reported to cause cardiomyopathy. In this case study we present reversal of Cardiomyopathy after treating malnutrition with total parenteral nutrition (TPN).
Case: Our patient is a 19 years old male who was diagnosed with severe Crohn's disease at the age of 8 years. The patient suffered from extensive intestinal strictures that eventually lead to ileocecal resection. Malabsorption and poor oral intake lead to severe malnutrition and growth impairment. At the age of 15 years his creatinine level was less than 15 mmol/L (Normal range 24-77mmol/L), albumin level was 21 mmol/L (normal range 35-52 mmol/L), His hemoglobin was 75 g/L, and His Body mass index (BMI) reached 14 kg/m2. Multiple attempts to enhance enteral feeding have failed. The patient was complaining of chronic fatigue, dyspnea and exertion intolerance. He was diagnosed with Heart failure with reduced ejection fraction of 25 %,gradual TPN refeeding program was started, the patient's nutritional status improved dramatically in the following 2 years ,Hemoglobin reached 105 G/L with normalized MCV of 84, BMI at the age of 19 years reached 23 kg/m2. His Heart failure symptoms improved, Follow up echocardiogram revealed reversal of cardiac impairment with left ventricular ejection fraction of 55%.
In Conclusion We believe that TPN (with proper portions of macronutrients, and micronutrients with trace elements) played a major role in the reversal of cardiomyopathy due to severe malnutrition in a patient with Crohn's disease, We strongly recommend aggressive and early nutritional management in patients suffering from malnutrition to avoid cardiac impairment. In addition, we believe that trace elements status should be monitored in these patients with adequate supplementation to avoid deficiencies.

913

NYHA class III chronic heart failure in 76-year old female with huge coronary fistula from LCx to coronary sinus and arterial pulmonary hipertension

S Nowak[1]; W Wojciech Kula[1]; G Sobieszek[1]; B Olajossy[1]
[1]*1st Military Hospital in Lublin, Cardiology, Lublin, Poland*

A 76-year-old female patient with history of hypertension and hypercholesterolemia, worsening symptoms of NYHA class III chronic heart failure, systolic heart murmur, with echocardiographic features of probable pulmonary hypertension, was referred to the Cardiology Department for diagnosis. The ECG recording revealed sinus rhythm, a dextrogram, an extension of the P-Q interval, and the right bundle branch block. The chest X-ray showed an enlarged heart profile and increased vascular drawing of the lungs. Transthoracic and transesophageal echocardiography reveals enlargement of the right heart cavity, normal left ventricle ejection fraction, moderate aortic and tricuspid regurgitation and the presence of arterial flow from the widened coronary sinus to the right atrium with a maximum speed of 3.1 m/s. Imaging diagnostics were supplemented with a computer tomography and coronary angiography, in which the presence of coronary anomaly was confirmed - widening of the pulmonary trunk to 42mm, dilatation of the left main up to 11 mm, dividing into the correct LAD and significantly widened (up to 22mm) and very twisted LCx, extending into the widened coronary sinus; right coronary artery without significant atherosclerotic lesions with a typical departure and course. In addition, right heart catheterization was performed, which showed pre-capillary pulmonary hypertension - mean pulmonary artery pressure 55 mmHg, total lung gradient 44mmHg, total pulmonary resistance 6.4 WU, heart index 3.8l / min * m2. In the six-minute walk test, the patient overcame a distance of 400m, fatigue assessed 8 points in the 10-point Borg scale. After consultation by the CardioGroup, the patient was qualified for conservative treatment due to the inability to undergo surgical and percutaneous treatment. At the moment, he is awaiting evaluation in the reference center of treatment of pulmonary hypertension against possible anti-proliferative pharmacotherapy.
Fistulas of the coronary arteries are a very rare anomaly observed in 0.05-0.25% of patients undergoing coronarography, the majority of which than the connections of the right coronary artery to the right ventricular cavity. The clinical case presented by us is an example of an extremely rare cause of pulmonary arterial hypertension and chronic heart failure, for which there are no unambiguous therapeutic recommendations



Fistula from LCx to coronary sinus

914

Iatrogenic pulmonary hypertension: a strange cause of heart failure.

J Ramos Jimenez[1]; M Maria Plaza Martin[1]; D Del Val Martin[1]; R Hernandez Antolin[1]; L Salido Tahoces[1]; R Rodriguez Olivares[1]; S Del Prado Diaz[1]; GL Alonso Salinas[1]; S Hernandez Jimenez[1]; JL Zamorano Gomez[1]
[1]*University Hospital Ramon y Cajal de Madrid, Madrid, Spain*

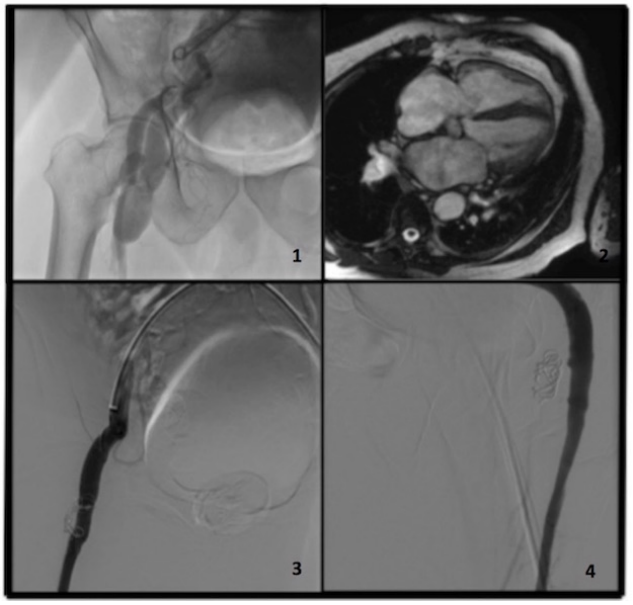
A 67-year-old man was admitted to our hospital in April 2017 due to shortness of breath and functional deterioration to NYHA class III. The patient had a first heart failure episode in January 2017 which was managed in a district hospital.
Respecting previous history, coronary artery disease was known since 2006, when he suffered a first myocardial infarction which was fibrinolysed. In 2014 the patient presented an episode of unstable angina and coronariography was performed by femoral approach. It revealed a total occlusion of right coronary artery, and severe stenosis in circumflex and first marginal arteries, with percutaneous revascularization of these last two. Besides, the patient was hypertensive, former smoker with COPD stage I (GOLD) and had moderate sleep apnea-hypopnea syndrome.

Physical exam showed jugular vein distension, loud second sound and light oedema lower limbs. Resting oxygen saturation was 85%. EKG consist of atrial fibrillation with controlled heart rate and right bundle branch block. Chest X-ray and blood test showed no relevant abnormalities. BNP was 389 pg/mL. Hypoxemic respiratory failure (pH 7,40, pO2 57, pCO2 43) was encountered in resting arterial blood gases. Infectious and autoimmune analysis were negative. Transthoracic echocardiography described preserved LVEF with impaired relaxation, whereas right ventricle was severely dilated with mild systolic dysfunction (TAPSE 15 mm) and PSAP was estimated in 67 mmHg. Right ventricle impairment was confirmed by cardiac-MRI, which also revealed inferior late gadolinium enhancement in relation to ancient myocardial infarction.

As a part of pulmonary hypertension study protocol, thorax-CT was demanded showing signs of mild centroacinar emphysema, dilatation of pulmonary artery trunk and both pulmonary branches. Pulmonary function was tested, with moderate obstruction to air flow (FEV1/FVC 0,67; FEV1 76%) and severely reduced DLCO (34%). That severe reduction and the severity of symptoms was not in concordance with mild imaging alterations. In this sense, a V/Q scintigraphy was performed with no signs of pulmonary embolism, and left-right heart catheterization was demanded with the following findings: PASP 74 mmHg, PADP 31 mmHg, PAMP 45, PWP 15 mmHg, CO 3,9 L/min and no changes in coronary anatomy. At the time of femoral puncture, thrilling was perceived by palpation. Selective iliac arteriography was done, showing arteriovenous fistula with important left to right shunt. Findings were confirmed by aortic-CT.

The patient was submited to percutaneous closure of the fistula with a remarkable improvement in his functional class and hemodinamics a few months after the procedure.

Arteriovenous fistula is responsible for a high output state which is identified as a cause of pulmonary hypertension included in the clinical group 5 of the recent classification. In this case, catheterization was the origin and the solution of this reversible ethiology of heart failure.



1AV fistula. 2RV dilatation. 3-4 result

Poster Session 2

Atrial Fibrillation - Epidemiology, Prognosis, Outcome

P915
Heart rate control in atrial fibrillation and outcomes in acute heart failure patients: the lower the best.

RM Agra Bermejo[1]; A Varela Roman[1]; I Gomez Otero[1]; A Ferrero-Gregori[2]; D Pascual Figal[3]; J Delgado Jimenez[4]; J Alvarez Garcia[4]; F Fernandez Aviles[5]; F Worner Diz[6]; L Alonso Pulpon[7]; J Cinca[2]; JR Gonzalez Juanatey[8]
[1]University Hospital of Santiago de Compostela, Santiago de Compostela, Spain; *[2]Hospital de la Santa Creu i Sant Pau, Barcelona, Spain*; *[3]Hospital Clínico Univeristario Virgen de la Arrixaca, Murcia, Spain*; *[4]University Hospital 12 de Octubre, Madrid, Spain*; *[5]University Hospital Gregorio Maranon, Madrid, Spain*; *[6]Hospital Arnau de Vilanova, Lleida, Spain*; *[7]University Hospital Puerta de Hierro Majadahonda, Madrid, Spain*; *[8]UNIVERSITY CLINICAL HOSPITAL OF SANTIAGO DE COMPOSTELA, DEPARTMENT OF CARDIOLOGY, SANTIAGO DE COMPOSTELA, Spain*

On behalf of: Red Española de Insuficiencia Cardiaca researchers (REDINSCOR II).

Introduction: The optimal resting ventricular rate in patients with AF and HF is uncertai. The ESC HF guidelines recommend that the target for rate control therapyshould be between 60-100 bpm.
Ventricular rates < 70 bpm are associated with a worse outcome.This may explain why betablockers titrated to guideline-target doses failed to reduce morbidity or mortality in patients with HFrEF and AF, and might also explain the association between digoxin and adverse outcomes reported in some observational studies of AF.

Purpose: The aim of the study was to evaluate the impact of the more strict rate control(< 60 bpm) in acute HF patients with atrial fibrillation on short and long- term mortality.
Methods: The analysis included acute heart failure and atrial fibrillation patients enrolled in the REDINSCOR Registry. Patients with sinus rhythm and/or paced rhythm presented during index hospitalization were excluded from the study. Patients were divided into two subgroups according to heart rate at discharge: < 60 bpm or > 60 bpm . The primary endpoint was 30- day and 1- year mortality.
Results: The final analysis included 653 patients; 128 with HR < 60 bpm (18.3%) and 535 with HR >60 bpm (75.1%). There were no differences in age, sex, cardiovascular risk factors, NT-proBNP levels or left ventricular ejection fraction. There were no differences in the use of betablockers but the use of digoxin was higher in the HR > 60 bpm group (36,7% vs 21,4%, p < 0,001). The heart rate at discharge was 54,9 ± 5 bpm in the HR < 60 bpm and 79,2 ± 13 in the HR > 60 bpm group (p < 0,001). There were no differences in the use of betablockers but the use of digoxin was higher in the HR > 60 bpm group (36,7% vs 21,4%, p < 0,001).
The 30 -day mortality was 1,6% in HR < 60 bpm group vs 6,5% in HR >60 bpm group (p = 0,029) and the 1- year mortality was 14,1% in HR < 60 bpm group vs 21.1% in HR >60 bpm group. The Kaplan Meier Curves showed that these differences were statistically significant (FIGURE1). In the multivariate analysis HR>60 bpm (HR 1.70, CI 95% 1.02-2,83, p 0.042), betablockers (HR 0.65, CI 95% 0.45-0.95, p 0.025) and digoxin HR 1.56, CI 95% 1.04-2.32, p 0.030) were predictors of mortality.
Conclusions: In acute heart failure patients with AF HR < 60 bpm is associated with better short and long term prognosis. The use of betablockers not digoxin in this population remains beneficial.

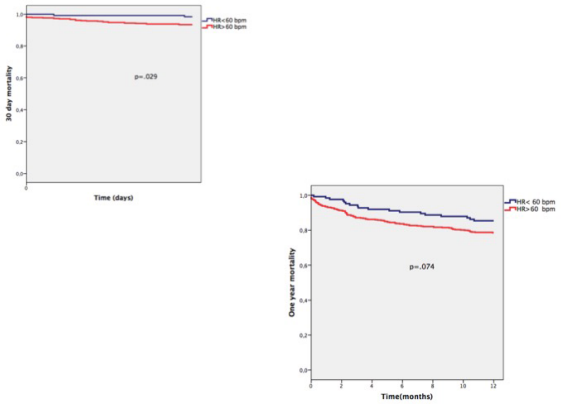


Figure 1

P916
Personalized left atrial substrate modification in patients with long-standing persistent atrial fibrillation and chronic heart failure.

VS Orshanskaya[1]; AV Kamenev[1]; MA Naimushin[1]; LA Belyakova[1]; EN Mikhailov[1]; DS Lebedev[1]
[1]Almazov Federal Heart Centre, Electrophysiology , Saint Petersburg, Russian Federation

Background: Emerging evidence suggests that left atrial (LA) electroanatomic substrate (EAS) outside the pulmonary veins (PV) plays a crucial role in the maintenance of persistent atrial fibrillation (PsAF) and chronic heart failure (CHF). Whether personalized LA EAS modification in addition to circular pulmonary vein isolation (PVI) improves the long-term procedure outcome and heart function in patients with long-standing persistent atrial fibrillation (PAF) and CHF with left ventricular (LV) systolic dysfunction (SD) is unknown.
Method: We prospectively analyzed electroanatomical high density bipolar maps (HDBM) in 125 subjects with long-persistent AF and chronic HF (group I with LVEF < 45%, n = 43 and group II with LVEF = 45 %, n= 82), who underwent circular PVI. Bipolar signals = 0.75mV outside PV, associated with local conduction velocity delay were tagged on LA maps, considered as EAS and measured. Patients in groups I and II were further divided according to whether LA EAS modification to addition to circular PVI was performed (group IA, n= 22; group IIA, n = 36) or not (group IB, n = 21, group II B, n = 46). Patients were followed up with implanted electrocardiographic monitors when possible (63%). Long-term ablation success and LV EF dynamics after procedure were analyzed.
Results: EAS areas were identified in 93 % and 57 % of patients in groups I and II respectively and a mean relative EAS area was 16.8 ± 10.3% and 32.6 ± 18.5% in groups I and II respectively(P = 0,003). The LA roof and the posterior, anterior and septal wall LA were most often affected. During a mean follow-up of 21 ± 8 months, long-term ablation success was higher in group IA than in group IB (64 % vs 38 %; P 0.025) as well as in group II A was higher than in group II B (67.0 % vs 40 %; P 0.03). The mean increase in LVEF following AF ablation was higher in IA group, than IB group (19 ± 9 % vs 8,4 ± 6 %, p = 0,001 respectively) and higher in IIA group than IIB group (11 ± 7 % vs 5,6 ± 5 %, p = 0.04 respectively).
Conclusion: In patients with long-standing persistent atrial fibrillation and heart failure, personalized LA EAS modification in addition to circular pulmonary vein isolation significantly improves their long-term procedure outcome and heart function.

P917

Maze III procedure in patients with heart failure, atrial fibrillation and valve disease

A A Kulikov[1]

[1]*Cardiology Research and Production Center, Moscow, Russian Federation*

Research objective: To estimate effectiveness of Maze III procedure combined with a mitral valve operation in patients with heart failure and long-standing atrial fibrillation.

Methods: In the study were included 100 adult patients (48 men) with heart failure, persistent and longstanding persistent forms of AF and valvular pathologies. Average age of patients was 59 years. Average AF duration was 4 years.

Functional class of heart failure on NYHA 2,7 ± 0,75. The size of the left atrium 5,1 ± 1,5 cm, average left ventricular ejection fraction 61 ± 8,6%.

Antiarrhythmic therapy was tried to all patients, however it was inefficient.

All patients had mitral valve pathology. Also 80% of patients had the tricuspid valve insufficiency.

To all patients the electric cardioversion was made. After restoration of a sinus rhythm, the EP was executed. Then, on the first or second day after EP, correction of valve pathologies combined with "Maze III" procedure was carried out.

Results: Following the results of Maze III procedure combined with correction of valve disease, disposal of AF was observed in 95% of patients. 46% of patients had stable sinus rhythm to the moment of discharge from the hospital. 24% of patients had atrial rhythm with the maximum heart rate of 80-110 bpm (according to results of 24-hour Holter monitoring). For 25% of patients, it was necessary to implant a pacemaker. According to results of EP study, 13% of these patients suffered from sick sinus syndrome before operation. For 9% of the remaining 12% of patients, the indications for pacemaker implantation were atrioventricular nodal rhythm with low heart rate and pauses more than 3 sec long. For 1% of patients the indication was second degree AV block (type 2) and second degree SA block (type 2); for 1% the indication was complete heart block, and for 1% it was atrial rhythm and pauses more than 3 sec long.

13% of patients with an atrial rhythm and normal heart rate developed typical atrial flutter (AFL) in the early postoperative period. For all of them the RF catheter ablation with linear ablation of the right atrial isthmus and creation of isthmus block was effective, and further recurrence of AFL was not observed.

Conclusions: In the early postoperative period Maze III procedure combined with a mitral valve operation proved to be an effective surgical technique of treatment of persistent and long-standing persistent forms of AF in patients with heart failure. NYHA class II heart failure was not an obstacle for surgical treatment of AF.

Ventricular Arrhythmias and SCD - Pathophysiology and Mechanisms

P918

Last but not least: second half of the QRS complex is more important for differential diagnosis between ventricular tachycardias and various aberrant supraventricular tachycardias.

HF Salami[1]; AA Zhambeev[1]; AGH Gasparyan[1]; PS Novikov[1]; NYU Mironov[1]; NB Shlevkov[1]

[1]*Research Institute of Cardiology, violation of rhythm and conductivity, Moscow, Russian Federation*

Background: Majority of known ECG criteria for differential diagnosis between various wide QRS complexes tachycardias (WCT) rely on either initial components of the QRS or the general polarity. The diagnostic significance of the components of the "second half" of the QRS is poorly understood. Aim: to compare the importance of initial and the late components of the QRS for differential diagnosis between various WCT.

Methods: 120 patients (83 M, 37 F, age 47 ± 19) with RBBB tachycardias (n = 60) or LBBB tachycardias (n = 60) were included into the study. All patients underwent EPS resulting in diagnoses of VT (n = 40), SVT with aberrant conduction (n= 40) or SVT with preexcitation (n = 40). Multifactorial and ROC-analyzes of the 240 ECG parameters were performed to compare the diagnostic value of initial (q-beginning to R-peak) and late (R-peak to S-end) components of QRS.

Results: identified 66 significant differences between LBBB groups as well as 140 differences between RBBB groups.

Conclusion: The final components of the QRS are at least highly underestimated for the differential diagnosis between various WCT.

1-?.The most powerful predictors of various LBBB tachycardias

?	ECG criteria	'VT' (n = 20)	'SVT'(n = 20)	'WPW' (n = 20)
1.	The interval R (peak) - S (end) in V2, ms	70 (40-80)	100 (100-120)	110 (100-120)
2.	The interval R (peak) - S (end) in V3, ms	50 (40-50)	105 (100-120)	110 (100-120)
3.	The interval R (beginning) - S (peak) in V2, ms	100 (90-120)	60 (60-70)	90 (80-100)
4.	The duration of the R wave in V5, ms	130 (115-155)	40 (40-78)	135 (120-148)
5.	M-shaped QRS in I	20%	85%	10%
6.	The presence of a wave S in AVL	55%	75%	0%
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1-B.The most powerful predictors of various RBBB tachycardias

1.	The duration of the QRS in II, ms	165 (160-200)	127 (120-135)	130 (118-140)
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3.	The duration of the wave R in I, ms	80 (50-116)	40 (30-40)	60 (40-105)
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6	The duration of the S wave in V6, ms	100 (80-113)	70 (60-80)	60 (40-70)

The cursor shows signs that relate mainly to the initial part of the QRS complex.The bold type indicates features that relate mainly to the final part of the QRS complex.

P919

Heart rate variability in patients with refractory epilepsy

T Faria[1]; M Campelo[2]; H Rocha[3]; R Rego[3]; P Barata[4]; G Pestana[5]; R Pinto[5]; M Silva[5]; D Souteiro[5]; D Alves[3]; JG Pereira[1]; F Rocha Goncalves[4]; E Elisabete Bernardes[4]

[1]*Sao Joao Hospital, Nuclear Medicine, Porto, Portugal*; [2]*Faculty of Medicine University of Porto, Cardiology, Porto, Portugal*; [3]*Sao Joao Hospital, Neurology, Porto, Portugal*; [4]*University of Porto, Faculty of Medicine, Porto, Portugal*; [5]*Sao Joao Hospital, Cardiology, Porto, Portugal*

Introduction: Autonomic heart function is impaired in patients with epilepsy (mainly drug-resistant).Their resting sympathetic tone is increased and their parasympathetic tone (vagus-mediated) is decreased. These conditions lead to diminished protection from the sympathetic stress occurring during seizures which can increase the risk of myocardial lesions and arrhythmias that can cause sudden unexplained death in epilepsy (SUDEP). In other cardiac pathologies, a decrease in heart rate variability (HRV) is associated with worse prognosis.

Objective: To evaluate basal HRV parameters in patients with drug-resistant epilepsy, trying to identify groups with increased risk, more likely to suffer SUDEP.

Material and Methods: From 25th April 2016 to 18th December 2017, we prospectively evaluated patients without known cardiac pathology, hospitalized in our Video-EEG Monitoring Unit, as part of their pre-surgical evaluation of drug-resistant epilepsy. We excluded patients with only psychogenic nonepileptic seizures and those with very frequent seizures which precluded 1-hour basal ECG recording.

All patients underwent a 48 hour single-lead ECG recording from which we evaluated 1 hour while awake and at rest. We included for analysis time and frequency dependent measures of HRV as recommended by the European Society of Cardiology.

Statistical analysis by SPSS version 24.

Results: 47 patients (28?), median age 41 (16-73) years, 51% with Temporal Lobe Epilepsy (TLE), 55.3% with right epilepsies (25.5% left and 19.1% bilateral), 36.2% with cardiovascular risk factors and median epilepsy duration 14 (1-67) years. The most frequent etiology was hippocampal sclerosis (23.4%), but in 34% the etiology remained undetermined.

We did not find any statistical difference in any of HRV parameters between TLE vs non-TLE patients or between right vs left epilepsy patients.
We found negative correlations between SDNN and the duration of the epilepsy (r=-0,458; p = 0,001), and between RMSSD and the duration of epilepsy (r=-0,327; p = 0,025).
Conclusion: In this specific population, there is lower HRV in patients with longer epilepsies, evaluated by the SDNN and the RMSSD parameters, which may point to a higher cardiac risk in those patients. Since the duration of the epilepsy is included in SUDEP risk scores, SDNN and RMSSD may present as biomarkers of that risk.

P920
Relationship between polymorphism of ADRA2B gene and primary cardiac conduction disorders

A Anna Chernova[1]; S YU Nikulina[1]
[1]*Krasnoyarsk State Medical University named prof. V. F. Voino-Yasenecky, Krasnoyarsk, Russian Federation*

Background: Cardiac conduction system (CCS) disease, which results in disrupted conduction and impaired cardiac rhythm, is common with significant morbidity and mortality. Current treatment options are limited, and rational efforts to develop cell-based and regenerative therapies require knowledge of the molecular networks that establish and maintain CCS function. Recent genome-wide association studies (GWAS) have identified numerous loci associated with adult human CCS function, including ADRA2B.
Materials and Methods: A family examination was performed in 71 patients with atrioventricular block (AVB). The control group consisted of 657 patients without clinical ECG manifestations of cardiac diseases. All the examinees have undergone ECG, echocardioscopy, electrophysiological examination of the heart.
Results: by results of research it is established that the frequency of carriers of a homozygous genotype on rare allel (DD) among patients with AVB (43,7% ± 5,9) was higher in comparison with control selection (16% ± 1,4). The obvious tendency to decrease in carriers of a heterozygous genotype (ID) among patients with AVB (23,9% ± 5,1) in comparison with group of control (51,1% ± 2,0) is also noted.
Conclusions: In this work we for the first time revealed on clinical - genetic material association between hereditary disturbances of cardiac conduction and polymorphism of 2-adrenergic receptor gene.

Genotypes:	AVB (n = 71)	Control group (n = 657)	?		
n	%±m	n	%±m		
II	23	32,4±5,6	216	32,9±1,8	?>0,05
ID	17	23,9±5,1	336	51,1±2,0	? <0,001
DD	31	43,7±5,9	105	16±1,4	? <0,001
Allels:					
Allel I	63	32,9±1,8	768	58,4±1,4	? <0,001
Allels D	79	51,1±2,0	546	41,6±1,4	? <0,001
?R; 95% CI OR	1,764;1,244-2,5				
Genotype II	23	32,4±5,6	216	32,9±1,8	?>0,05
Genotypes ID+DD	48	67,6±5,6	441	67,1±1,8	?>0,05
?R; 95% CI OR	0,978;0,58-1,65				

P921
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Conclusion: The final components of the QRS are at least highly underestimated for the differential diagnosis between various WCT.

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P922
The study of the relationship between C reactive protein and the severity of ventricular arrhythmia of non-coronary etiology

H Husniddin Kuchkarov[1]; G Mullabayeva[1]
[1]*Cardiology Center of Uzbekistan, Tashkent, Uzbekistan*

Purpose: The study of the relationship between C - reactive protein (CRP) and the severity of ventricular arrhythmia.
Materials and Methods: 43 patients (18 women, 25 men) with ventricular arrhythmias (VA) were included to the study. The mean age of the patients was 35,8 ± 8 years. All patients had a history of myocarditis, confirmed by extracts from the case histories, outpatient cards. The duration of the anamnesis for myocarditis was 3,2 ± 1,1 years. All patients underwent a 24 hour Holter ECG monitoring in outpatient conditions. The conventional classification of VA by Lown was used for separating of VA. VA of III and and upper classes (IV a and IV b) was assigned as high grades. The level of CRP was determined by using Dayton biochemical analyzer. Patients were divided according to the level of CRP into 2 groups: 1 group (n = 21) patients with CRP level of 6,7 ± 1,9 mg/dl, 2 group (n = 22) patients with CRP less than 5 mg/dl.
Results: as the comparative analysis showed, the groups did not differ in age and gender. But it should be noted that in the 1 group the number of men (16 men in the 1 group against 9 in the 2 group, p > 0,05) was unreliably more. The total number of

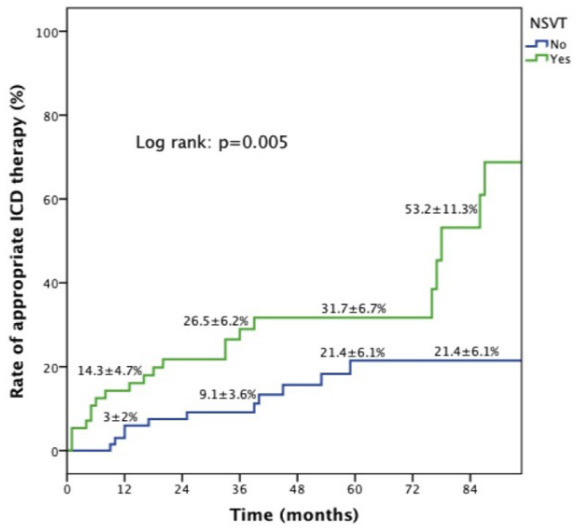
VA in the compared groups was almost similar and amounted to 6368 ± 956 per day and 6920 ± 1000 per day, respectively, in 1 and 2 groups (?>0,05). Structural analysis of VA showed that, the high grade VA prevailed in the 1 group. So VA of II class was observed in 2 (9,5%) and 9 (40,9%) patients, of III class in 3(14,3%) and 6 (27,3%) patients, VI a and IV b in 16 (76,2%) and 7 patients (31,8%) respectively in both groups. Statistical nonparametric analysis demonstrated a significant prevalence of patients with high - grade VA in a group with high level of CRP (?2= 6,8; ? = 0,009). In case of VA with different origins, there were no significant differences (?2 = 0,45; ? = 0,51). It should be noted that in the 2 group there were significantly more frequent cases of VA of II class according to Lown (?2 = 4,0; ? = 0,04).
Conclusion: thus, we identified an association of high levels of CRP with high - grade VA.

Implantable Cardioverter / Defibrillator

P923
Is there a role to implantable cardioverter defibrillator for primary prevention in non-ischemic dilated cardiomiopathy?

JN Neiva[1]; IR Rodrigues[2]; PSC Cunha[2]; BV Valente[2]; NS Nogueira Da Silva[2]; RP Pimenta[2]; ASD Delgado[2]; MB Bras[2]; RCF Ferreira[2]; MO Oliveira[2]
[1]Hospital de Vila Franca de Xira, Cardiology, Vila Franca de Xira, Portugal; *[2]Hospital de Santa Marta, Lisbon, Portugal*

During the last decade implantable cardioverter defibrillator (ICD) became the mainstay of sudden cardiac death (SCD) prevention, resulting in a marked increase of ICD implantation for primary prevention. Despite the proven survival benefit of ICD in patients (P) with severe left ventricular systolic dysfunction, there is much more robust evidence in ischemic cardiomyopathy (ICM). Recent evidence has questioned the benefit of ICD implantation in nonischemic dilated cardiomyopathy (NICM). The aim of this study was to evaluate the long-term clinical impact of ICD in P with NICM for SCD primary prevention, and to investigate the predictors of ventricular tachyarrhythmic events (VTE) in this population.
Methods: Retrospective, descriptive and correlation study extended to P with ICD for primary prevention in NICM. P with hypertrophic cardiomyopathy, right ventricular arrhythmogenic cardiomyopathy, left ventricle noncompaction and inherited channelopathies were excluded. Baseline clinical characteristics were analysed. Uni and multivariate analysis of markers for the occurrence of VTE with appropriate therapy (antitachycardia pacing and shock) via ICD and of overall mortality was performed. The statistical methods used were Mann-Whitney's U test, Chi-squared test and Cox regression.



Survival curve

Results: Within a population of 126P with NICM (69% male; age 60,8+11,2 years; NYHA class II/III; 69% with a cardiac resynchronization therapy system - CRT -), 28,8% had diabetes mellitus (DM); 38,4% dyslipidemia; 60,8% hypertension (HT) and 25% permanent atrial fibrillation (AF). The mean ejection fraction (EF) was 25%. Natriuretic peptides were high in 78,4% of the P, 29,8% had creatinine clearance <60mL/min and 45,5% had nonsustained ventricular tachycardia (NSVT) on 24h Holter recording before ICD implantation. After a median follow-up time of 61months (6-139), the mortality rate was 14,3% and 2P underwent heart transplantation. Appropriate therapies occurred in 27% of the cases. The first appropriate intervention occurred after a median of 49,2 months. P with NSVT had more appropriate therapy (12 months: 14,3 ± 4,7% vs. 3 ± 2%; 36 months: 26,5 ± 6,2% vs. 9,1 ± 3,6%; 84 months: 53,2 ± 11,3% vs. 21,4 ± 6,1%; p= 0,005). The occurrence of NSVT before implantation was a strong predictor of appropriate ICD therapy (HR 2,59, 95% CI 1.29-5.19; p = 0,008). Gender, age, EF, NYHA class, AF, DM, HT, dyslipidemia, CRT, renal dysfunction and elevation of natriuretic peptides were not predictors of therapy via ICD.
Conclusions: In a long-term follow-up period, 27% of NICM P received appropriate therapies after ICD implantation for primary prevention. NSVT seems to be a strong predictor of appropriate therapy delivered.

P924
Right ventricular septal pacing with narrow QRS less than 125ms is beneficial for preventing pacing induced cardiomyopathy

DH Kim[1]; SY Lee[1]; SW Park[1]
[1]Sejong General Hospital, Arrhythmia division, Cardiology department, Bucheon, Korea Republic of

Background: When ventricular pacing more than 40% is expected for patients with complete AV block, current guideline demonstrates that bi-ventricular pacing is recommended for preventing pacing-induced cardiomyopathy. However, it is not clear that right ventricular (RV) septal pacing is more beneficial than RV apical pacing.
Objective: Narrow QRS after pacing is more important factor than pacing site. We hypothesize that RV septal pacing with narrow QRS is beneficial for preventing pacing-induced cardiomyopathy.
Methods: Total 117 consecutive patients with complete AV block and pacemaker implantation were studied from 2014 to 2016. RV septal pacing was performed in 66 patients and RV apical pacing was performed in 51 patients. Pacing induced cardiomyopathy was defined as reduced left ventricular ejection fraction (LVEF) after pacing compared to baseline LVEF before pacing. We evaluated LVEF, aggravation of tricuspid regurgitation (TR), ventricular diastolic dimension (LVDD), and left ventricular systolic dimension (LVSD).
Results: QRS width after septal pacing is less than QRS width after apical pacing (122 ± 28ms vs. 137 ± 33ms, p = 0.007). During the mean 20.9 ± 17.7 months, there is no significant differences of change of LVEF between septal pacing and apical pacing (-5.57% vs. -3.94%, p = 0.292). Aggravation of TR is not different (12.1% vs. 23.5%, p = 0.138). The change of LVDD is not different (-1.8mm vs. -0.7mm, p = 0.614). The change of LVSD is not different (1.2mm vs. 1.5mm, p = 0.158). However, patients with narrow QRS less than 125ms after RV septal pacing have experienced less reduced LVEF than those with wide QRS more than 125ms after pacing (-2.56% vs. -6.35%, p = 0.040). Aggravation of TR is not different (15.2% vs. 18.3%, p = 0.803) after pacing. The change of LVDD (-1.9mm vs. -0.4mm, p = 0.348) and LVSD (1.8mm vs. 0.6mm, p = 0.827) is not different.
Conclusion: This study showed that RV septal pacing with narrow QRS less than 125ms is beneficial for preventing pacing-induced cardiomyopathy

Cardiac Resynchronization Therapy

P925
The significance of NT-proBNP plasma concentration at baseline for predicting outcomes after CRT-D implantation in heart failure patients

M Michal Kerekanic[1]; M Hudak[1]; S Misikova[1]; E Komanova[1]; A Boho[1]; B Stancak[1]
[1]East-Slovak Institute of Cardiovascular Diseases, Department of Arrhythmias, Kosice, Slovak Republic

Introduction: The efficacy of cardiac resynchronization therapy (CRT) in patients with heart failure (HF) in ambulatory class NYHA III or IV and wide QRS complex has been established in numerous clinical trials. N-terminal fragment produced from the cleavage of proBNP (NT-proBNP) is commonly used and well established in daily clinical practice in diagnostic and monitoring of treatment of HF. The importance of baseline levels of NT-proBNP in HF patients before CRT implantation and its impact on survival and mortality has not been enough evaluated until now. Aim of our study was evaluated whether it is possible to determine cutoff value of NT-proBNP level at baseline that can predict all-cause mortality after CRT implantation.
Methods: We realized prospective study and enrolled patients during the time period from May 2011 to April 2013. Eligible patients had advanced HF regardless of etiology, severe systolic dysfunction of left ventricle with ejection fraction (EF) = 35%, native QRS complex duration = 120 ms and optimal medical therapy. The primary endpoint was death from any cause. Serum concentrations of NT-proBNP levels at

baseline were analyzed by ROC analysis, and the cut-off value was calculated for primary endpoint. Patients were divided into two groups according to the cut-off value of serum concentration of NT-proBNP.
Results: We enrolled 90 patients. The primary endpoint occurred in 22 patients (24,4%). Cut-off concentration of NT-proBNP for primary endpoint was 1401 ng/ml at comparable values of sensitivity and specificity (AUC 0,8; p = 0,001). The primary endpoint was reached by 5 patients in group with NT-proBNT level less than 1401 ng/ml (entitled group A) and by 17 patients (51,5%) in group with level of NT-proBNP equal or more than 1401 ng/ml (entitled group B). Survival of patients in both groups was calculated using Kaplan-Meier analysis. Patients in group B had statistically significant survival, p <0,001 according to log-rang test. Impaired renal function (HR 1.04, p = 0.001) and elevated level of NT-proBNP (equal or more than 1401 ng/ml) (HR 5.26, p = 0.002) were independent predictors of increasing risk of all-cause mortality after adjusting using multivariable analysis.
Conclusion: The baseline NT-proBNP level is independent predictor of all-cause mortality of HF patients who undergoing CRT implantation. It can be used for selection high risk patients before CRT implantation. The choice of specialized treatment (assist devices, heart transplantation) in first line for high risk patients (elevated NT-proBNT level = 1401 ng/ml) could be potential possibility how to decrease high amount of nonresponders to CRT.

P926
Cardiac resynchronization therapy in the elderly

A Lorente Ros[1]; S Del Prado Diaz[1]; JM Vieitez Florez[1]; M Abellas Sequeiros[1]; J Moreno Planas[1]; E Franco Diez[1]; GL Alonso Salinas[1]; JL Zamorano[1]
[1]University Hospital Ramon y Cajal de Madrid, Cardiology Department, Madrid, Spain

Introduction: Chronic heart failure is a common and prevalent entity in elderly patients. However, the benefit and safety of cardiac resynchronization therapy (CRT) in this patient population are not well defined. The objective of this study was to analyse the safety and outcomes after CRT in elderly patients.
Methods: Patients aged = 80 years referred to CRT in 2015 and 2016 in a tertiary care hospital were consecutively included. Baseline demographics, complications and outcomes were retrospectively analysed. Functional class, left ventricle ejection fraction (LVEF) and number of hospitalizations over a one-year period were registered and compared before and after the procedure.

Figure 1.

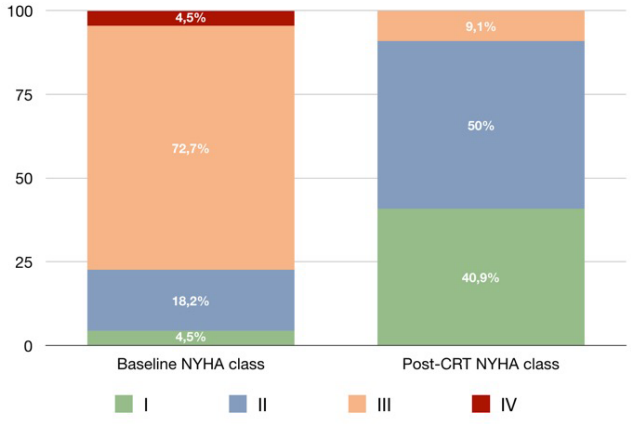


Figure 1

Results: Patient characteristics: A total of 22 consecutive elderly patients were included with a median follow-up of 383.0 (329.5-620.0) days. Age at implantation was 83.6 ± 2.5 years and 14 (63.6%) were male. Cardiovascular risk factors were prevalent: 18 (81.8%) patients suffered hypertension, 11 (50%) diabetes, and 13 (59.1%) dyslipidaemia. 11 (50%) patients presented atrial fibrillation, ischemic aetiology was present in 9 (19.1%) patients and 16 (72.7%) were in NYHA functional class III at baseline. 6 cases (27.3%) were upgrades from previously implanted pacemakers. No defibrillator therapy was implanted. Atrioventricular node ablation was performed in 5 (22.7%) patients. Median serum creatinine and BNP were 1.1 (0.9-1.3) mg/dl and 574 (216-1281) pg/dl, respectively.
Outcomes: Improvement in functional class was observed in 16 patients (72.7%) and was significant (Figure 1). The number of heart failure admissions over the first year of follow-up decreased compared with the year before implantation (0.6 ± 0.7 vs 0.2 ± 0.4; p = 0.021). LVEF significantly improved (34.9% ± 7.7 vs 43.8% ± 9.4, p = 0.021). There was only one complication (4.5%) reported that required medical assistance: a device infection requiring explant and surgical re-implantation. Two deaths were reported, both after the first year of follow-up: a sudden death and a non-cardiovascular death.
Conclusions: In the subgroup of patients aged = 80 years, CRT is safe and effective. It improves functional class and decreases the number of hospital admissions due to heart failure on the first year of follow-up.

P927
Correlation between change in QRS duration and responsiveness in patients with heart failure and CRT device.

J Joao Pedro De Sousa Bispo[1]; D Carvalho[1]; P Azevedo[1]; J Guedes[1]; T Mota[1]; R Fernandes[1]; D Bento[1]; R Candeias[1]; A Camacho[1]; I Jesus[1]
[1]Faro Hospital, Cardiology, Faro, Portugal

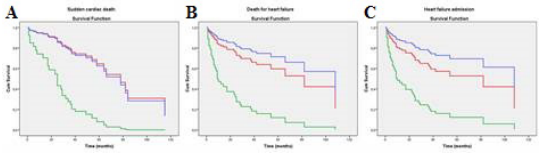
Introduction: Prediction of responsiveness to cardiac resynchronization therapy (CRT) in heart failure patients remains a challenge. This study intends to determine whether the degree of change in QRS duration is a good predictor of responsiveness and lower mortality.
Methods: Retrospective study of a group of patients with heart failure that have CRT device. QRS duration change was calculated from pre- and post-implantation 12-lead ECG, and correlated with LVEF and symptom improvement, all-cause mortality and all-cause hospitalization.
Results: A total of 55 patients were included, 38 (69,1%) were male, and average age was 67,0 ± 15,5 years. Follow-up was 25,1 ± 17,8 months. Most common diagnosis were dilated cardiomyopathy in 28 (50,9%) patients and ischemic cardiopathy in 20 (36,4%). Previously to implantation, QRS duration was 170,5 ± 24,2 msec, 23 (42,9%) patients were in NYHA classification of 3 or 4, and average LVEF was 27,5% ± 6,2. The device implanted was a CRT-D in 44 (80,0%) cases. After implantation, there was a significant decrease in QRS duration (170,5 ± 24,2 vs 139,2 ± 24,3 msec, p-value <0,001), in NYHA classification (42,9% in NYHA III or IV vs 18%, p-value <0,001) and a significant increase in LVEF (27,5 ± 6,2 vs 42,6 ± 14,2, p-value < 0,001). There was no direct correlation between degree in decrease of QRS duration and increase in LVEF (Pearson correlation = 0,072, p-value = 0,63).
A total of 13 (23,6%) patients were hospitalized and 10 (18,2%) patients died during follow-up. There was a non-significant trend towards lower QRS duration change among patients that died (16,9 ± 28,8 vs 35,3 ± 27,4, p-value = 0,051). There was no difference between hospitalization status (23,1 ± 28,7 vs 34,5 ± 28,1, p-value = 0,71). In the composite end-point of hospitalization and mortality, there was a significantly lower QRS duration change in patients that had an event (19,3 ± 29,9 vs 36,5 ± 26,8, p-value = 0,045).
Conclusion: Change in QRS duration had no correlation with less symptoms and higher LVEF after device implantation. A higher QRS duration change showed a non-significant trend towards lower all-cause mortality, and a significant reduction in a composite end-point of all-cause mortality and hospitalization.

P928
Electrophysiological parameters predictive of clinical response to cardiac resynchronization therapy.

M Matteo Casale[1]; M Mezzetti[2]; M Gigliotti De Fazio[1]; M Morelli[2]; L Caccamo[2]; P Busacca[2]; G Dattilo[1]
[1]University of Messina, Messina, Italy; *[2]Hospital S. Maria della Misericordia, Operative Unit of UTIC and Cardiology, Urbino, Italy*

Background: Left ventricular lead implantation in maximally electrically delayed site recently allowed optimal results in patients undergoing to CRT. However most of the studies had small follow up periods without prospective evaluation.
Purpose: We assessed in a prospective way the long term clinical response to CRT in patients undergoing to left ventricular stimulation in sites of maximum delay.
Methods. 130 consecutive patients underwent to CRT. In 86 the maximum local delay (QLV) was electrophysiologically assessed and the remaining 44 underwent to a standard implantation technique of the left ventricular lead. Clinical status was evaluated within a median period of 25 (IQR = 13-47) months. The presence of heart failure (HF) rehospitalizations, HF death or sudden cardiac death (SCD) identified the nonresponders.
Results: Receiver operating characteristic (ROC) curve analyzes for QLV were significant for all the study endpoints: p= 0.015 for SCD; p= 0.015 for death due to HF; p= 0.035 for HF re-hospitalizations. A cutoff of 25 msec had a sensibility of 12.5% and a specificity of 100% for SCD and HF death, a specificity of 100% and a sensibility of 11.8% for HF re-hospitalizations. Survival analysis by Cox proportional hazards regression showed a significantly worse clinical outcome for patients with a QLV = 25 msec (Figure - green line) in comparison to patients with QLV>25 msec

(blue line) and to patients with standard implantation technique (red line). SCD was significantly higher (p = 0,024; HR= 5,74) compared to patients with a QLV>25 msec (Figure - Panel A). There was a significant (p = 0,015; HR= 6,3) better long-term survival free from HF death in patients with a QLV>25 msec in comparison to those ones with QLV = 25msec (Figure - Panel B). HF re-hospitalizations were significantly (p = 0,021; HR= 5,76) less for patients with a QLV>25 msec compared to those ones with QLV = 25 msec (Figure - Panel C).
Conclusion: Targeting sites with a QLV < 25 msec is associated with a long term poor prognosis due to sudden cardiac death, heart failure death and heart failure re-hospitalizations. This intraoperative assessment is easy and cost effective, being feasible also by standard programmer. Clinical response to CRT is improved by this simple assessment.



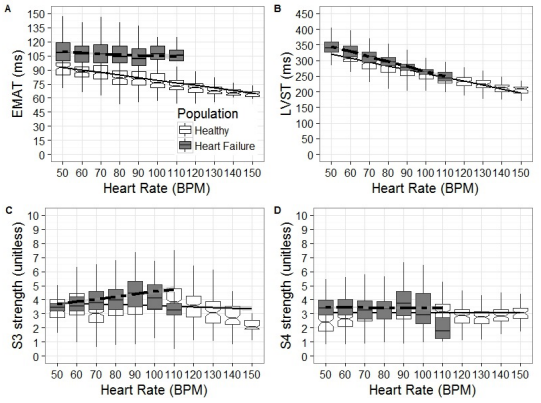
Home and Remote Patient Monitoring

P929

Heart rate affects cardiac acoustic biomarkers: implications for ambulatory management of heart failure patients

R Perumal[1]; T Masuda[1]; M Shozakai[2]
[1]*ZOLL, Pittsburgh, United States of America*; [2]*Asahi Kasei Corporation, Kanagawa, Japan*

Purpose: Ambulatory management of heart failure (HF) is challenging. Cardiac acoustic biomarkers (CABs) can be recorded noninvasively using an accelerometer on the chest and timing these heart sounds to ECG signals, thus enabling remote monitoring. CABs are related to both systolic and diastolic function. However, it has not been determined that CABs can be used independent of heart rate. The purpose of this study is to define the relationship of CABs and heart rate in healthy and HF subjects.
Methods: CABs were collected from 15 healthy volunteers (87% male, age: 33 ± 15 years), wearing an acoustic cardiography enabled accelerometer with ECG electrodes during graded exercise. CAB and heart rate data were also accumulated from 1433 acute HF patients with EF = 35% (78% male, age: 58 ± 13 years), who wore an acoustic cardiography enabled wearable cardioverter defibrillator. The following systolic and diastolic CABs were calculated from the recorded heart sounds and ECG signals: electromechanical activation time (EMAT) measured from the onset of the Q wave to 1st heart sound; left ventricular systolic time (LVST) measured from 1st heart sound to 2nd heart sound; S3 and S4 "strengths" (calculated based on the third and fourth heart sounds intensity and persistence, and expressed as a continuous variable on a scale of 0 to 10). Analysis of variance were used examine the impact of heart rate changes on CABs in both healthy and acute HF groups.



Box-plot with linear trend line

Results: For healthy subjects, both EMAT and LVST showed a significant (p <0.05) decrease with increased heart rate (Figure). For acute HF patients, EMAT did not significantly change with increased heart rate whereas LVST showed a significant decrease as heart rate increased. S3 strength did not change with heart rate in healthy subjects, but showed a significant though modest increase with heart rate in the HF group. S4 strength did not change significantly with heart rate in either group.

Conclusions: In contrast to healthy subjects, EMAT did not change with heart rate in the HF group, implying an inability to increase contractility with demand. S3 strength showed an increase with heart rate in the HF group suggesting reduced ventricular compliance in early diastole. EMAT, S4, and possibly S3 could be used independent of, or in conjunction with, heart rate for ambulatory monitoring of HF. Ongoing evaluations will determine if changes in CABs are associated with outcomes, thereby providing a useful signal by which to guide therapy.

P930

Therapeutic approach to implantable haemodynamic monitoring: a strategy based on timing of haemodynamic recordings

S Shankho Ganguli[1]; C Sauld[1]; O Cheema[1]; TE Hastings[1]; E Roberts[1]; A Ghafoor[1]; DL Zwicke[1]; V Thohan[1]; N Sulemanjee[1]
[1]*Aurora Sinai/Aurora St. Luke's Medical Centers, Aurora Cardiovascular Services, Milwaukee, United States of America*

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Background: Despite significant advancements in management, heart failure (HF) exacerbation is still the leading cause of hospitalisation in the western world. Until recently, there was no definitive way to predict those who are on the precipice of another exacerbation. Now, with remote implantable haemodynamic monitoring (RIHM) devices assessing pulmonary artery (PA) pressures, heart failure (HF) patients can be diagnosed prior to another heart failure exacerbation and prevent hospitalisation with appropriate titration of medications. We propose that optimising the timing of PA pressure measurements will lead to a more accurate reflection of haemodynamics and thus better treatment.
Purpose: RIHM device has been growing as an effective strategy to manage HF and reduce hospitalisations. Unlike standard drug regimen, current practice leaves the timing of these haemodynamic measurements to the patients, leading to large variances in observations. We hypothesize that standardising the timing of these measurements will lead to an accurate reflection of response to therapy and effective utilisation of this technology.
Methods: This is a prospective randomised study. We included all patients in the Advanced Heart Failure Clinic implanted with RIHM in 2015. Out of 27 patients, 12 met the inclusion criteria. First, everyone underwent a 3-day period of checking PA measurements twice a day, once before and then 1 hour after taking their morning meds. Next, the patients were randomised in a 1:1 manner into two groups. Group 1 took all measurements per patient preference and Group 2 took all their measurements 1 hour after. We collected PA pressure trends, medication adjustments and HF hospitalisations at baseline, 1 and 4 months. We also collected additional information on 6-minute walk test (6MWT) and heart failure QoL questionnaire.
Results: There was no statistically significant difference in PA systolic pressure (PASP), pulmonary artery diastolic pressure (PADP) and mean pulmonary artery pressure (PAP) obtained pre- and post-medication during the initial 3 days prior to randomisation. Timing of the readings had no statistically significant effect on change in PASP (p = 0.683), PADP (p = 0.485), or mean PAP (p = 0.254) from baseline to 4 months, and had no statistically significant effect on change in creatinine from baseline to 4 months (p = 0.320). Repeated measure ANOVA showed no statistically significant effect of timing of readings on HF QoL (p = 0.445) and 6MWT (p = 0.146) Results: There was no statistically significant difference in number of medication adjustments between the groups.
Conclusion: Our pilot study tried to answer the clinically relevant question of whether timing of haemodynamic (PA pressure) measurements affects observations and clinical outcome. We did not find any statistical difference in the PAPs or clinical outcomes in pre- vs post-medications groups; however, a larger sample size may be required to be conclusive.

Chronic Heart Failure - Pathophysiology and Mechanisms

P931

Cardiopulmonary exercise testing in pulmonary hypertension associated with congenital heart disease vs. other forms of pulmonary hypertension: physiological insights

FM Righini[1]; A Apostolo[1]; C Carlo Vignati[1]; P Bambul Heck[2]; S Farina[1]; A Hager[2]; M Correale[3]; R Badagliacca[4]; S Sciomer[4]; P Agostoni[1]

[1]Cardiology Center Monzino IRCCS, Heart Failure Unit, Milan, Italy; [2]Deutsches Herzzentrum Technische Universitat, Department of Pediatric Cardiology and Congenital Heart Disease, Munich, Germany; [3]UTIC Universitaria Ospedali Riuniti OO.RR , Cardiologia-UTIC Universitaria, Foggia, Italy; [4]Sapienza University of Rome, Dipartimento di Scienze Cardiovascolari, Respiratorie, Nefrologiche, Anestesiologiche e Geriatriche, Rome, Italy

Background: Cardiopulmonary exercise testing (CPET) allows the assessment of integrative cardiopulmonary response to exercise.
Objectives: To evaluate CPET parameters behaviour in adult pulmonary hypertension (PH) patients with congenital heart disease (CHD) and without CHD.
Methods: The present is a multicenter retrospective study which includes PH Group 1 and 4 patients. All subjects underwent full clinical and instrumental evaluation, including CPET and right heart catheterization.
Results: 166 PH patients (92 women and 74 men, 56 CHD and 110 non-CHD) were enrolled. CHD patients had higher pulmonary pressure (mPAP: 60.1 ± 19 mmHg vs 43.1 ± 16.2 mmHg, p<.0001) and lower systemic cardiac output (3.8 (3.1;4.4) L/min vs 4.5 (3.9;5.4) L/min, p = 0.0094). At CPET they had lower peakVO2/kg (13 ± 3.6 ml/kg/min vs 15.5 ± 4.2 ml/kg/min, p = 0.0002) and higher VE/VCO2 slope (54.6 ± 15.9 vs 45.6 ± 14.3, p = 0.0003). Moreover patients were paired for gender and peakVO2 (± 1 ml/min/kg), obtaining 47 pairs and even so CHD patients had higher pulmonary pressure (mPAP: 58.7 ± 19.9 mmHg vs 43.9 ± 17 mmHg, p = 0.0004) and VE/VCO2 slope (54.2 ± 15.3 vs 47 ± 15.1, p= 0.0248). VE/VCO2 slope correlated with SpO2 at peak exercise only in CHD patients.
Conclusions: In PH CHD patients, pulmonary pressure and VE/VCO2 are higher compared to non-CHD PH patients, while CO and peakVO2 are lower. After matching patients for peakVO2, pulmonary pressure and VE/VCO2 remains higher in ACHD patients suggesting that the long term adaptation to high pulmonary pressure, hypoxia and low systemic cardiac output, as well as a persisting shunt has, at least partially, preserved exercise performance of PH-ACHD patients.

P932

The occurence of Heart failure result in low weight at birth in woman with congenital heart disease

S Sonila Bele[1]; A Rrugia[2]; E Petrela[3]
[1]University Hospital"Queen Geraldine" Tirana, Tirana, Albania; [2]University Hospital"Koco Glozheni" , Tirana, Albania; [3]University Hospital Centre "Mother Theresa",Tirana, Tirana, Albania

Background: Obsetric and neonatal complications are common during pregnancy and delivery in woman with congenital heart disease. Heart failure can cause premature labor or arrhythmias Risk of maternal or fetal death correlates with NYHA functional classification.
Objective: To evaluate the course of pregnancy in patients with Congenital Heart Disease in severale cases that referred to our clinic.
The Material and Methods: This study was monitored in a single-centre cohort between Janary 2000 and December 2016 The data and information have been collected through clinical record sheets. Patients with valvular heart disease were excluded and only patients with documented unrepaired or repaired Congenital Heart Disease(CHD) entered the study.
Results: Pregnancy outcomes were analyzed in 352 consecutive women aged 29.8 ± 5.5 years with heart disease. The patients with corrected CHD including 19 % of all cases and patients with uncorrected CHD including 19,3 % of all cases .These including Atrial Septal Defect, Ventricular Septal Defect, Tetralogy of Fallot ,Coarctation of the Aorta, The ductus Botalli, Pulmonary Stenosis, Transposition of the Great Arteries,Ebstein 'Anomaly,Eisenmenger Syndrome.There was no maternal mortality. Primipare were 47,6% of women.
Average birth number is 1,71 ± 0.89.Average baby weight is 2829.4 ± 629 gr. The occurrence of Heart failure were 18.7% of all cases. Preeclampsia (28.4 %% of all cases with corrected CHD and 36.6%% of all cases with uncorrected CHD) may be modifiers of the risk of CV complications. By looking through correlation Kendal's coeficient, a relation was found between weight at birth and Heart failure (p <0.001), uncorrected CHD(p = 0.017), weight and Tetralogy of Fallot(p = 0.029), weight and Coarctation of the Aorta(p = 0.018). As well as weight and Pulmonary Hypertension at birth (p = 0.003). The occurence of such pathologies result in low weight at birth.
Conclusion: Most women with successful repair CHD can have a successful pregnancy Risk is increased even such women have symptoms. Women with class III or IV heart failure or may be advised to obtain an early therapeutic abortion

P933

Relationship between serotonergic-modulating psycoactive treatments and 24-hour Cheyne-Stokes respiration occurrence in systolic heart failure.

G Gianluca Mirizzi[1]; C Borrelli[1]; A Giannoni[2]; F Bramanti[2]; G Iudice[2]; M Emdin[1]; C Passino[1]
[1]Sant'Anna School of Advanced Studies, Pisa, Italy; [2]Gabriele Monasterio Foundation, Department of Cardiovascular Medicine, Pisa, Italy

Background: central apneas (CA) in the form of Cheyne-Stokes respiration in systolic heart failure (HF) occur frequently during the 24-hour and are associated with excess mortality. In animal models, enhanced brainstem serotoninergic neurotransmission has been linked to central apneas development via enhancement of central chemoreflex sensitivity. Psychiatric comorbidities are frequently diagnosed in HF and often treated with central serotonergic-modulating drugs.
Purpose: to evaluate the relationship between serotonergic-modulating treatments and CA occurrence in systolic HF.
Methods: among 667 patients with systolic HF (mean left ventricular ejection fraction -LVEF- 32 ± 9, age 67 ± 12 years, 75% males, BMI 27.5 ± 5.4 kg/m2, N-terminal fragment of pro-brain natriuretic peptide, NT-proBNP, 1435 ng/L, interquartile range -IR- 585-3615), 438 (65.7%) showed CA, expressed by an apnea/hypopnea index (AHI) = 5 and CA/total apnea = 50% (mean AHI 18/h, IR 9-27). Psychoactive treatment was prescribed in 25% of patients, with 11% taking benzodiazepines, 17% serotonergic modulating drugs (selective serotonin or serotonin/norepinephrine reuptake inhibitors, SSRI/SNRI in 11% of patients, trazodone in 9.8%). Patients on psycoactive treatment showed similar levels of 24-h AHI (17.0/h, interquartile range -IR- 8.0-28.0 vs. 18.0 ev/h, IR 9.0-27.0 p = ns) and 24-h central apnea index (CAI; 6.1 ev/h, IR 1.2-17.7 vs. 5.8 ev/h, IR 1.6-15.6, p = ns); similar results were observed for nighttime and daytime AHI and CAI and in specific therapeutic subgroups of patients. Among patients with the highest risk of having CA (expressed by levels of NT-proBNP = 1680 ng/l), psycoactive treatment was not associated with differences in AHI or CAI. Treatment with SSRI/SNRI was associated with a trend towards increased levels of 24-h CAI (14.2 ev/h, IR 9.5-20.9 vs. 12.1 ev/h, IR 3.6-28.4, p = 0.08).
Conclusion: among systolic HF patients and CA/CSR, psychoactive treatments modulating serotonergic neurotransmission are very often prescribed; CA occurrence, albeit significant, is however not influenced by serotonergic drugs.

P934

The association between markers of fibrosis and myocardial dyssynchrony in patients with CHF

OV Bilchenko[1]; TA Rudenko[1]
[1]Kharkiv Medical Academy for Postgraduate Education , Internal medicine and Nephrology, Kharkiv, Ukraine

Background: Pathological activation of fibroblasts and collagen synthesis contributes to increased reactive interstitial myocardial and substitutional fibrosis, which leads to myocardial dyssynchrony and the progression of CHF.
Purpose: To study the association between markers of fibrosis and myocardial dyssynchrony in patients with CHF and DM type 2.
Methods: 106 patients (63 women and 43 men) with CHF of ischemic origin examined. The mean age of patients was (67.45 + 10.32) years; age (65 + 10.62) years. All patients divided into two groups depending on the presence of DM. The first group consisted of patients with DM (83 persons - 78.3%). The second group - patients without DM (23 - 21.7%). All patients were subjected to a standard 12 leads electrocardiography (ECG) according to the generally accepted method. To detect electrical dyssynchrony, the criteria of a narrow QRS complex <120ms and an extended QRS complex = 120ms were used. Myocardial dyssynchrony was divided into intraventricular, interventricular, atrial-ventricular (atrioventricular) and combined. The presence of myocardial fibrosis was assessed by the content of galectin (Gal) -3 in the blood serum by an enzyme immunoassay (EIA) and the content of matrix metalloproteinase (MMP) 1. The interstitial collagen volume fraction (ICVF) was calculated using the J. Shirani method.
Results: In patients with myocardial dyssynchrony on the background of DM type 2, compared with the group without DM, there was an increase in Gal-3 (7.49 + 0.6) ng/ml and ICVF (7.6 ± 4.03%) and a decrease in MMP-1 (0.46 + 0.2) ng/ml (p <0.05). Gal-3 increased in the presence of combined forms of mechanical dyssynchrony. Thus, with simultaneous combination of intra-ventricular and interventricular or Atrioventricular myocardial dyssynchrony, the level of Gal-3 was the highest (9.03 + 4.63) ng/ml against a background of a decrease in MMP-1 (0.2 ± 1.7) ng/ml. In patients with the presence of one of the forms of myocardial dyssynchrony, Gal-3 was lower (6.67 + 5.14) ng / ml, but the level of MMP-1 (0.78 + 1.55) ng/ml increased (p <0, 05). In patients with CHF of ischemic genesis without DM type 2 and myocardial dyssynchrony, the level of Gal-3 was the lowest (5.13 ± 0.37) ng/ml. A high content of Gal-3 was observed in patients without DM type 2 with manifestations of myocardial dyssynchrony (7.92 ± 0.95) ng/ml.

Conclusions: when there is a combination between CHF of ischemic genesis and DM type 2, there is an increase in the serum level of Gal-3, which correlates with the progression of mechanical dyssynchrony, an increased Functional class (FC) of CHF, development of systolic and diastolic failure. The content of MMP-1 depends on the form of mechanical myocardial dyssynchrony - decreases in combined forms.

P935

Circulating biomarkers of inflammation and left ventricular hypertrophy in patients with heart failure with preserved ejection fraction

A V Alexandr Bilchenko[1]; AA Bilchenko[2]; MA Khvysiuk[1]
[1]Kharkiv Medical Academy for Postgraduate Education , Internal medicine and Nephrology, Kharkiv, Ukraine; *[2]Kharkiv National Medical University, Internal medicine, Kharkiv, Ukraine*

Background: The association between left ventricular hypertrophy (LVH) and high sensitivity CRP values has recently been investigated. Little is known, however, about the association between LVH and the new biomarkers of inflammation P-selectin and galectin-3 in patients with HFpEF.
Purpose: The goal of our study was to investigate the relations between several inflammatory markers (P-selectin and galectin-3) and LV geometry in patients with HFpEF.
Methods: 73 patients with HFpEF NYHA II-III (28 men and 44 women; mean age 72.2+5.1 years) were included in the study. All subjects underwent routine laboratory tests, as well as specific biomarkers assessment (P-selectin, galectin-3) by using standard kits. Left ventricular mass index (LVMI) was measured. LV geometry was divided into four categories: normal LV geometry, concentric LVH, eccentric LVH and concentric remodeling.
Results: In patients with concentric left ventricular hypertrophy P-selectin level was significantly higher as compared with patients without left ventricular hypertrophy (98,1+4,3 vs 86,3+3,2 ng/ml) ($p < 0.05$). In patients with eccentric LVH and concentric remodeling P-selectin levels were not increased as compared with patients without left ventricular hypertrophy (88,1+3,3 ng/ml and 84,9+2,6 ng/ml, respectively, ($p > 0.05$). There was no significant difference in galectin-3 levels in four groups (10,2+3,4 ng/ml; 9,8+2,5 ng/ml; 9,7+4,1 ng/ml and 10,5+3,7 ng/ml, respectively, ($p > 0.05$).
Conclusions: P-selectin was increased significantly in HFpEF patients with concentric left ventricular hypertrophy but did not in patients with eccentric LVH and concentric remodeling. There was no difference of galectin-3 levels in HFpEF patients with all types of LVH as compared with patients without left ventricular hypertrophy.

P936

Radiation induced valve disease and cardiotoxicity induced heart failure is frequent

J Bergler-Klein[1]; M Schneider[1]; M Frey[1]; M Gyongyosi[1]; T Binder[1]
[1]Medical University of Vienna, Dept. of Cardiology, Vienna, Austria

Radiation of the mediastinum causes direct linear damage of the myocardium. Additional chemotherapy and oncologic therapies may cause cardiotoxicity of the left and right ventricular systolic and diastolic function. This study aims to demonstrate typical findings of radiation induced valve disease (RIVD) in the long term follow up. Considering the relatively younger age of e.g. lymphoma or breast cancer patients, cardiovascular disease after 10-20 years is clinically demanding.
Methods: 25 Pts with breast cancer, lymphoma, gastric cancer, or survivors of childhood cancer, after chemotherapy and/ or radiation were examined by echo and underwent coronary angiography or valve interventions as clinically indicated. Appropriate heart failure medication was initiated and pts followed up accordingly.
Results: In 4 survivors of Hodgkin's lymphoma, radiation induced valve disease was prominent of the aortic valve and rigid anterior mitral valve leaflet, causing low flow aortic stenosis leading to valve replacement in 2 pts. In contrary 1 pt showed only highly reduced LV function with typical thinned myocardium. Pericardial constriction was observed in a lymphoma pt after 15 y. In a pt with breast cancer irradiation left side additionally to aortic stenosis and basal anterior mitral leaflet calcification, severe stenosis of the left subclavian artery and carotids were observed at 20 y FU. After right side radiation the tricuspid valve and RV were dilated in another breast cancer pt. Another pt underwent TAVR due to low flow AS after radiation. Aortic regurgitation due to sclerosis after radiation of metastatic gastric cancer was observed with additional LV systolic impairment by previous multiple chemotherapy cycles including anthracyclines and cisplatin. Additional chronic thromboembolism and pulmonary hypertension complicated a case of breast cancer with aortic stenosis undergoing TAVR and balloon pulmonary angioplasty. Subclinical forms with only mild valvular thickening or reduced LV strain were frequently observed in the breast cancer pts.
Conclusion: Patients with radiation especially in left, but also right breast cancer or mediastinal radiation demonstrate typical premature calcifications and thickening of the aortic valve and the mid to basal part of the anterior mitral leaflet and mitral ring. Patients should be followed closely and cardiac treatment initiated early. Studies to prevent further sclerosis progression e.g. with statins should be performed in the future.

P937

Dual cardioprotection improves right and left ventricular systolic function in patients receiving cardiotoxic chemotherapy

AGF Ana Ferreira[1]; G Lloyd[1]; S Woldman[1]; M Westwood[1]; T Crake[1]; M Maxwell[1]; LR Lopes[1]; C Manisty[1]; AK Ghosh[1]
[1]Barts Health NHS Trust, Barts Heart Centre, London, United Kingdom

Introduction: Cardiotoxicity is a side effect of many chemotherapeutic agents. Cardioprotective therapy (CP) [Angiotensin Converting Enzyme Inhibitors (ACEi) or Angiotensin Receptor Blockers (ARB) and/or beta blockers (BB)] may prevent chemotherapy-related left ventricular (LV) dysfunction. Advanced echocardiographic measurements of cardiac function may help guide CP.
Methods: We retrospectively reviewed patients (pts) seen in the Cardio-Oncology service over a 28-month period. 46 pts [57.6 ± 10.9ys, 35 (76.1%) females] had received potentially cardiotoxic chemotherapy [20 (43.5%) also had radiotherapy] and at least one echocardiographic evaluation before and another after CP.
Results: 24 pts had breast cancer (52%), 7 lymphoma (15%), 7 myeloma (15%), 4 other haematological (9%) and 4 gastrointestinal malignancies (9%). 15 pts received anthracyclines, 9 trastuzumab, 13 anthracyclines and trastuzumab, 9 other chemotherapy. 34 pts (73.9%) received dual CP (BB and ACEI/ARB), 8 (17.4%) ACEI/ARB, and 4 (8.7%) BB only. Baseline and follow-up echocardiographic values shown in table 1. Time interval between assessments was 130 ± 100 days. GLS, LVEF, e' septal, e' average and TAPSE improved with dual CP.

P937 Table 1

	FIRST ECHO	SECOND ECHO							
	All	Dual therapy	ACEI/ARB only	All	P value vs 1st echo	Dual therapy	P value vs 1st echo	ACEI/ARB only	P value vs 1st echo
GLS (%)	-13.7±3.3	-13.9±3.3	-14.0±3.0	-16.4±3.1	<0.0005	- 16.4±3.3	<0.0005	-16.5 ± 3.1	0.127
LVEF Biplane (%)	46.3±8.3	46.0±8.6	49.9±4.7	50.2±13.4	0.049	50.4±12.7	0.031	48.4 ± 21.5	0.960
S' Lateral (cm/s)	8.5 ± 2.8	8.4 ± 2.9	8.0 ± 1.9	8.5 ± 2.4	0.94	8.3 ± 2.6	0.933	9.0 ± 2.2	0.050
S' Septal (cm/s)	6.9 ± 2.0	6.6 ± 1.8	7.6 ± 1.8	7.1 ± 1.7	0.568	7.2 ± 1.8	0.051	6.6 ± 1.4	0.206
S' avg	7.7 ± 2.2	7.5 ± 2.2	8.0 ± 1.5	7.8 ± 1.9	0.611	7.7 ± 2.0	0.355	8.0 ± 1.6	0.959
E/e' avg	9.5 ± 5.4	9.3 ± 4.9	9.4 ± 4.6	9.0 ± 4.2	0.446	8.7 ± 4.6	0.367	10.7 ± 2.8	0.481
e' Lateral (cm/s)	8.6 ± 2.8	8.5 ± 3.1	8.4 ± 2.1	9.3 ± 2.7	0.087	9.4 ± 2.9	0.081	9.4 ± 2.3	0.170
e' Septal (cm/s)	6.5 ± 2.3	6.4 ± 2.4	6.7 ± 1.7	7.0 ± 2.3	0.06	7.3 ± 2.5	0.015	6.0 ± 2.0	0.220
e' avg	7.5 ± 2.1	7.6 ± 2.3	7.2 ± 1.8	8.3 ± 2.5	0.011	8.5 ± 2.7	0.006	7.9 ± 2.0	0.531
TAPSE (mm)	18.96±3.33	18.95±3.33	20.00±3.61	20.81±3.87	0.004	20.76±4.11	0.029	21.1 ± 3.8	0.270
S' RV (cm/s)	12.4±3.0	12.4 ± 3.1	14.0±2.8	12.1 ± 3.2	0.679	12.0 ± 3.4	0.672	12.5 ± 7.1	0.500

Measurements of systolic and diastolic function at first and second echocardiography. GLS - Global longitudinal strain, LVEF - Left ventricular ejection fraction, avg - average, cm/s - centimetres/second, TAPSE - Tricuspid annular plane systolic excursion, RV - Right ventricle.

Conclusions: Early effects of CP in left and right ventricular function are identifiable by GLS, LVEF, e' and TAPSE, with dual CP demonstrating an early beneficial effect.

P938

Cancer therapeutic related cardiac dysfunction among active breast cancer patients: A Cardio-Oncology registry

M Laufer Perl[1]; A Milwidsky[1]; L Mor[1]; D Ravid[1]; N Amrami[1]; M Derakhshesh[1]; J Sherez[1]; G Keren[1]; Y Arbel[1]; Y Topilsky[1]
[1]*Tel Aviv Sourasky Medical Center, Cardiology, Tel Aviv, Israel*

Background: Progress in the treatment of breast cancer during the past two decades has led to substantial improvement in survival but at the cost of increased side effects, with cardio-toxicity being the most significant one with a mortality rate reaching as high as 60% in two years. The most commonly used definition is cancer therapeutic related cardiac dysfunction (CTRCD), defined as a left ventricular ejection fraction (LVEF) reduction of >10 %, to a value below 50%. Latest studies have implied that the incidence of CTRCD among breast cancer patients is decreasing resulting from the lower doses of anthracyclines and lower correlation for Trantszumab and Pertuzumab treatment.
Objectives: Evaluating the incidence of CTRCD among breast cancer patients and identifying significant predictors for its development.
Methods: Data was collected as part of the International Cardio-Oncology Registry (ICOR), enrolling all patients evaluating in the cardio-oncology clinic in our institution. All patients performed at least two echocardiograms.
Results: Among 103 consecutive patients, 5 (5%) developed CTRCD and 10 (10%) developed LVEF reduction of 5% and above. Mean time for CTRCD development was 171days (range 66 to 231). There were no significant differences in the baseline cardiac risk factors (hypertension, diabetes, hyperlipidemia or smoking) between the groups. Significant predictors for developing CTRCD were treatment with Trantszumab (80% vs. 18%, p = 0.001) or Pertuzumab (80% vs. 14%, p <0.001) and low systolic blood pressure (100 ± 13 vs. 132 ± 22, p = 0.006). Interestingly, Doxorubicin was not. Significant predicting echocardiography parameters included lower baseline global longitudinal strain (GLS) (18 ± 3 vs. 21 ± 2, p = 0.016), increased left ventricular end systolic diameter (LVESD) (35 ± 6 vs. 25 ± 4, p <0.001) and low e' septal (5.2 ± 0.5 vs. 7.4 ± 2.6, p <0.001).
Conclusions: CTRCD is frequent among active cancer patients and relates to Trantszumab and Pertuzumab treatment. Early GLS evaluation may identify it and allow cardio-protective treatment in order to prevent it.

P939

Mesalazine-induced cardiotoxicity: a retrospective study initial results

C Goena Vives[1]; L Quintas Ovejero[1]; R Garcia Martin[1]; I Luis Serret[1]; E Zapata Morcillo[2]; A Castiella Eguskiza[2]; L Zubiaurre Lizarralde[2]; A Iribarren Etxeberria[2]; JI Emparanza Knorr[3]; I Urreta Barallobre[3]
[1]*Mendaro's Hospital, Cardiology, Mendaro, Spain*; [2]*Mendaro's Hospital, Gastroenterology, Mendaro, Spain*; [3]*Donostia University Hospital, Clinical epidemiology, Donostia, Spain*

Introduction: Cardiac complications in inflammatory bowel disease (IBD) may be associated with the disease or due to Mesalazine (M) used in the treatment.The cardiac toxicity may appear after 2-4 weeks and as infrequent,its diagnosis is difficult in daily practice.Early drug cessation is enough to achieve improvement with no apparent long-term sequelae.
Purpose: Estimate the prevalence of M-related cardiomyopathy in IBD, asses feasibility of a simple screening protocol and present its initial results.
Methods: Observational retrospective cohort study EPA-SP (CGV-EII-2015-01). Inclusion criteria: ambulatory patients>16 years with >30 days of treatment at the moment of the evaluation and prior signed informed consent.Exclusion criteria: < 16 years and previous cardiopathy.Collected data:age, gender,type of IBD,NYHA,M dose and time of treatment.Every patient underwent a physical examination, ECG and transthoratic echocardiogram (TTE).If anomalies were detected, M was stopped, the patient underwent a CMR and NTproBNP and medical treatment and follow-up.

Table 1

	Case 1	Case 1
Age/Gender	17/Male	67/Female
IBD	Non controlled	Controlled
M treatment duration (months)	3	20
Basal ECG and 6 months after cessation	Sinus rythm	Sinus rythm+ LBBB
TTE	Dilated LV. LVEF 45%. RV affected.Pericardial effusion.	Dilated LV. LVEF 30%, RV affected. Paradoxical septal movement.
CMR/CMR 6 months after cessation	No late enhancement/=	No late enhancement/=
NYHA/NYHA 6 months after cessation	I/I	IIb/I
TTE 6 months after cessation	Non dilated LV.LVEF 60%.RV ok.	Non dilated LV.LVEF 47%.RV ok.

Results:84 patients (86 screened) between December 2015 and December 2016.83 were NYHA I/IV and one NYHA II/IV.42.86%women.The average time of treatment was 102 month(3-360). 2 patients had AF without structural cardiac disease.TTE evaluation revealed that the great majority of patients had good biventricular function.6 patients had reduced LVEF (1 alcoholic myocardiopathy and 3 coronary multivessel disease) and among these patients 2 cases of toxicity were reported (see table 1). Biventricular function normalized in less than 6 months after treatment disruption.
Conclusion: M is a frequent treatment in IBD with infrequent severe paucysintomatic cardiac adverse effect, potentially reversible with the drug withdrawal.Conventional TTE provides enough information for the initial screening.

P940

Haemodynamic changes associated with Cheyne-Stokes respiration in patients with heart failure: an echocardiographic study

A Giannoni[1]; V Raglianti[1]; C Taddei[1]; C Chiara Borrelli[2]; V Chubuchny[1]; A Valleggi[1]; C Passino[1]; E Pasanisi[1]; G Mirizzi[1]; M Cameli[3]; M Emdin[1]
[1]*Gabriele Monasterio Foundation, Pisa, Italy*; [2]*Sant'Anna School of Advanced Studies, Pisa, Italy*; [3]*University of Siena, Siena, Italy*

Background: Although Cheyne-Stokes respiration (CSR) is an oscillatory phenomenon, the effects of CSR phases (hyperventilation and apnea) on cardiopulmonary hemodynamics have never been investigated.
Purpose: The aim of the study is to examine the echocardiographic changes associated with CSR in a group of patients with systolic heart failure (HF).
Methods: 12 HF patients (age 69.7 ± 9.1 years, LVEF 24.1 ± 5.5%) underwent, beyond 24-hour polysomnography, chemoreflex tests by rebreathing technique, neuro-hormonal assessment and simultaneous echocardiographic and respiratory monitoring by inductance plethysmography.
Results: All patients had 24-hour CSR (24-hour apnea-hypopnea index, AHI: 25.0 IR 18.0-39.0). During CSR, systolic pulmonary artery pressure increased from hyperventilation (H) to apnea (A) (H 48.0 ± 9.6 versus A 53.5 ± 14.6 mmHg, p = 0.002), acceleration time of the pulmonary artery decreased (H 110.3 ± 20.9 versus A 92.1 ± 21.6 ms, p = 0.009) and pulmonary vascular resistances increased (PVR: H 3.8 ± 2.7 versus A 5.5 ± 3.5 wood units, p = 0.005) (Figure 1). During apnea a reduction of right and left ventricular outflow tract VTI (right VTI: H 12.5 ± 5.2 versus A 10.1 ± 3.3, p = 0.015; left VTI: H 30.1 ± 15.9 versus A 25.9 ± 13.2 mm, p = 0.009) and a reduction in tricuspid annular plane systolic excursion (H 15.8 ± 4.6 versus A 14.5 ± 4.2 mm, p = 0.03) was also observed, while no significant change in left ventricular systolic and diastolic function was found. Notably, PVR variation strongly correlated with norepinephrine levels (Rho = 0.93, p = 0.001), and chemosensitivity to hypercapnia (n = 7; Rho = 0.82, p = 0.023).
Conclusions: In HF patients with CSR, recurrent chemoreflex-mediated adrenergic discharge may cause pulmonary vasoconstriction and increase in pulmonary arterial pressure during apnea, with undesirable changes in right and left ventricular hemodynamics.

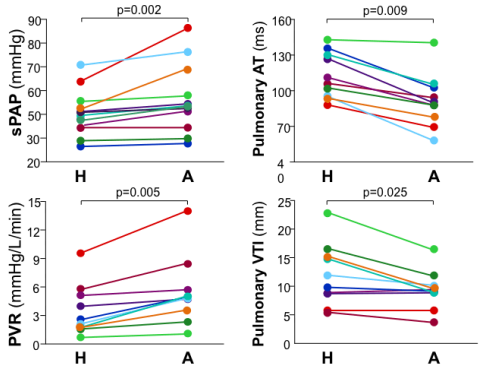


Figure 1. Haemodynamic changes from hyperventilation (H) to apnea (A) in patients with HF and CSR
AT: acceleration time, CSR: Cheyne-Stokes respiration, HF: heart failure, PVR: pulmonary vascular resistances, sPAP: systolic pulmonary arterial pressure, VTI: velocity-time integral

P941

Combined post- and pre-capillary pulmonary hypertension in heart transplant candidates with ischemic versus nonischemic etiology

Z Bayram[1]; C Dogan[1]; RD Acar[1]; B Guvendi[1]; A Karaduman[1]; T Unkun[1]; OY Akbal[1]; A Hakgor[1]; S Uysal[1]; C Kaymaz[1]; N Ozdemir[1]
[1]Kartal Kosuyolu Heart Education and Research Hospital, Department of Cardiology, Istanbul, Turkey

Background: A pulmonary hypertension (PH) is relevant complication of left ventricular heart failure. We aimed to investigate the effect of heart failure etiology (ischemic or non-ischemic) on the presence of isolated postcapillary PH (Ipc-PH) or combined pre-and postcapillary PH (Cpc-PH) or no-PH.
Methods and Results: A total of 210 patients with end-stage heart failure undergoing evaluation for heart transplantation were stratified into two groups; namely, those with ischemic cardiomyopathy (ICMP) and nonischemic cardiomyopathy (NICMP). The patients with left ventricle ejection fraction (LVEF) = 25%, NYHA class III or IV and INTERMACS III and VII levels were included to study.Ninety seven patients had ICMPand 113 patients had NICMP. There were no differences in terms of left ventricular ejection fraction, NYHA, INTERMACS grades, presence of severe mitral regurgitation, left ventricular diastolic dysfunction and duration of heart failure betweengroups. The systolic pulmonary pressures, PAPm and PVR were higher in ICMP group compared to NICMP group [57 ± 18 vs. 47.2 ± 15.1, p < 0.001; 35.8 ± 11.5 vs. 30.6 ± 10.7 p = 0.001 and 3.4 (1.7-6.5) vs. 2.4 (1.0-4.4); p = 0.007]. Although more Cpc-PH was found in ICMP it didn't reached statistically significance (55.6% vs. 40.7%, p = 0.07). The patients with ICMP and NICMP had similar rate of Ipc-PH and no-PH (25.7% vs. 33.6%, p= 0.216; and 19.5% vs. 28.3%, p = 0.150; respectively).The patients with ICMP had a similar rate of PVR= 3 but significantly increased rate of PVR = 5 WU compared to NICMP (56.7% vs. 44.2%, p = 0.05 and 32.9% vs. 17.6%, p = 0.008). In subgroup analysis of patients who don't require inotropic treatment (170 patients), patients with ICMP had higher rate of Cpc-PH compared to NICMP (55.8% vs. 337.7%,p = 0.043).
Conclusions: It seems that heart failure etiology, ischemic or nonischemic, didn't affect the rate of Ipc-PH, Cpc-PH and No-PH. However, more Cpc-PH was determined in patients with ICM who didn't require inotropic treatment.

P942

Effect of ischemic versus nonischemic cardiomyopathy on invasive hemodynamic findings in heart transplant candidates

Z Zubeyde Bayram[1]; C Dogan[1]; RD Acar[1]; B Guvendi[1]; A Karaduman[1]; OY Akbal[1]; T Unkun[1]; A Hakgor[1]; S Uysal[1]; C Kaymaz[1]; N Ozdemir[1]
[1]Kartal Kosuyolu Heart Education and Research Hospital, Department of Cardiology, Istanbul, Turkey

Background: Results of studies evaluating the effect of heart failure (HF) etiology (ischemic or nonischemic) on invasive hemodynamic measurements are inconsistent because of heterogeneities of studies and relatively small number of patients in those studies. We aimed to investigate how does etiology of HF affects the invasive hemodynamic findings about right ventricular function, including novel parameters such as pulmonary artery pulsality index (PAPi), pulmonary arterial capacitance (PAC) and pulmonary arterial elastance (PAE).
Methods and Results: A total of 215 patients with end-stage heart failure undergoing evaluation for heart transplantation were stratified into two groups; namely, those with ischemic cardiomyopathy (ICMP) and nonischemic cardiomyopathy (NICMP) and all of the patients underwent right heart catheterization. One hundred and one patients had ICM and 114 patients had NICM. Patients with left ventricle ejection fraction (LVEF) = 25%, NYHA class III or IV and INTERMACS IV and VII levels were included to study. There was no difference in terms of LVEF, duration of HF,NYHA and INTERMACS grades between ICMP and NICMP (p>0.05). The patients with ICMP had higher pulmonary artery systolic and mean pressures, pulmonary vascular resistance (PVR) compared to NICMP [59.0 (42.0-73.0) vs. 46.0 (37.0-59.0), p < 0.001; 35.0 (27.0-46.0) vs. 31.0 (23.0-39.0), p = 0.002 and 3.5 (1.8-6.6) vs. 2.4 (1.0-4.4), p = 0.007; respectively]. The cardiac output, cardiac index, stroke volume, right atrial pressure, pulmonary wedge pressure and pulmonary artery diastolic pressure were similar between group [3.3 ± 0.81 vs.3.4 ± 0.96, 1.7 ± 0.45 vs. 1.8 ± 0.5, 41.6 ± 12.9 vs. 41.4 ± 15.1, 10.0 (5.0-15.0) vs. 11.0 (6.0-16.0), 23.7 ± 7.8 vs. 22.0 ± 7.3 and 24.0 (16.0-30.0) vs.31.0 (23.0-39.0); p>0.05 in all]. While the right ventricular stroke work index (RVSWI) and PAPi were higher and PAC was lower in patients with ICMP compared to NICM [6.5 (4.8-8.2) vs. 5.4 (3.7-7.7), p = 0.007; 3.4 (2.2-5.2) vs. 2.5 (1.7-4.0) p = 0.004 and 1.2 (0.8-1.8) vs. 1.5 (1.0-2.2), p = 0.002; respectively], the PAE was similar between groups [1.3 (0.92-2.0) vs. 1.2 (0.81-1.6), p = 0.638]. Among to PVR= 3 WU, higher PAPi and lower PAC was determined among to ICM group compared to NICMP group (3.8 ± 2.1 vs. 2.9 ± 1.5, p = 0.026 and 1.1 ± 0.55 vs. 1.4 ± 0.79, p = 0.017), and RVSWI and PAE were similar between groups (7.6 ± 3.1 vs. 6.6 ± 2.7, p = 0.122; 1.89 ± 0.78 vs. 1.69 ± 0.58, p = 0.317).Among to PVR < 3 WU, PAC and PAE were similar between in ICM and NICMP (p = 0.243 and p = 0.662). While patients with ICMP had higher RVSWI and PAPi, it didn't reach statistically significance in patients with PVR < 3 WU (6.2 ± 3.2 vs. 4.9 ± 2.9, p = 0.051; 4.4 ± 3.2 vs. 3.3 ± 2.4, p = 0.05).
Conclusions: The patients with ICM had higher RVSWI, PAPI and PAC than patients with NICM.It seems that the ischemic cardiomyopathy is better than nonischemic cardiomyopathy in terms of RVSWI, PAPiand PAC of which are invasively determined risk factors for RVF.

P943

Experience using sacubitril/valsartan in real life: tolerability and clinical evolution in a long term

R Rafael Bravo Marques[1]; E Timonet Andreu[1]; JL Rodriguez Martinez[1]; S Lopez Tejero[1]; PA Chinchurreta Capote[1]; C Corona Barrio[1]; JR Siles Rubio[1]; A Valle Alberca[1]; FE Mesa Prado[1]; C Martin Dominguez[1]; F Ruiz Mateas[1]; FJ Torres Calvo[1]
[1]Hospital Costa del Sol, Cardiology, Marbella, Spain

Introduction: The prevalence of chronic heart failure (HF) has been increased, due to the improvement in the management and treatment of most of heart diseases and the longer life expectancy of the population, becoming an important public health problem. The clinical practice guidelines of HF have aproved using Sacubitril/Valsartan in patients with HF with reduced eyection fraction (HfrEF) and functional class (FC) = II.
Material and Methods: We conducted a prospective observational study of patients with HfrEF assessed in our outpatient clinic, who started treatment with Sacubitril/Valsartan between October 2016-Febrery 2017. We analyzed their baseline characteristics and the one year evolution in functional class, analytical parameters and drug tolerance.
Results: We analyzed 57 patients, with a mean age of 69.1 ± 10,1 years, being 80.7% male. 57,9 were hypertensive, 33.3% diabetic and 45.6% dyslipemic. The mean FG of 65.2ml/min (CKD-EPI). The cause of heart failure was dilated cardiomyopathy in 68.4% and in ischemic heart disease in 29.8%. The mean telediastolic diameter of left ventricle was 63.8 ± 6.6mm, with an average LV ejection fraction of 33.6 ± 6.4%. Atrial fibrillation was present in 31.6%.
At the beginning, the majority were in FC II (43.9%), 43.9% in FC III/IV. Mean baseline systolic blood pressure was 117.2 ± 20.4mmHg and diastolic 69.7 ± 12.4mmHg and mean heart rate was 69.4 ± 14.1bpm. Pretreatment was optimal in all cases (maximum tolerated doses of ACEI, ARB II, BB, mineralcorticoids). ARNI was started (after stopping ACE inhibitors in 56.2% and the rest ARI II), at low doses in 57.9%, at medium doses 29.8% and the rest at high doses. In a review at 7 months follow-up, 18 patients improved functional class (3 patients from IV to III, 10 patients from III to II and 5 patients to FC I). Concerning analytical parameters, we observed a reduction of NT-ProBNP (from 1813 to 813µg/L; this parameter was measured one month after initiating ARNI and after 6 months) and uric acid (from 10.9 to 6.9mg/dL). We found a significant decrease in blood pressure at month and the six months (115.2/67.8mmHg and 109.8/65mmHg respectively; p = 0,034 and 0,005) but allowed us to optimize the treatment with LCZ696, being at medium dose 40.5%, at high dose 38.1% and the rest at low doses. We did not find significant differences in renal function or in potassium levels during follow-up. The LV ejection fraction improved significantly to 37.3 ± 10.2% (p = 0,034) on echocardiogram 7 months after starting treatment with ARNI. Only one patient stopped taking medication due to pruritus.
Conclusions: The treatment with LCZ696 in a group of patients in real-life was well tolerated in all cases, with a significant decrease in blood pressure, being able to

optimize the dose of LCZ696. It was related to improvement in the functional class, LV ejection fraction and in analytical parameters, even with a long follow-up.

P944

What is the significance of right ventricular dysfunction in patients with preserve, mid-range and depressed LVEF?

M Plaza Martin[1]; S Del Prado Diaz[1]; G Alonso Salinas[1]; J Ramos Jimenez[1]; S Hernandez Jimenez[1]; A Pardo Sanz[1]; M Valverde Gomez[1]; VC Lozano Granero[1]; M Pascual Izco[1]; JL Zamorano Gomez[1]
[1]*University Hospital Ramon y Cajal de Madrid, Madrid, Spain*

Introduction: European Society of Cardiology (ESC) guidelines establish three categories of heart failure (HF) based on left ventricular ejection fraction (LVEF). Meanwhile the presence of right ventricular (RV) dysfunction is not considered.
Methods: An observational study was designed in order to evaluate differences in baseline characteristics and functional class between consecutive patients with and without RV dysfunction followed in HF Unit.
Results: A total of 200 patients were included. Mean age was 74.5 ± 12.5 years, 60% were men, 62% hypertensive, 17% diabetic, 43% dyslipidemic and 56% were on atrial fibrillation or flutter. There was RV dysfunction in nearly 30% of patients. According to ESC recent classification, the majority of patients (58%) had depressed LVEF, 18% mid-range and 24% preserved LVEF. There was no difference in baseline characteristics between patients with and without RV dysfunction except higher rate of atrial arrhythmias in the group with RV dysfunction (69% vs 51%, p = 0,020). The proportion of patients in the three cathegories based on LVEF was similar in both groups. However, irrespective of left ventricular function, patients with RV dysfunction showed worse functional class (p = 0,041) and higher natriuretic peptides levels (829 ± 623 vs 656 ± 558, p = 0,021).
Conclusions: In this cohort, RV dysfunction was related with worse functional class and higher natriuretic peptides regardless of left ventricular dysfunction degree. As a result, it would be reasonable performing studies focused on the analysis of RV dysfunction to evaluate its role in the follow up of patients with HF.

Baseline characteristics

	Right ventricular function preserved	Right ventricular dysfunction	p
Age (X ± SD)	75,09 ± 11,7	74,0 ± 12,8	0,572
Hypertension	63%	61%	0,086
Diabetes mellitus	38%	42%	0,069
Dyslipidemia	41%	49%	0,302
Smoking	12%	5%	0,148
COPD	23%	20%	0,624
Atrial arrhythmias	51%	69%	0,020
Depressed LVEF	55%	63%	0,510
Mid-range LVEF	20%	14%	0,510
Preserved LVEF	25%	24%	0,510

X mean, SD standard deviation, COPD chronic obstructive pulmonary disease, LVEF left ventricular ejection fraction

P945

Echocardiographic evaluation of left ventricular filling pressures in patients with pulmonary hypertension

M Matthias Schneider[1]; H Ran[2]; A Pistritto[3]; C Gerges[1]; I Lang[1]; T Binder[1]; G Goliasch[1]
[1]*Medical University of Vienna, AKH - Vienna, Cardiology Clinic, Vienna, Austria*; [2]*Nanjing 1st Hospital, Department of Echocardiography, Nanjing, China People's Republic of*; [3]*San Paolo Hospital, Emergency Department, Division of Cardiology, Savona, Italy*

Background: Echocardiographic estimation of diastolic function is an essential part of every comprehensive transthoracic echocardiographic examination. The 2009 recommendations for the evaluation of left ventricular (LV) diastolic function combined a series of parameters to a diagnostic algorithm for the echocardiographic diagnosis of LV diastolic dysfunction. In 2016, an updated version was published, proposing a more simplified approach. Both recommendations primarily rely on the secondary findings left atrial dilatation, tricuspid regurgitation velocity, and the Doppler criteria E/A, e' and E/e'. Tricuspid regurgitation velocity plays a major role in this algorithm. This can lead to false interpretation of LV diastolic function in patients with pulmonary hypertension.
Purpose: We aimed to compare the accuracy of the 2009 and the 2016 recommendations in patients with pulmonary hypertension.
Methods: We prospectively evaluated all adult patients with clinically indicated right heart catheterization between July 2015 and July 2016. For the final analysis, only patients with pulmonary hypertension were included. All patients had a complete transthoracic echocardiographic examination shortly before right heart catheterization. In a subgroup of patients LV end-diastolic pressure was measured via left heart catheterization when clinically indicated.
Results: A total of 63 patients were included in the final analysis, 35 patients (56%) were female. Mean age was 68 years (range 21-91). All patients had pulmonary hypertension (mean pulmonary artery pressure = 25 mmHg). A total of 27 patients (43%) had elevated left ventricular filling pressures (defined as mPCWP >12 mmHg and/or LVEDP >16 mmHg). Left ventricular systolic function was normal in all patients. Right ventricular systolic function was graded normal in 40% of the patients. Mean TAPSE was 17 ± 4 mm, and mean longitudinal strain of the free lateral wall of the right ventricle was -18 ± 6 %. At least moderate tricuspid regurgitation was present in 27 patients (43%), at least moderate mitral regurgitation was present in 11 patients (17%). Sensitivity for correct echocardiographic classification of diastolic function was 67% and 84%, specificity was 82% and 80%, in the 2009 and 2016 recommendations, respectively. The area under the curve (AUC) for the 2016 guidelines with 0.82 was significantly better compared to the AUC of 0.74 for the 2009 guidelines (P = 0.0427)
Conclusion: Our study demonstrates that the 2016 recommendations for echocardiographic evaluation of diastolic function are superior to the 2009 recommendations in estimating left ventricular filling pressures in patients with pulmonary hypertension.

P946

Metabolic syndrome phenotypes have different effects on the diastolic function of the left ventricle and arterial ageing

AM Jakstaite[1]; J Celutkiene[2]; S Solovjova[2]; J Badariene[2]
[1]*Vilnius University, Medical faculty, Vilnius, Lithuania*; [2]*University Hospital Santariskiu Klinikos, Clinic of Cardiac and Vascular Diseases, Centre of Cardiology and Angiology, Vilnius, Lithuania*

Background: It was shown that some metabolic syndrome (MetS) clusters are associated with significantly stiffer arteries.
Purpose: We aimed to investigate the association between MetS phenotypes, left ventricle diastolic function [LVDF] and arterial markers.
Methods: 357 high cardiovascular risk patients were recruited prospectively. Inclusion criteria: defined MetS, echocardiographic LVDF evaluation, arterial markers (pulse wave velocity [PWV], augmentation index [AI], common carotid artery intima-media thickness [IMT], common carotid artery stiffness [CAS], cardio-ankle vascular index [CAVI]). According to the combination of MetS components (increased waist circumference [W], increased triglyceride [T], increased plasma glucose [G], low high-density lipoprotein [H], arterial hypertension [B]) subjects were divided into MetS phenotypes. Impaired relaxation was described as E/A < 1.0 and E/e'mean < 13. Pseudonormal or restrictive diastolic dysfunction- as E/e'mean = 13. In case of E/A>1.0, e'septal = 8 cm/s and e'lateral = 10 cm/s- as normal diastolic function.
Results: Subjects composed 15 phenotypes, the most common being WTGHB (n = 72), WGB(n = 66), WTGB(n = 58), WTB(n = 48), WTHB(n = 33), WGHB(n = 26). All MetS phenotypes mostly presented with impaired relaxation. About ? of WGHB and WTHB subjects had pseudonormal or restrictive diastolic dysfunction. Furthermore, the majority of WGHB subjects had impaired diastolic function. Significant differences of arterial markers (PWV, AI, CAVI, IMT) were found between MetS phenotypes (Table 1.).
Conclusion: Specific MetS phenotype is associated with particular stage of diastolic dysfunction and arterial ageing, being WGHB type the strongest predictor of high impairment degree.

P947

Diastolic dysfunction of the right ventricle as an early diagnostic marker of heart failure

V Kirillova[1]; E YU Prosviryakov[2]
[1]*Ural State Medical Academy, biochemistry, Ekaterinburg, Russian Federation*; [2]*Institute of Engineering Science, UB RAS, Laboratory of Nonlinear Vortex Hydrodynamics, Ekaterinburg, Russian Federation*

Right ventricular (RV) diastolic function is associated with outcomes for patients with pulmonary hypertension.
Echocardiographic evaluation of right and left ventricular (LV) diastolic function in hypertensive patients with different duration of disease.

P946 Table 1.

Diastolic function and arterial markers	WGB	WTGHB	WGHB	WTGB	WTHB	WTB
Normal diastolic function(%)	28.8	27.8	19.2	25.9	24.2	33.3
Impaired relaxation(%)	56.1	52.8	50.0	58.6	48.5	56.3
Pseudonormal or restrictive filling(%)	15.2	19.4	30.8	15.5	27.3	10.4
PWV femoral(m/s)	8.7±1.2	8.9±1.4	9.2±1.7*	8.9±1.7	8.5±1.2	8.2±1.4
AI	25.3±8.0*	22.4±8.4	24.2±9.5	22.2±10.1	24.3±12.8	19.7±9.3
CAVI right	7.8±1.7	8.0±1.7	8.3±2.7	8.3±1.8	8.0±1.8	7.8±1.6
CAVI left	8.2±2.3*	7.5±1.1	7.4±2.2	7.8±1.5	7.2±1.4	7.5±1.6
IMT right(μm)	663.9±107.7	653.1±116.9	680.2±143.1*	641.6±109.1	630.4±96.9	601.5±163.7
IMT left(μm)	657.7±127.9	683.4±120.1	703.0±144.0	652.9±106.1	673.5±133.4	648.7±154.7
CAS right	3.9±1.7	3.8±1.3	4.3±2.3	3.9±1.8	3.7±1.4	3.9±1.5
CAS left	3.9±1.8	4.0±1.6	4.3±2.2	3.7±1.4	4.2±1.6	3.8±1.2

* p value < 0.05

The study included 152 hypertensive patients (61.4 ± 1.4 years, 74.7% women). The control group was 55 people without cardiovascular disease (37.1 ± 1.3 years, 66.6% women). RV and LV diastolic function was assessed using early (E) and late (A) transtricuspid and transmitral flow velocities, E/A ratio, and e' and a' tissue Doppler velocities.

The hypertensive patients had right ventricular diastolic dysfunction with left ventricular diastolic dysfunction with and without pulmonary hypertension (mean systolic pressure of pulmonary artery in the patients was 23.9 ± 1.2 Hg vs 15.8 ± 0.59 Hg in the control group, p < 0.05). The hypertensive patients had different types of right and left ventricular diastolic dysfunction. 55 patients had early diastolic dysfunction of the right and left ventricles (LV: E/A = 0.7 ± 0.02, e' = 7.9 ± 0.3 m/s, a' = 12.8 ± 0.5 m/s; RV: E/A = 0.76 ± 0.01, e' = 8.2 ± 0.29 m/s, a' = 14.8 ± 0.54 m/s vs control LV: E/A = 1.65 ± 0.05, interventricular septum: e' = 12.4 ± 0.33 m/s, a' = 8.9 ± 0.17 m/s, lateral wall: e' = 16.2 ± 0.48 m/s, a' = 10.1 ± 0.33 m/s; RV: E/A = 1.4 ± 0.02, e' = 14.3 ± 0.36 m/s, a' = 10.4 ± 0.36 m/s). 27 patients had early diastolic dysfunction of the left ventricle and pseudonormal diastolic dysfunction of the right ventricle (LV: E/A = 0.76 ± 0.03, e' = 9.2 ± 0.37 m/s, a' = 14.4 ± 0.5 m/s; RV: E/A = 1.26 ± 0.04, e' = 9.1 ± 0.5 m/s, a' = 15.6 ± 0.7 m/s). 20 patients had pseudonormal diastolic dysfunction of the right and left ventricles (LV: E/A = 1.17 ± 0.03, e' = 8.7 ± 0.29 m/s, a' = 11.4 ± 0.49 m/s; RV: E/A = 1.25 ± 0.02, e' = 8.8 ± 0.24 m/s, a' = 14.1 ± 0.38 m/s). 50 patients had normal diastolic function of the left lateral ventricular wall and pseudonormal diastolic dysfunction of the right ventricle; the interventricular septum, which is shared by both ventricles, had early diastolic dysfunction (LV: E/A = 1.29 ± 0.05, interventricular septum: e' = 11.0 ± 1.64 m/s, a' = 12.4 ± 1.89 m/s, lateral wall: e' = 13.7 ± 0.29 m/s, a' = 9.8 ± 0.29 m/s; RV: E/A = 1.38 ± 0.03, e' = 9.4 ± 0.37 m/s, a' = 13.8 ± 0.47 m/s). The last group with right ventricular diastolic dysfunction and normal left ventricular diastolic function had a short duration of disease (less than 7 years) versus the other groups having more than 10 years of hypertension.

This study has demonstrated that, in hypertensive patients, the right ventricular diastolic dysfunction accompanies the left ventricular diastolic dysfunction. The right ventricular diastolic dysfunction has been demonstrated in cases without pulmonary hypertension. The patients with a short period of hypertensive disease have only pseudonormal right ventricular diastolic dysfunction, which can be an early diagnostic marker of heart failure.

P948

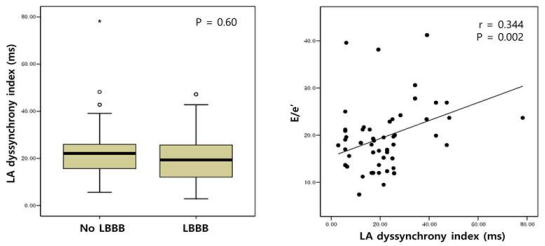
Impact of left bundle branch block on left atrial dyssynchrony and its relationship to left ventricular diastolic function in dilated cardiomyopathy

SM Seong-Mi Park[1]; DH Cho[1]; MN Kim[1]; WJ Shim[1]
[1]*Korea University College of Medicine, Seoul, Korea Republic of*

Background: The impact of left bundle branch block (LBBB) on left atrial (LA) dyssynchrony in heart failure (HF) patients with non-ischemic dilated cardiomyopathy (DCM) has not been clearly elucidated.

Methods: Eighty consecutive symptomatic HF patients with non-ischemic DCM (left ventricular ejection fraction, LVEF < 35%) were included. LBBB was defined according to standard electrocardiographic criteria on a 12-lead electrocardiogram. LV systolic and diastolic dyssynchrony index and LA dyssynchrony index were obtained by color-coded tissue Doppler imaging.

Results: There was no significant difference in LV size, LVEF, and LA volume between patients with LBBB (n = 38) and no LBBB (n = 42). NT-pro BNP level was similar between two groups. There was a significant difference in LV systolic dyssynchrony index (P = 0.014) and there was a mild difference in LV diastolic synchronicity index between patients with LBBB and no LBBB (P = 0.045). However, there was no difference in LA dyssynchrony index between the two groups (P = 0.60). LA dyssynchrony index was not related to LV systolic and diastolic dyssynchrony indexes, but it was related to the deceleration time of mitral early diastolic velocity



LA dyssynchrony index (E) (r = -0.249, P = 0.029), the ratio of E to mitral annular early diastolic velocity (E/e', r = 0.344, P = 0.002) and LA volume (r = 0.242, P = 0.031). E/e' was most related to LA dyssynchrony index (r^2 = 0.325, P = 0.002).

Conclusion: LBBB influences both LV systolic and diastolic dyssynchrony, but not LA dyssynchrony. LA dyssynchrony was related to LV diastolic function and the improvement of LV diastolic function by HF therapy may improve LA mechanical dysfunction regardless of the presence of LBBB in in patients with non-ischemic DCM.

P949

Early circulating predictors of post-infarction myocardial remodeling pattern

M Ivanov[1]; I Popovici[1]; V Ivanov[1]; D Dragoi[1]; V Cobet[2]; M Popovici[1]
[1]*Institute of cardiology , Chisinau, Moldova Republic of*; [2]*State University of Medicine and Pharmacy, Chisinau, Moldova Republic of*

Aim: Daily assaying of serum level of pro- and anti-inflammatory cytokines during first 7 days of post-infarction evolution in patients with STEMI exposed to angioplasty as well as MMP-8 in correlation to installed myocardial remodeling pattern estimated echocardiography at 4-6 month period after revascularization.

Material and methods. From a big group (n = 238) of patients with STEMI exposed to angioplasty in first 12 hours since infarction onset have been selected 56 pts who developed adaptive (AMR) myocardial remodeling and 57 pts who developed pathological (PMR) myocardial remodeling according to geometric (concentric or eccentric remodeling) and functional (end diastolic volume rise more than 20%) criteria. Using ELISA method daily serum concentrations of pro-inflammatory ((high sensitive C reactive protein, interleukins (IL) 1, 6, tumor necrosis factor alpha and monocyte chemoattractant protein 1)), anti-inflammatory biomarkers (IL-4, IL-10, IL-33, IL-1 receptor antagonist and heregulin-1beta) ?s well as ???-8 have been determined in the first 7 days after myocardium revascularization.

Results: Initial serum content of the explored pro-inflammatory biomarkers was in both groups significantly bigger than control value. Their dynamics did not differ in patients with AMR and PMR after revascularization. It was characterized by a significant biomarker increase at 3-rd day followed by a decline toward 7-th day up to initial level. Among anti-inflammatory biomarkers IL-4 and IL-10 have manifested by a distinct dynamics in concern to myocardial remodeling pattern. In both groups these interleukins decreased after angioplasty, reaching a minimal level at 3-rd day.

However, in patients with AMR since 4-th day has been established an increase of serum content of IL-4 and IL-10, their increment being at 7-th day in a range of 52-55% ($p < 0,05$). In patients with PMR the interleukins rise was negligible: 5,7-5,8%. MMP-8 dynamics also has been different in groups and was correlated with dynamics of IL-4 and IL-10. Thus, in patients with AMR its level has fallen since 3-rd day up to 7-th day by 46,6%, while in group with PMR metalloproteinase level in this period practically did not change, remaining significantly higher than control by 45-53%.

Conclusion: In patients with STEMI determining of serum content of IL-4 and IL-10 in the first 7 days after angioplasty is important in regard to myocardial remodeling pattern prediction in post-infarction period. Their rise more than 50% since 4-th day up to 7-th day (period of anti-inflammatory macrophages, M2, activation) testifies priority of AMR developing, while a negligible increment (up to 6%) is a predictor of PMR. The MMP-8 dynamics correlated with dynamics of IL-4 and IL-10.

P950

Early left ventricular reverse remodelling after sacubitril/valsartan treatment in clinical practice

M Groba-Marco[1]; M Singh[1]; M Galvan Ruiz[1]; M Fernandez-De-Sanmamed-Giron[1]; R Montiel Quintero[1]; E Perez-Nogales[2]; JM Medina Gil[2]; M Blanco-Nuez[1]; E Caballero Dorta[1]; JR Ortega Trujillo[1]; I Menduina Gallego[1]; J Morales Gonzalez[1]; V Quevedo Nelson[1]; H Mendoza Lemes[1]; A Antonio Garcia Quintana[1]
[1]University Hospital De Gran Canaria "Dr. Negrin", Las Palmas de Gran Canaria, Spain; *[2]University Hospital Insular of Gran Canaria, Las Palmas De Gran Canaria, Spain*

Background: Sacubitril/Valsartan is an angiotensin receptor-neprilysin inhibitor (ARNI), recommended to further reduce morbidity and mortality in ambulatory patients with heart failure with reduced ejection fraction (HFrEF) symptomatic despite optimal treatment. Few data on echocardiographic parameters of remodelling has been published after ARNI treatment.

Purpose: To analyse the evolution of left ventricle ejection fraction (LVEF) and end diastolic diameter (LVEDD) in patients with stable symptomatic HFrEF and optimized treatment after ANRI, and study whether aetiology of HF and early initiation of this drug after diagnoses of HFrEF is associated with better outcomes.

Methods: We performed a retrospective study of 17 patients with ARNI treatment. Clinical characteristics, date of HFrEF diagnoses and ARNI treatment initiation, LVEF and LVED were collected. Follow-up transthoracic echocardiography was performed after mean time of 4.91 ± 3.05 months of treatment with ANRI.

Results: Mean age was 60.6 ± 10.93 years, 13 patients (76%) men and 4 (24%) women. Aetiology of HFrEF was 41.2 ischemic and 58.8 non-ischemic. Along with ANRI treatment, 88.2% of patients received beta-blocker, 56.2% mineralocorticoid receptor antagonist and 29.2% Ivabradine. 3 patients (17%) had cardiac resynchronization therapy before ANRI. ARNI dose was 24/26mg 3 patients (17,6%), 49/51mg 9 patients (52,9%) and target dose 97/103mg 5 patients (29,5).

Mean LVEF before and after ANRI was $30 \pm 7.9\%$ and $35.47 \pm 10.3\%$ respectively, with mean improvement $5.47 \pm 9.5\%$ (p value = 0,031). Mean LVED before and after ANRI was 66.42 ± 6.74mm and $62,42 \pm 7,5$mm respectively, with mean reduction $4 \pm 5,3$mm (p-value = 0,025). Baseline LVEF in ischemic and non-ischemic HF was 29.14% and 31.14% and after ARNI 20,60% and 38.50% respectively ($p = ns$).

Mean improvement of LVEF and LVED with ARNI initiation before 12months of HFrEF diagnoses was $14,0 \pm 17,5\%$ and 2.2 ± 4mm respectively and in patients with ARNI initiation after 12months of HFrEF diagnoses $2,8 \pm 3,6$ % ($p = 0,036$) and 4.9 ± 5.8mm respectively ($p = ns$).

Conclusions: A statistically significant improvement in LVEF and LVED is observed in patients with ARNI and optimal heart failure treatment. A more significant increase in LVEF is observed in patients with non-ischemic HFrEF and in patients with earlier ARNI treatment initiation. However, extended data with larger cohort size is needed to confirm these results and enlighten the role of ARNI in ventricular reverse remodelling process.

P951

Pathological left ventricle remodelling and electric instability in patients with myocardial infarction

E Dushina[1]; Y Barmenkova[1]; V Galimskaya[1]; N Burko[1]; V Valentin Oleinikov[1]
[1]Penza State University, Penza, Russian Federation

Aim: analysis of the effect of left ventricle pathological remodeling in patients in the postinfarction period on the detecting of late ventricular potentials (LVP), pathological turbulence of the heart rhythm (HRT), and the development of ventricular arrhythmias (VA).

Methods: 100 subjects aged from 35 to 65 years were examined at the 7th-9th day, and 24 weeks after STEMI. Daily 12 leads ECG monitoring with the analysis of LVP and HRT was performed using the Holter Analysis-Astrocard complex (Meditek, Russia). The presence of LVP was established if at least two of the following conditions existed: QRSf = 120 ms, HFLA = 39 ms, RMS = 25 μV. The normal ranges of the parameters were used in HRT assessing: TO less than 0% and TS more than 2.5 ms/RR. The pathological HRT was determined in deviation of any of these parameters. The Lown and Wolf classification was used for the VA evaluation. Echocardiography was performed on MyLab 90 scanner (Esaote, Italy), end-diastolic volume index (EDVi) was determined. The patients were separated onto two groups depending on the EDVi increase: one group included 43 (58%) people without echocardiographic signs of LV remodeling; group 2 comprised 31 (42%) patients with an EDVi increase by 20% or more.

Results: the frequency of impaired HRT registration in group 1 decreased significantly from 31% (18 patients) to 12.1% (7 patients) ($p = 0.02$), this positive intra-group dynamics was accompanied by a marked decrease in absolute values of TO with -0,42% (95% CI -2.22, 1.38%) at 7-9th days to -2.47 ms/RR (95%CI -3.58, -1.35 ms/RR) at the 24-week ($p = 0.007$). In the compared group, the incidence of pathological baroreflex sensitivity was not significantly changed and was 23.8% (10 subjects) at the 7-9th days, and 11.9% (5 patients) at the end of follow-up. VA of high grades (gradation 3 and above on Lown and Wolf) was more often in group 2 (45.2%), compared to group 1 (22.4%) ($p = 0.02$). There was no significant change in the LVP registration in both groups.

Conclusion: pathological remodeling of the left ventricle in the post-infarction period adversely affects the baroreflex sensitivity, and also promotes the life-threatening arrhythmias development.

P952

Dynamical 3D modeling possibilities in the left ventricle reconstructions Personalized surgical approach in cardiac surgery

J Imre Barabas[1]; Z Szabolcs[1]; F Horkay[1]; T Huttl[1]; L Fazekas[1]; M Polos[1]; L Daroczi[1]; K Benke[1]; P Kovacs[1]; A Koszegi[1]; R Toth[1]; B Gasz[2]; B Merkely[1]; I Hartyanszky[1]
[1]Semmelweis University Heart Center, Budapest, Hungary; *[2]University of Pecs, Department of Surgical Research and Techniques, Pecs, Hungary*

Development of computer science, more accurate planning and simulation spread into the medical patient care. Although the surgical specialties utilized static model but by the evolution of dynamical planning method and practical usage of computer simulations created the possibility of introduction of dynamical parameters in cardiac surgery.

Our aim was the amelioration and application of 3D models in cardiac surgical practice wherewith the prediction of fluid dynamical variables and remaining ventricle shape, volume and function in surgical ventricle restoration cases.

Using own developed script, the raw Dicom files were imported, the dilated left ventricle was modeled and fluid dynamical parameters simulated, such as flow kinematic and profile analysis, turbulence calculation and myocardial response to shear stress.

Then step-by-step simulation of the surgical ventricle restoration procedure was accomplished and the calculated variables were imbedded in silico model of the left ventricle reconstruction. The extension and length of resection lines were modified based on the previous computer simulation. Optimal resection of the myocardium was applied during the operation, considering the all feasibility. The sphericity and conicity indexes were improved significantly in postoperative period (0,42vs. 0,67 és 0,36vs. 0,72, $p < 0,05$, Student t-test). The occurred shear stress at endocardium decreased 83% due to the normalization of flow kinematic pattern of the ventricle in postoperative period (54 ± 12vs. 32 ± 9 $p < 0,02$, Student t-test). The postoperative turbulent flow pattern - based on Reynolds number - significantly decreased, according to our computational method (2712vs. 1823, $p < 0,0001$, Student t-test). With our method, the standardization of the surgical ventricle reconstruction was achievable and the surgical steps were predictable. Therefore, a new decision making support system was established in cardiac surgery for high risk patients. Consequently, a personalized surgical technique was offered our patients, improving their life expectancy and quality of life.

P953

Corrected QT interval and right shifted association with mortality in acute heart failure patients

HY Hae-Young Lee[1]; HJ Cho[1]; BH Oh[1]
[1]Seoul National University Hospital, Seoul, Korea Republic of

On behalf of: KorAHF registry
Funding Acknowledgements: Korea CDC

This study sought to investigate the predictive power of corrected QT (QTc) interval in acute heart failure patients. In this prospective cohort study, we analyzed 4,990 patients who were followed up to 5 years. They had QTc interval of = 350 msec and did not have pacing rhythm, and history of malignant neoplasm. Patients were

grouped according to QTc intervals as follows: normal QTc (350-439 msec, n = 1,022), prolonged QTc (440-479 msec, n = 1,849), and longest QTc (= 480 msec, n = 2,119) groups. Kaplan-Meier survival analysis showed that the longest QTc group had significantly higher 30-day and 5-year mortalities than the prolonged QTc group (P = 0.018 and P = 0.037). Cox regression analysis showed that all-cause death was more frequent within the longest QTc group than the prolonged QTc group in both univariate analysis [Hazard ratio (HR) 1.105; 95% confidence interval (CI) 1.006-1.213; P = 0.037] and multivariate analysis (HR 1.153; 95% CI 1.042-1.276; P = 0.006]. Interestingly, there was no significant difference in clinical outcomes between the normal QTc and prolonged QTc groups. Modeling with multivariable fractional polynomials showed a J-shaped association between QTc interval and 5-year all-cause mortality. In patients with AHF, QTc interval was an independent predictor of overall death. Patients with QTc interval up to 440-479 msec had a neutral prognosis, while patients whose QTc intervals were longer had higher risk of mortality.

P954

Long term outcome and factors associated with reduced systolic ventricular function in survivors of sudden cardiac arrest

H Helle Soeholm[1]; JK Kjaergaard[1]; JHT Hartvig Thomsen[1]; EH Hadziselimovic[1]; FKL Lippert[2]; LK Kober[1]; CH Hassager[1]
[1]Rigshospitalet - Copenhagen University Hospital, Heart Centre, Department of Cardiology, Copenhagen, Denmark; [2]Emergency Medicine and EMS, Head Office, Copenhagen, Denmark

Funding Acknowledgements: The Danish Foundation Trygfonden

Background: Outcome after sudden cardiac arrest (SCA) outside hospital has increased in recent years but is still only 10%. Nearly 50% of successfully resuscitated patients survive to discharge, however little is known about the association between post-SCA comorbidity, systolic LV function and long-term survival.
Purpose: In SCA survivors we aimed to describe long-term outcome and predictors of discharge with reduced systolic ventricular function defined by left ventricular ejection fraction (LVEF) < 40% at hospital discharge.
Methods: From a consecutive cohort in 2002 to 2011 of SCA-patients with cardiac cause in the Copenhagen area we report long-term outcome up to 11 years (median 3.6 years) presented as Kaplan-Meier curves. Logistic regression analyses were used to assess factors associated with discharge with LVEF = 40% vs. < 40% in patients without pre-SCA congestive heart failure according to the Danish National Patient Registry.
Results: A total of 497 SCA survivors with a mean age of 61 years were discharged alive from hospital (44% of patients admitted with successful resuscitation). Patients with LVEF = 40% had higher survival rates with 78% being alive at follow-up compared to 70% in patients with LVEF < 40%. (p logrank = 0.02). The difference in survival rates according to LVEF at discharge was primarily noted in patients with other causes than Acute Coronary Syndrome (ACS) as cause of SCA (Figure 1). Independent factors associated with LVEF < 40% at discharge were older age (odds ratio (OR) pr 5 years = 1.14 (95% CI: 1.03 - 1.26) and ACS (OR = 1.90 (1.01 - 3.50), whereas gender, time to return of spontaneous circulation (ROSC), bystander cardiopulmonary resuscitation (CPR), shockable initial rhythm nor being conscious at hospital arrival were not.
Conclusion: SCA survivors discharged alive with LVEF < 40% had significantly lower long-term survival rate compared to patients with preserved LVEF. Independent factors associated with reduced EF at discharge were older age and ACS as cause of SCA.

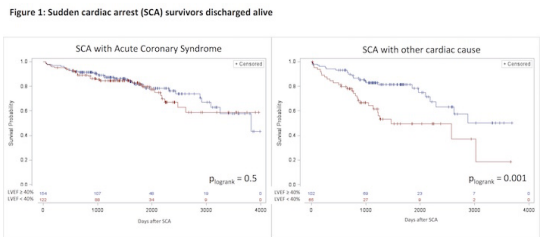


Figure 1

P955

Ivabradine in the treatment of heart failure with reduced ejection fraction

GM Dadashova[1]; NZ Farajova[1]
[1]Scientific Research Institute of Cardiology, Heart Failure, Baku, Azerbaijan

Background: Elevated heart rate represents an important risk factor for adverse outcomes in patients with heart failure. As heart rate is associated with hospital admissions and mortality, the open question is whether early treatment to achieve heart rate reduction with an If-channel inhibitor - ivabradine could reduce the high readmission rate and mortality.
Objectives: We aimed to assess the effect of heart-rate reduction by the selective sinus-node inhibitor ivabradine on outcomes in heart failure.
Material and methods - A prospective observational study that included 50 consecutive patients with hospitalized systolic heart failure, sinus rhythm and heart rate >70 b/min in whom ivabradine was administered during hospitalization or early after discharge. Clinical data, echocardiography, follow-up events were recorded at baseline and after 6 months, 12 months of follow-up; 1 year mortalty and rehospitalization rates for heart failure were compared with ivabradine and placebo groups. Patients were randomly assigned by computer-generated allocation schedule to ivabradine titrated to a maximum of 7·5 mg twice daily or matching placebo.
Results: 50 patients were randomly assigned to treatment groups (26 ivabradine, 24 placebo). Ivabradine was administered in 52,1%. Median follow-up was 12 months. 11 (42%) patients in the ivabradine group and 16 (66%) of those taking placebo had a hospitalization in one year period. The hospitalization rate (number of hospitalization) in the placebo group was much higher than in the ivabradine group (9 [37,5%] vs 3 [11%]; p < 0,001), and the deaths due to heart failure (14 [58%] vs 1 [3,8%]. One year all cause mortality was 30%. Fewer serious adverse events occurred in the ivabradine group (3 events) than in the placebo group (8 events, p < 0,001).
Conclusion: Ivabradine therapy in patients hospitalized for decompensated heart failure improve of clinical outcomes,well tolerated, reduce mortality and rehospitalizations.

P956

Endocrine hormonal imbalance in heart failure with reduced ejection fraction

M Matthias Naegele[1]; J Barthelmes[1]; S Cantatore[1]; F Ruschitzka[1]; I Sudano[1]; AJ Flammer[1]
[1]University Heart Center, Cardiology, Zurich, Switzerland

Funding Acknowledgements: LHW Foundation, Swiss Heart Foundation, University Hospital Zurich, Zurich Heart House

Background: Neurohormonal activation is an important pathophysiologic component of heart failure with reduced ejection fraction (HFrEF). Alterations in thyroid, parathyroid, sex and glucocorticoid hormones have also been described in isolated studies. A systemic analysis of these hormones in a contemporary cohort of well-treated patients is lacking.
Objective: Study the difference in thyroid hormone status (TSH, fT3/fT4 ratio), parathyroid hormone (PTH), estradiol, progesterone, prolactin, testosterone and cortisol in compensated patients with HFrEF compared to a cohort of healthy controls (HC).
Methods: In this prospective observational study, patients with compensated HFrEF with a last known LVEF of <40% and healthy controls, = 40 years of age, free of cardiovascular disease and major risk factors (smoking, hypertension, dyslipidemia or diabetes), were included. Exclusion criteria were use of hormone supplements, anti-thyroid therapy or amiodarone. Fasting morning blood samples were obtained and analyzed using established methods. All patients signed informed consent.
Results: We included 38 patients with HFrEF (mean age 62 ± 10 years, 29% female, mean LVEF 28 ± 7%, median NT-pro BNP 824 ng/L, 61% ischemic cardiomyopathy, 29% dilated cardiomyopathy) and 52 healthy controls (mean age 62 ± 12 years, 29% female). The majority of patients were on guideline-recommended therapies (ACE-inhibitor or angiotensin receptor blocker 95%, beta-blocker 95%, mineralocorticoid antagonist [MRA] 74%, diuretic 71% and CRT 32% of patients respectively). While there were no significant differences in TSH (2.1 ± 0.9 vs. 2.8 ± 2.5 mU/l, p = 0.15), HFrEF patients had a significantly lower fT3/fT4 ratio compared to controls (0.29 ± 0.06 vs 0.33 ± 0.05, p <0.01). PTH was significantly elevated in HFrEF patients vs. controls (74 ± 45 vs. 47 ± 12 p <0.01). Regarding steroid hormones, HFrEF patients had significantly elevated cortisol levels vs. controls (521 ± 155 vs. 418 ± 114 nmol/l, p <0.001). The difference in cortisol was observed in patients both with and without MRA therapy as well as with and without diabetes. Male HFrEF patients had lower testosterone levels than male controls (14 ± 6 vs. 19 ± 5 nmol/l, p <0.01). Estradiol, progesterone and prolactin levels were not different between both groups stratified by gender. The fT3/fT4 ratio correlated inversely with Log(NT-pro BNP) and high-sensitivity troponin T in HFrEF patients (r2 = 0.21, p <0.01 and r2 = 0.3, p <0.001). A significant positive association between PTH and Log(NT-pro BNP) was found (r2 = 0.36, p <0.001) which was stronger than the inverse correlation between PTH and eGFR (r2 = 0.16, p = 0.01). Cortisol correlated inversely with eGFR (r2 = 0.25, p = 0.001).

Conclusions: There is evidence of significant endocrine hormonal imbalance in HFrEF despite use of guideline-recommended therapies. A lower fT3/fT4 ratio, elevated PTH and elevated cortisol are associated with important prognostic biomarkers of HFrEF patients.

P957
Reduction in the number of heart failure hospitalizations in patients included in a heart failure unit.

V Victor Martinez Dosantos[1]; D Iglesias Del Valle[1]; E Garcia Ramirez[1]; Z Blazquez Bermejo[2]; J De Juan Baguda[3]; E De La Cruz Berlanga[1]; C Casanova Rodriguez[1]; R Cadenas Chamorro[1]; B Paredes Gonzalez[1]; A Martin-Penato Molina[1]; E Prieto Moriche[1]; R Cano Carrizal[1]; I Plaza Perez[1]
[1]University Hospital Infanta Sofia, Madrid, Spain; *[2]Hospital del Mar, Barcelona, Spain*; *[3]University Hospital 12 de Octubre, Madrid, Spain*

Background and objectives: The prevalence of heart failure (HF) is approximately 1-2% of the adult population in developed countries, and is increased in/to 10% of the population over 70 years old. The mortality rates for any cause at 12 months in hospitalized and ambulatory patients with HF are 17% and 7% respectively, as well as hospitalization rates at 12 months are 44% and 32% respectively in both groups. The main causes of deaths are related to cardiovascular disease.
The objectives of this study were to demonstrate the reduction of admissions for HF at 12 months after the inclusion of patients diagnosed with HF in our heart failure unit (HFU) and identify their causes.
Methods: We studied all patients included in our HFU between July 2014 and December 2016. All patients received an education focused on self-care behaviors and a contact telephone. A structured follow-up was carried out within the unit. Demographic and clinical data were collected per protocol. All relevant clinical changes, emergency visits, hospital admissions and deaths were documented. We counted all HF admissions in the year before and in the year after inclusion.
Results: We collected 137 patients with a mean age at inclusion of 65.1 years (±12.7), 73.7% men. They had a mean left ventricular eyection fraction of 28.1% (±9.7) and a baseline NT-proBNP levels of 5403.8 µg/L (±5162.3). Regarding the cardiovascular risk factors, 69.3% had hypertension, 35.0% had diabetes mellitus, 51.8 had dyslipidemia and 23.4% were smokers. The most frequent etiologies of HF were ischemic 35.8%, idiopathic 23.4, enolic 11.7% and hypertensive 10.2%. 47.4% were in functional class NYHA III, 39.4% in NYHA II, 9.5% in NYHA I and 3.6% in NYHA IV. 48.9% of patients were included after a first episode of HF, the rest was diagnosed with chronic HF. The mean number of admissions in the year prior to inclusion in the specific HF program was 1.04 admissions per patient, compared to 0.31 admissions in the following year. This implies a relative reduction of 69,9% (95% CI 51,6%-88.3%, $P < 0.0001$). In the year following the inclusion there were 43 hospitalizations in 24 patients. In 5 of them the patient died. 113 patients (82,5%) did not need any hospital admission in the following year. The most frequent causes of hospitalization in the following year were infection (34.9%), acute kidney injury (7.0%), arrhythmia (4.7%), anemia (4.7%) and therapeutic noncompliance (4.7%) The mortality rate at one year of follow-up was 9.7%.
Conclusion: In view of these results, there is evidence of the need for specific HFU for the management of this type of patients in order to reduce the number of HF admissions. HF hospitalizations were due to non-preventable causes in most cases, such as infection, acute renal failure, anemia and arrhythmic events.

P958
Predictors of recovery of left ventricular ejection fraction in patients included in a heart failure unit

D Iglesias Del Valle[1]; V Martinez Dosantos[1]; E Garcia Ramirez[1]; JS De Juan Baguda[2]; Z Blazquez Bermejo[3]; E De La Cruz Berlanga[1]; R Cano Carrizal[1]; C Casanova Rodriguez[1]; E Prieto Moriche[1]; A Martin Penato Molina[1]; R Cadenas Chamorro[1]; A Garcia Garcia[1]; MB Paredes Gonzalez[1]; I Plaza Perez[1]
[1]University Hospital Infanta Sofia, Madrid, Spain; *[2]University Hospital 12 de Octubre, Madrid, Spain*; *[3]Hospital del Mar, Barcelona, Spain*

Introduction: Left ventricular ejection fraction (LVEF) is the main parameter for measurement of left ventricular systolic function. It also allows us to differentiate between heart failure (HF) with preserved, mid-range or reduced ejection fraction. In case of reduced LVEF, it can remain stable or variate over time. It would be interesting to know what factors can predict a recovery of LVEF.
Purpose: To analyze predictors of recovery of LVEF in patients with heart failure with reduced ejection fraction (HFrEF) included in a heart failure unit (HFU).
Methods: We collected all patients with HFrEF included in our unit from July 2014 to December 2016. We collected prospectively data of baseline characteristics as well as LVEF measurements at baseline and at 1 year follow-up. For each patient, we calculated variation between LVEF at baseline and at 1 year. We analyzed predictors of variation in LVEF by simple and multiple linear regression. We obtained standardized regression coefficient (Beta) and statistical significance (P) for each possible predictor.
Results: We included a total of 112 patients. Mortality rate at 1 year was 7.6%. In 97 patients (86.6%) we were able to measure LVEF at 1 year. Mean age was 65.0 years (±12.7) and 70.1% were male. Considering the time course, 18.6% had chronic stable HF, 28.9% had chronic decompensated HF and 52.6% had new-onset HF. As cardiovascular risk factors, 70.1% had hypertension, 36.1% had diabetes, 49.5% had dyslipidemia and 22.7% were smokers. The most frequent etiologies of HFrEF were ischemic 35.1%, idiopathic 26.8%, hypertensive 11.3% and enolic 8.2%. As comorbidities, 39.2% had coronary artery disease, 14.4% had previous stroke, 16.5% had chronic obstructive pulmonary disease, 27.8% had anemia and 25.8% had chronic kidney disease. NYHA functional class at baseline was I 9.3%, II 41.2%, III 46.4% and IV 3.1%. Mean NT-proBNP levels at baseline were 5577.5 µg/L (±5558.2). Mean LVEF at baseline was 25.6% (±7.3) and at 1 year was 39.5% (±14.2), which means an average change of 14.0 (95% confidence interval 11.2-16.8, $P < 0,0001$). 48.5% of patients had LVEF = 40% at one year. In univariate linear regression analysis the variables age (Beta=-0.218, $P = 0.032$), new-onset versus chronic HF (Beta = 0.544, $P < 0.0001$), ischemic etiology (Beta=-0.347, $P = 0.0005$), coronary artery disease (Beta=-0.386, $P = 0.0001$), chronic kidney disease (Beta=-0.213, $P = 0.036$) and narrow QRS (Beta = 0.369, $P = 0.0002$) were associated with LVEF variation. In multivariate linear regression analysis only the variables new-onset HF (Beta = 0.428, $P < 0.0001$), coronary artery disease (Beta=-0.267, $P = 0.001$) and narrow QRS (Beta = 0.219, $P = 0.009$) remained as independent predictors of LVEF variation.
Conclusions: HFU represent the appropriate scenario for implementation of measures that can lead to a recovery in LVEF. New-onset versus chronic HF, absence of coronary artery disease and presence of narrow QRS are variables capable of predicting this recovery.

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Reduction of the need for diuretic treatment in patients included in a heart failure unit

V Victor Martinez Dosantos[1]; D Iglesias Del Valle[1]; E Garcia Ramirez[1]; Z Blazquez Bermejo[2]; J De Juan Baguda[3]; E De La Cruz Berlanga[1]; C Casanova Rodriguez[1]; A Martin-Penato Molina[1]; R Cadenas Chamorro[1]; B Paredes Gonzalez[1]; R Cano Carrizal[1]; E Prieto Moriche[1]; A Garcia Garcia[1]; I Plaza Perez[1]
[1]University Hospital Infanta Sofia, Madrid, Spain; *[2]Hospital del Mar, Barcelona, Spain*; *[3]University Hospital 12 de Octubre, Madrid, Spain*

Background and objectives: The prevalence of heart failure (HF) is approximately 1-2% of the adult population in developed countries, and is increased in/to 10% of the population over 70 years old. Most of these patients needs loop diuretic to reduce congestive symptoms. The objective of this study was to demonstrate the reduction of the need for diuretic treatment in patients diagnosed with HF during the first 12 months after inclusion in our heart failure unit (HFU).
Methods: We studied all patients included in our HFU between July 2014 and December 2016. Demographic and clinical data were collected per protocol. We measured the daily dose of loop diuretics at baseline, at 6 months and at 1 year of follow-up.
Results: We collected 114 patients with a mean age at inclusion of 64.9 years (±13.1). 70.2% of them were men. According to time course, 29.8% were included with chronic decompensated HF, 21.1% with chronic stable HF and 49.1% with new-onset HF. The mean left ventricular eyection fraction was 28.4% (±10.2) and mean baseline NT-proBNP levels were 5408.2 µg/L (±5292.6). Regarding the cardiovascular risk factors, 66,7% had hypertension, 36.8% had diabetes mellitus, 51.8 had dyslipidemia and 22.8% were smokers. The most frequent etiologies of HF were ischemic 33.3%, idiopathic 24.6, enolic 13.2% and hypertensive 10.5%. In terms of functional class, 49.1% had NYHA III and 39.5% NYHA II. The mortality rate during the first year was 7.4%. At inclusion, 64.9% of the patients were treated with furosemide, 9.6% with torasemide and the remaining 25.4% were not taking loop diuretics. At 6 months the percentages were 44.4%, 9.3% and 46.3% and at 1 year 40.6%, 8.9% and 50.5%, respectively. The mean daily dose of furosemide or equivalent (torasemide, assuming a 2:1 ratio) taken by the patients was 38.8, 25.7 and 24.8 mg at baseline, 6 months and 1 year after inclusion. There was an average reduction of 12.3 mg of the furosemide daily dose (95% CI 7.2-17.4, $p < 0.001$) in patients with treatment at baseline and at 6 months (108) and 12.2 mg (95% CI 6,1-18.1, $p < 0.001$) in those with treatment at the baseline and at 1 year (101). According to the time course of HF, the mean daily doses of furosemide are shown in the table 1.
Conclusion: The inclusion in our HFU meant a significant reduction in the doses of loop diuretics, mainly in the new-onset HF group.

1

	Baseline	6 months	1 year
Chronic decompensated HF	57,9	44,7	45.3
Chronic stable HF	23,8	24,8	19,5
New-onset HF	33,7	15,3	14,7

Table 1. Daily dose of furosemide (mg) according to the time course.

P960

Ejection fraction monitoring in patients with heart failure: the improved ejection fraction as a prognostic marker

ML Maria Lorena Coronel[1]; JP Cimbaro Canella[1]; MJ Blanchet[1]; SM Macin[1]; JI Parras[1]; BN Gonzalez Arjol[1]; L Borgo[1]; ER Perna[1]
[1]*J.F. Cabral Cardiology Institute, Corrientes, Argentina*

In patients with heart failure, ejection fraction (EF) was historically associated with prognosis. The "improved" ejection fraction has emerged in recent years, with diverse implicancy on prognosis. Data in our country about the role of this condition is limited.
Objective: Characterize the long-term outcome of patients with heart failure according to the EF at baseline and at follow-up.
Methods: Between January and August 2011, 79 patients with chronic heart failure (CHF) and 98 with acute heart failure (AHF) who survive at discharge, were prospectively included. At the moment of enrollment, an echocardiogram was performed (baseline-B) and it was repeated during follow up (S). A final follow up was done in August 2016, where we evaluated survival (SUR) and survival without hospitalization due to AHF (SURH). Cox proportional hazard model was built, which included significant variables in the univariate analysis. Patients were classified according to baseline EF in B1 = 40%, B2 41-49% and B3 = 50%; and according with EF during follow up in S1 = 40%; S2 >41% current and previous and improved EF (iEF) with previous EF = 40 and current >40%).
Results: Of the cohort of 177 patients; the mean age was 65 ± 12 years, male 66%, 39% with ischemic heart disease, 28% with diabetes; 68% with previous hospitalization due to AHF and 46% were in functional class III-IV. According to the baseline EF, the distribution was B1 = 58; B2 = 12 and B3 = 30%; and according to EF during follow up was S1 = 51; S2 = 34; iEF = 15%. From 102 patients with EF-B = 40%, 27 (26.5%) improved the EF; 11 of 21 with EF-B 41-49%, deteriorated the EF (52.4%) and only 4 of 54 patients with EF-B = 50%, deteriorated the EF during follow up.
The survival at five years in groups B1, B2 and B3 was 53; 55 and 50% (p = 0.586), while in S1, S2 and iEF was 52; 51 and 61% (p = 0.04). The survival free of hospitalization in B1, B2 and B3 was 35; 39 and 37% (p = 0.669) and in S1, S2 and iEF was 33; 37 and 44% (p = 0.043). In the Cox proportional hazard model, only the improved EF was associated with better survival free of hospitalization (HR = 0.44, 95%CI = 0.24-0.83, p = 0.01) and better survival at 5 years of follow up (HR = 0.47, 95%CI = 0.25-0.89, p = 0.0019).
Conclusion: One out four subjects with reduced EF improved the EF during follow up; and this group presented a better clinical course than those who maintain the EF reduced or preserved

P961

Efficacy of heart failure reversal treatment followed by 90 days follow up in chronic heart failure patients with low ejection fraction

RM Sane[1]; R Mandole[2]; D Amin[3]; G Amin[3]; R Singh[4]
[1]*Madhavbaug Multidisciplinary Cardiac Care Clinics and Hospitals, Mumbai, India*; [2]*Madhavbaug Cardiac Rehabilitation Center, Department of Research and Development, Raigad, India*; [3]*Madhavbaug Cardiac Rehabilitation Center, Department of Ayurvedic Medicines, Raigad, India*; [4]*Madhavbaug Cardiac Rehabilitation Center, Department of Exercise and Cardiac Investigations, Raigad, India*

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Objectives: The present study was designed to evaluate efficacy of heart failure reversal therapy (HFRT) that uses herbal procedure (panchakarma) and allied therapies, in chronic heart failure (CHF) patients with low ejection fraction.
Methods: This efficacy study was conducted in CHF patients (aged: 25-65 years, ejection fraction (EF) < 30%) wherein HFRT (60-75 minutes) consisting of snehana (external oleation), swedana (passive heat therapy), hrudaydhara (concoction dripping treatment) and basti (enema) was administered twice daily for 7 days. During this therapy and next 30 days, patients followed the study dinarcharya and were prescribed ARJ kadha in addition to their conventional treatment. The primary endpoint of this study was evaluation of maximum aerobic capacity uptake (MAC) as assessed by 6 minute walk distance (6MWD) using Cahalins equation from baseline, at end of 7 day treatment, follow-up after 30 days and 90 days. EF was assessed by 2D Echo at baseline and after 30 days of follow-up.
Results: CHF patients with < 30% EF (N = 52, mean [SD] age: 58.8 [10.8], 85% men) were enrolled in the study. There was a 100% compliance to study therapy. A significant improvement was observed in MAC levels (7.11%, p = 0.029), at end of 7 day therapy as compared to baseline. This improvement was maintained at two follow-up visits. Moreover ejection fraction was observed to be increased by 6.38%, p = 0,012 as compared to baseline at day 7 of the therapy
Conclusion: This 90 day follow up study highlights benefit of HFRT, as a part of maintenance treatment for CHF patients with reduced ejection fraction.

P962

The impact of coronary artery disease on clinical outcomes in heart failure with mid-range ejection fraction patients

JC Choe[1]; JH Choi[1]; SH Lee[1]; J Ahn[1]; JP Park[1]; HW Lee[1]; JH Oh[1]; HC Lee[1]; KS Cha[1]; TJ Hong[1]
[1]*Pusan National University Hospital, Department of Cardiology, Pusan, Korea Republic of*

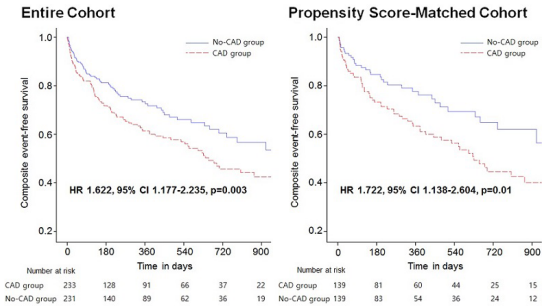
Background: Limited data are available on the role of coronary artery disease (CAD) in heart failure with mid-range ejection fraction (EF) (HFmrEF).
Purpose: We evaluated the association of CAD with outcomes and prognostic impact of revascularization in HFmrEF patients.
Methods: Among 464 consecutive patients with primary diagnosis of HFmrEF (EF 40-49%) in an urban tertiary referral center from October 2013 to March 2017, 233 (50.2%) were in CAD group and 231 (49.8%) were in no-CAD group. We compared the characteristics and composite event (all-cause death and cardiovascular readmission) in the entire and propensity score (PS)-matched cohorts.
Results: HFmrEF patients with CAD vs. no-CAD had higher incidence of hypertension, diabetes mellitus, peripheral artery disease, and right ventricular dysfunction and increased value of B-type natriuretic peptides and troponin I. Composite event occurred in 169 patients (36.4%), with a significantly higher rate in CAD group. After risk adjustment, the presence of CAD (entire: hazard ratio [HR] 1.622, 95%

P962 Clinical Outcomes

	Entire Cohort (n = 464)		Propensity Score-Matched Cohort (n = 278)		
CAD group (n = 233)	No-CAD group (n = 231)	p	CAD group (n = 139)	No-CAD group (n = 139)	p
All-cause death	28 (12.0%)	18 (7.8%)	0.048	16 (11.5%)	10 (7.2%)	0.047
CV death	15 (6.4%)	6 (2.6%)	0.017	9 (6.5%)	2 (1.4%)	0.049
CV readmission	73 (31.3%)	50 (21.6%)	0.031	49 (35.3%)	25 (18.0%)	0.016
CV death and CV readmission	88 (37.8%)	56 (24.0%)	0.004	58 (41.7%)	27 (19.4%)	0.006
All-cause death and CV readmission	101 (43.3%)	68 (29.4%)	0.003	65 (46.8%)	35 (25.2%)	0.01

confidence interval [CI] 1.177-2.235, p = 0.003; PS-matched: HR 1.722, 95% CI 1.138-2.604, p = 0.01) and age (entire: HR 1.028, 95% CI 1.013-1.043, p <0.001; PS-matched: HR 1.058, 95% CI 1.032-1.085, p <0.001) were predictive for the increased risk of composite event. In CAD group, coronary revascularization (n = 212) were associated with the improved risk of composite event (entire: HR 2.368, 95% CI 1.541-3.640, p <0.001; PS-matched: HR 3.631, 95% CI 2.018-6.531, p <0.001), with a similar composite event rate of no-CAD group (HR 0.942, 95% CI 0.669-1.326, p = 0.731). Additionally, the prescription of beta-blocker (HR 0.556, 95% CI 0.333-0.929, p = 0.025) and inhibitor of renin angiotensin system (HR 0.482, 95% CI 0.290-0.801, p = 0.005) were predictors of lower risk of composite event in CAD group.

Conclusions: CAD presented in approximately one-half of patients with HFmrEF and was associated with the unfavorable outcomes. However, coronary revascularization and optimal medical treatment could contribute to better outcomes in HFmrEF patients with CAD.



KM curve for composite event

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The value of bioimpedance vector analysis in decompensated heart failure patients with mid-range ejection fraction

A Klimenko[1]; S Villevalde[1]; Z Kobalava[1]
[1]*RUDN University, Moscow, Russian Federation*

Background: Volume overload is the known main driver for morbidity, mortality and hospital readmission in patients with decompensation of heart failure (DHF). Acute kidney injury (AKI) occurs up to 70% in DHF. But the prevalence remains unclear in DHF patients with mid-range ejection fraction (DHFmrEF). Bioimpedance vector analysis (BIVA) is a non-invasive accurate technique for hydration status (HS) evaluation. The aim of the study was to evaluate HS in DHFmrEF patients by BIVA and clinical/ radiographic criteria and to determine the diagnostic and prognostic value of these methods.

Methods: in 65 patients admitted with DHFmrEF (53 male, 69 ± 9 years (M ± SD), arterial hypertension 94%, ischemic heart disease 63%, myocardial infarction 51%, atrial fibrillation 49%, diabetes mellitus 26%, known chronic kidney disease 51%, ejection fraction (EF) 44.7 ± 3.0%) HS was assessed by BIVA and clinical/ radiographic criteria. AKI was defined using 2012 KDIGO Guidelines. Mann-Whitney test was performed. P < 0.05 was considered statistically significant.

Results: In 88% overhydrated patients clinical evaluation corresponded to BIVA results (G1), 12% patients were overhydrated only by BIVA (G2). Patients G1 compared with patients G2 had more marked clinically presentation of systemic congestion: ascites (22 vs 0%, p < 0.01), Rg-hydrothorax 49 vs 0%, p < 0.001), echo-hydropericardium (28 vs 0%, p < 0.05), oedema (93 vs 50%, p < 0.01), bilateral crackels (79 vs 50%, p < 0.05). Patients G1 compared with patients G2 were older (71 ± 7 vs 57 ± 7 years, p < 0.01), lower EF (44 ± 2.0 vs 47 ± 0.5 %, p < 0.01), higher level of NT-proBNP (12515 ± 3319 vs 9145 ± 2618 fmol/ml, p < 0.05) and tendence to higher rate of prior HF hospitalizations (57 vs 50%,p>0.05). There was lower frequency of AKI in G1 (29 vs 50% in G2, p < 0.05), but all AKI in G2 was transient (100 vs 41%, p < 0.01). Patients G1 compared with patients G2 had higher rate of HF rehospitalization (14 vs 0%, p < 0.001) and 30-days mortality (9 vs 0%, p < 0.01).

Conclusions: In 88% of patients with DHFmrHF and overhydration clinical/ radiographic criteria corresponded to BIVA results, 12% patients were overhydrated by BIVA only. Patients with overhydration by BIVA only had less evident systemic congestion; AKI was more frequent but transient and was not associated with poor short-term and long-term outcomes. Hydration status evaluation by BIVA has no independent prognostic value in patients with DHFmrHF.

Left ventricular systolic dysfunction before planned surgical revascularization: "grey area" features

P964

O Yepanchintseva[1]; K Mikhaliev[2]; O Zharinov[3]
[1]*Heart Institute of the Ministry of Healthcare of Ukraine, Kiev, Ukraine*; [2]*State Scientific Institution "Scientific and Practical Center of Preventive and Clinical Medicine", Kiev, Ukraine*; [3]*National Medical Academy of Postgraduate Education, Kiev, Ukraine*

Background: Left ventricular (LV) ejection fraction (EF) is a key parameter for risk stratification and decision-making in the management of patients with coronary heart disease (CHD) and heart failure (HF), including myocardial revascularization. The heterogeneity of HF with mid-range LV EF (HFmrEF) determines the need to study the clinical profile of these patients, compared to patients with preserved and reduced LV EF.

Purpose: to study the clinical characteristics of patients with stable CHD and HFmrEF (LV EF 40-49%), selected for the planned coronary artery bypass grafting (CABG) in the real-life settings.

Methods. A cross-sectional one-center study included 622 consecutive patients with stable CHD (mean age [61 ± 9] yr, 526 [84,6%] males and 96 [15,4%] females), selected for planned CABG. We analyzed demographic, clinical, laboratory, echocardiographic and coronary angiographic data. The population of enrolled patients was stratified into three groups according to LVEF: group 1 (G1; LVEF = 50%, n = 350 [56,3%]); group 2 (G2; LVEF 40-49%, n = 115 [18,5%]); and group 3 (G3; LVEF < 40%, n = 157 [25,2%]).

Results: The G2 profile was similar to G1 by parameters, such as frequency of functional class IV angina and mild tricuspid regurgitation, the severity of heart failure and mitral regurgitation. At the same time, G2 and G3 were comparable by gender; the frequency of earlier ST-elevation myocardial infarction; baseline diuretics use; serum potassium and estimated glomerular filtration rate; the frequency of moderate-to-severe tricuspid regurgitation; the frequency of significant left anterior descendent artery stenosis. Parameters in G2, having intermediate values compared to G1 and G3, were (shown as G1 vs. G2. vs. G3): the frequency of baseline aldosterone antagonists administration (8,3%; 24,3% and 41,4%, respectively; pG1-G2 < 0,001; pG1-G3 < 0,001; pG2-G3 = 0,017); the frequency of patients without mitral (71,2%; 36,5% and 18,4%, respectively; p < 0,001) and tricuspid regurgitation (87,1%; 70,5% and 41,4% in , respectively; p < 0,001); the frequency of moderate-to-severe mitral regurgitation (4,5%; 13,0%; and 38,9%, respectively; p < 0,001); mean systolic pulmonary artery pressure (30 [28-36]; 35 [30-40]; and 43 [35-62] mm Hg, respectively; pG1-G2 = 0,003; pG1-G3 < 0,001; pG2-G3 < 0,001); the frequency of LV aneurysm at coronary ventriculography (4,6%; 27,8%; and 47,1%, respectively; pG1-G2 < 0,001; pG1-G3 < 0,001; pG2-G3 = 0,007).

Conclusion: The population of patients with CHD and HFmrEF, undergoing CABG in the real-life clinical practice settings, is associated with clinical heterogeneity by vast majority of parameters, which influence the decision to perform CABG. Further studies are needed to determine LVEF changes after CABG in these patients.

P965

Heart failure with mid-range ejection fraction: characteristics and outcome in patients with and without acute kidney injury

IR Lala[1]; DA Darabantiu[1]; A Pop-Moldovan[1]; RM Christodorescu[2]; M Puschita[1]
[1]*Vasile Goldis Western University, Cardiology, Arad, Romania*; [2]*University of Medicine Victor Babes, Timisoara, Romania*

Background: Worsening renal function during hospitalization is associated with increased mortality among patients with heart failure and reduced ejection fraction (HFrEF) however in patients with HF and mid range ejection fraction (HFmrEF) such information is lacking.

Purpose: To evaluate incidence and prognostic implications of acute kidney injury (AKI) during hospitalization in HFmrEF patients.

Methods: Of 556 consecutive patients with a primary diagnosis of acute heart failure included in our regional heart failure registry 2014-2016, we identified 144 with HFmrEF (EF 40-49%). Patients were divided into two groups: with or without AKI (defined as an increase of serum creatinine by = 0.3 mg/dl within 48 hours from admission). For statistical analysis we used independent t test for comparison of continuous values, Pearson x^2 test for comparison of categorical values, multivariate logistic regression, survival curves and Cox regression for predictors of in-hospital mortality.

Results: Mean age was 68 ± 11 years and 42% were female regardless of AKI development. The percentage of patients with AKI was 27%. The AKI group presented higher systolic blood pressures compared to the non-AKI group (161 ± 41mmHg vs 146 ± 32mmHg p = 0.038). Previous history of chronic kidney disease was more often described among patients with AKI (64% vs. 31% p = 0.001). Hyperglycemia and QRS length were predictive factors for AKI development during hospitalization (OR = 1.05, p = 0.009; OR = 1.01, p = 0.01). Patients with AKI had a significantly

worse survival profile during hospitalization (log-rank test, p = 0.014) and Cox proportional hazards modelling showed a crude HR = 4.7 (95%CI [1.5.-14], p < 0.007) for in-hospital mortality.
Conclusion: Within the current group of HFmrEF, AKI is quite often and these patients are more likely to have a history of Chronic Kidney Disease and Hypertension. Hyperglycemia is of predictive value for AKI development during hospitalization. AKI was linked with worse in-hospital survival rates, thus this information might be important for future HFmEF outcome studies.

P966
Mortality in patients with heart failure and midrange ejection fraction

A Antonio Xavier Fontes[1]; C Serena[1]; L Oliveira[1]; S Moura-Ferreira[1]; C Almeida[1]; C Machado[1]; R Dourado[1]; E Santos[1]; N Pelicano[1]; AM Pacheco[1]; A Tavares[1]; F Melo[1]; D Martins[1]
[1]Hospital Divino Espirito Santo, Cardiology, Ponta Delgada, Portugal

Introduction: In 2016 the recommendations of the European Society of Cardiology introduced the concept of heart failure (HF) with mid-range leff ventricle ejection fraction (MREF) and suggested research by the scientific community around this concept, once patients (pts) shared characteristics of populations with reduced and preserved ejection fraction (EF). There is little data regarding mortality predictors in this population.
Objective: To identify predictors of mortality in patients with HF and MREF.
Methods: Retrospective study, which included 255 pts consecutively admitted to a center from January to December 2011, with the main diagnosis of decompensated HF. We performed 5 years follow-up. Clinical characteristics and exams results were evaluated. The binary logistic regression model was used to identify independent predictors of mortality.
Results: Of the 255 pts included, 87 (34.8%) presented MREF and 40 (45.9%) male gender. A complete follow-up time of 5 years was obtained in 98% of the cases, with a cumulative mortality of 50.0% in men and 55.3% in women (p = 0.620). Pts who died were an older population (73.6 ± 12.2 VS 63.5 ± 3.7 years old, p = 0.001), more cases of chronic kidney disease (69.7 VS 32.1%, p = 0.014), EF between 40-44% (67.4 VS 32.6%, p = 0.007) and with usual NYHA functional classes 2 or 3 (67.9% VS 32.1%, p < 0.001). They had higher levels of creatinine (1.41 (1.10-1.99) VS 1.04 (0.91-1.22 mg/dL, p < 0.001) and urea (60.5 (41.75-114.0) VS 45 (30.5-56.5) mg/dL, p = 0.001) and lower levels of hemoglobin (11.5 ± 2.0 VS 13.7 ± 1.8 g/dL, p = 0.001), hematocrit (35.2 ± 7.6 VS 42.2 ± 6.0%, p < 0.001) and sodium (135.7 ± 3.7 VS 137.7 ± 3.7mEq/L, p = 0.017). In terms of multivariate analysis the only independent predictor of mortality was the ejection fraction between 40-44% (OR = 4.5, 95% CI 1.31-15.53 p = 0.017).
Conclusion: Patients with HF and an episode of hospitalization due to decompensation present high mortality at 5 years. An EF between 40-44% was the independent predictor of mortality in pts at a 5-year follow-up.

P967
Impact of hypoalbuminemia in heart failure with preserved ejection fraction: a future therapeutic target?

M I Maria Ines Pires[1]; L Goncalves[1]; H Antunes[1]; J Gil[1]; L Abreu[1]; I Almeida[1]; J Costa Cabral[1]
[1]Hospital Sao Teotonio, Cardiology, Viseu, Portugal

Background: Hypoalbuminemia is common in heart failure (HF), particularly in elderly patients with multiple comorbidities, and is associated with a negative prognosis. This study aims to evaluate the impact of hypoalbuminemia in the prognosis of patients with heart failure with preserved ejection fraction (HFpEF).
Methods: All patients admitted for acute HFpEF between 2009 and 2015 in a Cardiology Department were enrolled in this study. Patients with cardiogenic shock were excluded from the analysis. Hypoalbuminemia was defined by serum albumin concentration < 3.5 g/dL. In-hospital mortality and mortality at 3, 6, 12, 18 and 24 months after discharge were assessed. Chi-square and Mann-Whitney U tests were used for group comparisons; survival analysis used Kaplan-Meier curves and log-rank tests; and predictors of mortality were assessed with logistic regression analysis.
Results: 473 patients were included in the study. Mean patient age was 79.4 ± 8.3 years, and 38.7% were male. Hypoalbuminemia occurred in 102 (21.6%) patients, and was associated with greater in-hospital mortality (53.3% vs. 46.7%; ?2 = 9.24; p = 0.002). In survival analysis, there was greater mortality in hypoalbuminemic patients in the follow up at 3 months (9.3% vs. 2.4%; ?2 = 8.10; p = 0.004), 6 months (14.9% vs. 6.6%; ?2 = 5.37; p = 0.020), 12 months (19.2% vs. 10.1%; ?2 = 4.03; p = 0.045), 18 months (21.1% vs. 11.1%; ?2 = 4.33; p = 0.037) and 24 months (23.2% vs. 11.5%; ?2 = 5.96; p = 0.015) after discharge. Univariate logistic regression identified the following predictors of in-hospital mortality: hypoalbuminemia (OR 4.426; 95% CI 1.565-12.513; p = 0.005), female gender (OR 9.232; 95% CI 1.204-70.812; p = 0.032), hemoglobin (OR 0.765; 95% CI 0.586-0.998; p = 0.048), urea (OR 1.013; 95% CI 1.001-1.026; p = 0.029), and B-type blood natriuretic peptide (OR 1.000; 95% CI 1.000-1.001; p = 0.035). At multivariate analysis hypoalbuminemia (OR 5.098; 95% CI 1.518-17.128; p = 0.008) and female gender (OR 11.396; 95% CI 1.352-96.031; p = 0.025) were the only independent predictors of in-hospital mortality. Hypoalbuminemia was also a predictor of 24 month-mortality (OR 2.314; 95% CI 1.189-4.507; p = 0.014), and in multivariate analysis was an independent predictor of worse survival at 24 months (OR 3.439; 95% CI 0.981-12.049; p = 0.05).
Conclusion: In this study, hypoalbuminemia was associated with greater in-hospital mortality as well as worse prognosis in the 24-month follow up, in patients with acute HFpEF. It was also an independent predictor of in-hospital and 24-month mortality. Since there are no disease-modifying therapies available for HFpEF and treatment of comorbidities has an important role in the management of these patients, in the future, albumin replacement treatment may arise as an option to reduce mortality in this subgroup of HF patients.

P968
Improvement in quality of life in patients with hereditary transthyretin amyloidosis with polyneuropathy and cardiomyopathy treated with inotersen in the phase 3 study NEURO-TTR

T Thibaud Damy[1]; M Maurer[2]; S Heitner[3]; B Drachman[4]; C Whelan[5]; D Judge[6]; S Guthrie[7]; L Tai[7]; S Hughes[7]; B Monia[7]; E Ackermann[7]; M Benson[8]
[1]Centre Hospitalier Universitaire Henri-Mondor, Creteil, France; *[2]Columbia University Medical Center, New York, United States of America*; *[3]Oregon Health & Science University, Portland, United States of America*; *[4]University of Pennsylvania, Philadelphia, United States of America*; *[5]University College London-National Amyloidosis Centre, London, United Kingdom*; *[6]Medical University of South Carolina, Charleston, United States of America*; *[7]Ionis Pharmaceuticals, Carlsbad, United States of America*; *[8]Indiana University School of Medicine, Indianapolis, United States of America*

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Introduction: Hereditary transthyretin (TTR) amyloidosis (hATTR) is a rare, progressive, and fatal disease. The disease is caused by misfolded TTR that builds up as amyloid in major organ systems, especially cardiac tissue and nerves, causing cardiomyopathy (CM) and polyneuropathy (PN), respectively. hATTR causes significant morbidity and a progressive decline in patient quality of life (QOL), severely limiting activities of daily living.
Purpose: To evaluate the effect of inotersen, an antisense oligonucleotide inhibitor of TTR protein production, on QOL of patients with hATTR with CM and PN.
Methods: NEURO-TTR (NCT01737398) is a global, randomised, double-blind, placebo-controlled phase 3 study. Adults (n = 172) with hATTR-PN (stage 1 or 2) with or without CM were randomly assigned 2:1 and received 300-mg weekly subcutaneous inotersen or placebo for 15 months. CM was defined as diagnosis of hATTR-CM or = 1.3 cm interventricular septum thickness (by echocardiography) at baseline. Primary endpoints were change from baseline to week 66 in Norfolk Quality of Life–Diabetic Neuropathy (Norfolk QOL-DN) total score and the modified Neuropathy Impairment Score+7 (mNIS+7). The Optum SF-36v2 Health Survey (SF-36v2) score was an exploratory outcome.
Results: At baseline, 69% of patients were male, mean age was 59 years (range, 27-81 years) and 63% (108/172) had CM. Of patients given placebo and inotersen, 55% (33/60) and 67% (75/112), respectively, had CM. Patients with CM had higher baseline mNIS+7 scores (higher scores indicate worse neuropathy), higher Norfolk QOL-DN total scores (higher scores indicate worse QOL) and lower SF-36v2 physical component summary scores (lower scores indicate worse QOL) than patients without CM. Inotersen-treated patients achieved highly statistically significant benefit compared with placebo in Norfolk QOL-DN total score (P = 0.0006) and mNIS+7 (P < 0.0001), irrespective of CM status. In patients with CM, inotersen treatment demonstrated significant improvement compared with placebo in Norfolk QOL-DN total score (P = 0.036) and the physical component summary score of SF-36v2 (P = 0.025). Most adverse events were mild or moderate. Key safety findings of thrombocytopenia and renal events were monitorable and manageable.
Conclusion: Significant improvement in Norfolk QOL-DN and SF-36v2 scores, which include several domains related to patient well-being and activities of daily living, suggest that inotersen improves the QOL of patients with hATTR-PN with CM, the hATTR population with the greatest disease burden.

P969
Impact of gender on the association between diastolic function and left atrial strain in atrial fibrillation patients with preserved ejection fraction

A Shavarov[1]; E Kokhan[2]; G Kiyakbaev[1]; Z Kobalava[1]
[1]RUDN University, Moscow, Russian Federation; *[2]Lomonosov Moscow State University, Moscow, Russian Federation*

Background: Diastolic dysfunction (DD) is one of the main causes of structural and functional changes of the left atrium (LA) that are substrate for atrial fibrillation (AF). Some studies have found that the rate of DD is higher in women compared to men. However, the influence of gender on the association between diastolic function and LA remodeling is yet to be established.
Purpose: We aimed to investigate the influence of gender on the relationship between left ventricle (LV) diastolic function parameters and LA strain in patients with AF and preserved ejection fraction.
Methods: Twenty seven men and 28 women (median age of 65 [60;72]) with recurrent non-valvular AF and mild to moderate DD were enrolled in the study. All patients had preserved LV ejection fraction (<50%). Beyond conventional echocardiographic protocol, global peak LA longitudinal strain (PALS, %) in the reservoir (r) and contractile (c) phases was measured using two-dimensional speckle tracking echocardiography. We used the diastolic index [(E/E')/LV-end diastolic volume] as a measure for LV stiffness.
Results: There were no significant differences in LA structural and functional parameters between men and women. However, despite the similar number of patients with E/E'>14 in both groups (9 vs 10 pts in men and women, respectively; p = 0.99), the medians of LV diastolic function parameters were worse in women than in men: E/E' (13 vs 11.2; p = 0.03) and diastolic index (0.13 vs 0.09 ml-1; p = 0.001). Women, but not men, had significant association between diastolic index and LA size (r = 0.52; p = 0.005 vs r=-0.32; p = 0.14, respectively); PALSr (r=-0.53; p = 0.004 vs r=-0.1; p = 0.62, respectively); PALSc (r = 0.51; p = 0.005 vs r=-0.1; p = 0.65, respectively); p for all interactions < 0.05.
Conclusion: A greater impairment of LV diastolic function was significantly associated with worsening of LA strain in the reservoir and contractile phases in women only. It could indicate a higher susceptibility of the women's LA to increased hemodynamic overload caused by DD.

P970

Effect of inspiratory muscle training on functional capacity in patients with heart failure with preserved ejection fraction: does baseline inspiratory muscle function matters?

P Palau Sampio[1]; E Dominguez[1]; JM Ramon[2]; L Lopez[2]; E Santas[2]; A Mollar[2]; E Valero[2]; J Melero[1]; JP Tormo[1]; A Briatore[1]; A Bellver[1]; FJ Chorro[2]; J Sanchis[2]; J Nunez[2]
[1]Hospital General de Castellón. Universitat Jaume I, Cardiology Department, Castellón, Spain; [2]Cardiology Departament, Hospital Clínic Universitari de Valencia, Valencia, Spain

Background: Heart failure with preserved ejection fraction (HFpEF) is a clinical syndrome characterized by severely impaired exercise capacity. Some evidence has shown that simple and home-based program of inspiratory muscle training (IMT) offers promising results in terms of functional capacity improvement. However, whether this effect is only limited to patients with inspiratory muscle weakness it is a matter of debate.
Purpose: We sought to evaluate whether the baseline inspiratory muscle function predicts the changes in peak oxygen uptake (peakVO2) after a program of IMT in HFpEF.
Methods and Results: A total of 45 stable symptomatic patients with HFpEF and NYHA II-III receive a 12-week home-based program of IMT between June 2012 and May 2016. They underwent a cardiopulmonary exercise test pre- and post-training and serial measurements of maximum inspiratory pressure (MIP) and peakVO2 were registered. Inspiratory muscle weakness (IMW) was defined as maximum inspiratory pressure (MIP) < 70% of normal predicted values. Multivariate linear regression analysis was used to assess the association between changes in peakVO2 (?-peakVO2) and baseline predicted MIP (pp-MIP).

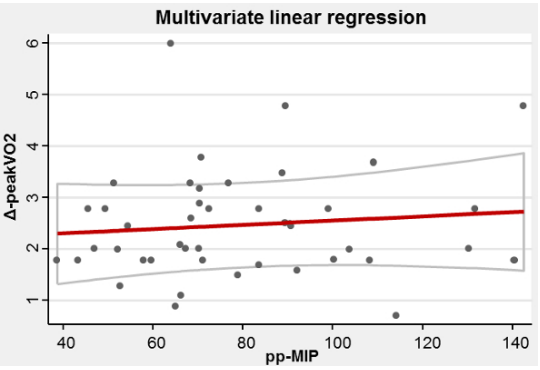

Figure 1

Mean (SD) age was 71.4 ± 9.7 years, 53.3% were women, and 35.1% displayed NYHA III. The mean peakVO2 and pp-?-peak VO2 were 10.4 ± 2.8 ml/min/kg and +2.2 ± 1.3 ml/min/kg (+21.3%), respectively. The median (IQR) of pp-MIP and ?-MIP were 71% (64-92) and 39.2 (26.7-80.4) cmH2O, respectively. After a multivariate analysis, baseline pp-MIP remained not associated with ?-peakVO2 (ß coefficient = 0.004, CI 95%: -0.009-0.017, p = 0.529) and is shown in figure 1.
Conclusions: In symptomatic and de-conditioned elderly patients with HFpEF, IMT offers an alternative to exercise training that improves maximal functional capacity regardless of baseline MIP.

P971

Potential usefulness of diastolic stress-test echocardiography in patients with suspicion of heart failure with preserved ejection fraction - a pilot study

E Belyavskiy[1]; DA Morris[1]; M Url-Michitsch[2]; N Verheyen[2]; AK Radha Krishnan[1]; A Frydas[1]; F Huang[1]; M Kropf[1]; R Lindhorst[1]; A Bobenko[1]; M Tadic[1]; C Tschoepe[1]; F Edelmann[1]; E Pieske-Kraigher[1]; B Pieske[1]
[1]Charite - Campus Virchow-Klinikum (CVK), Department of Internal Medicine and Cardiology, Charité - Universitätsmedizin Berlin, Berlin, Germany; [2]Medical University of Graz, Department of Cardiology, Graz, Austria

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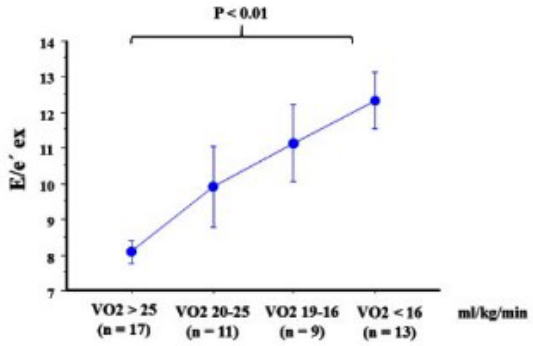
Aim: The purpose of this pilot study was to assess the potential usefulness of diastolic stress test echocardiography (DST) in patients with suspicion of heart failure with preserved ejection fraction (HFpEF).
Methods: Patients with suspicion of HFpEF (undetermined dyspnea NYHA class I-II, septal E/e' at rest 9 - 14, and NT-proBNP at rest < 220 pg/ml; n = 13) and a control group constituted by asymptomatic patients with arterial hypertension (HT) (n = 19) and healthy subjects (n = 18) were included. All patients were analyzed by 2D and Doppler echocardiography at rest and during exercise (DST) and underwent cardiopulmonary exercise test and NT-proBNP analysis during exercise. HFpEF during exercise was defined as exertional dyspnea and peak VO2 = 20.0 ml/kg/min.
Results: In patients with suspicion of HFpEF at rest, 84.6% of these patients developed HFpEF during exercise, whereas in the group of asymptomatic patients with HT and healthy subjects the rate of developed of HFpEF during exercise was 0%. Regarding the diagnostic performance of DST to detect HFpEF during exercise, an E/e' ratio > 15 during exercise was the most accurate parameter to detect HFpEF (accuracy 86%), albeit a low sensitivity (45.5%). Nonetheless, combining E/e' with tricuspid regurgitation (TR) velocity during exercise provided a significant increase in the sensitivity to detect patients with HFpEF during exercise (sensitivity 72.7%,

Diagnostic Performance of DST

Variable	Sensitivity	Specificity	VPP	VPN	Accuracy
E/e´> 15 or TR > 2.8 m/s during exercis	72.7%	79.5%	50%	91.2%	78%
E/e´> 15 during exercise alone	45.5%	97.4%	83.3%	86.3%	86%
TR > 2.8 m/s during exercise alone	36.4%	79.5%	33.3%	81.6%	70%
No increase of SV during exercise	9.1%	97.4%	50%	79.1%	78%
NT-proBNP during exercise > 125 pg/ml	36.4%	89.7%	50%	83.3%	78%
NT-proBNP during exercise > 220 pg/ml	18.2%	97.4%	66.7%	80.8%	80%

DST - diastolic stress test; VPP - positive predictive value, VPN - negative predictive value, TR-tricuspid regurgitation velocity, SV-stroke volume



Association of E/e' with peak VO2

specificity 79.5%, and accuracy 78%).In line with these findings, an increase of E/e' was significantly linked to worse peak VO2 and the combination of an increase of E/e' and TR velocity with elevated NT-proBNP values during exercise

Conclusion: The findings of this pilot study suggest that diastolic stress test using E/e' ratio and TR velocity could be of great usefulness to diagnose HFpEF during exercise in patients with suspicion of HFpEF at rest.

P972

Design and rationale of the EMPagliflozin outcomE tRial in patients with chrOnic heaRt failure (EMPEROR-Preserved)

J Butler[1]; M Packer[2]; G Filippatos[3]; F Zannad[4]; A Salsali[5]; K Kimura[6]; J Schnee[5]; C Zeller[7]; S Pocock[8]; J George[9]; M Brueckmann[9]; S D Anker[10]

[1]Stony Brook University Medical Center, Medicine, Stony Brook, United States of America; *[2]Baylor Heart and Vascular Institute, Dallas, United States of America*; *[3]University of Athens, Athens, Greece*; *[4]Institut Lorrain du Coeur et des Vaisseaux, Nancy, France*; *[5]Boehringer Ingelheim Pharmaceuticals, Ridgefield, United States of America*; *[6]Boehringer Ingelheim Canada Ltd., Burlington, Canada*; *[7]Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach, Germany*; *[8]London School of Hygiene and Tropical Medicine, London, United Kingdom*; *[9]Boehringer Ingelheim Pharma GmbH & Co. KG, Ingelheim, Germany*; *[10]Charité - Universitätsmedizin Berlin, Berlin, Germany*

Background and aims: Heart Failure with preserved ejection fraction (HFpEF) increasingly contributes to heart failure (HF) hospitalizations with outcomes as poor as in patients with HF and reduced ejection fraction (HFrEF), and there is no evidence-based therapy for HFpEF patients. In the EMPA-REG OUTCOME trial, the sodium-glucose co-transporter-2 (SGLT-2) empaglifozin reduced the risk of cardiovascular (CV) mortality by 38% and the risk of HF hospitalizations by 35% in patients with type 2 diabetes mellitus (T2DM) and established cardiovascular disease. Several mechanisms have been put forward to explain these benefits, which may go beyond the blood glucose lowering effect of empaglifozin. This raises the possibility of using empagliflozin as treatment for patients with established HF regardless of the presence or absence of diabetes.

Methods: The phase III randomized, double-blind EMPEROR-Preserved trial will explore the efficacy and safety of once daily empagliflozin 10 mg compared to placebo, in patients with chronic HFpEF with left ventricular ejection fraction (EF) > 40%. Patients are required to have elevated NT-proBNP levels (< 300 pg/ml for patients without atrial fibrillation (AF), or > 900 pg/ml for patients with AF), and structural heart disease or documented hospitalisation for HF within 12 months. The composite primary endpoint for this trial is the time to first adjudicated CV death or HHF. Approximately 4130 patients are planned to be randomized. The number of patients in this event-driven trial may be increased based on a blinded assessment of the primary event rate. The incidence of adjudicated HHF (first and recurrent) and the renal outcome of eGFR slope of change from baseline are key secondary endpoints.

Perspectives: As yet, EMPEROR-Preserved is the only phase III outcome study to evaluate an SGLT-2 inhibitor in patients with chronic HFpEF. Together with the EMPEROR-Reduced study, which is evaluating empaglifozin in patients with reduced ejection fraction (EF= 40%), these trials are expected to deliver conclusive insights regarding the value of empagliflozin treatment for patients with HF.

P973

Independent predictors of sudden cardiac death in patients with ischemic chronic heart failure with preserved ejection fraction and renal dysfunction

D Dmytro Lashkul[1]

[1]Zaporizhzhya State Medical University, Zaporizhzhya, Ukraine

The aim of the study was to determine the independent predictors of sudden cardiac death in patients with ischemic chronic heart failure (CHF) with preserved ejection fraction (EF) and renal dysfunction.

Materials and methods: The study included 243 patients (200 (80.3%) men) with (CHF), with an average age of 58.7 ± 9.3 years. CHF was diagnosed according to the Recommendations (2012) of the Association of Cardiologists of Ukraine, preserved EF were determined at EF>45%. The etiology of CHF: in 221 (90.9%) patients was a combination of coronary heart disease (CHD) and arterial hypertension, in 22 (9.1%) - CHD. II functional class (FC) was diagnosed in 112 (46.1%), III FC - 126 (51.8%), IV FC - 5 (2.1%), prior myocardial infarction in 165 (67.9%) patients. The glomerular filtration rate (GFR) was calculated according to the MDRD formula. Echocardiography was performed on ultrasound scanner GE VIVID 3 PRO EXPERT (USA). Primary endpoint: events of sudden cardiac death registered within 3 years after the signing of informed consent. To study the predictive value of the indicators the Receiver operating characteristic analysis, univariate and multivariate Cox's regression analysis was performed. The log rank test was used to compare different strata in Kaplan-Meier analyses of survival.

Results: As a result of the univariate analysis of Cox proportional risks, there are associated risk factors that have a reliable prognostic value for the risk of developing a three-year mortality in patients with ischemic CHF with preserved EF and renal dysfunction: matrix metalloproteinase-9 (odds ratio [OR] 12.66; 95% confidence interval [95% CI] 1.32-120.7; p = 0.02), age (OR 13.32; 95% CI 4.79-37.01; p < 0.0001), LV mass index (OR 5.61; 95% CI 1.79-17.54; p = 0.003), right ventricular pressure (RVPs) (OR 10.4; 95% CI 1.29-83.9; p = 0.02); Borg scale (OR 7.64; 95% CI 2.16-26.94, p = 0.001), GFR (OR 8.09; 95% CI 2.29-28.55, p = 0.001), creatinine (OR 6.38; 95% CI 1.81-22.50, p = 0.004), heart rate (OR 3,8; 95% CI, 1.38-10.43, p = 0.009), NTproBNP (OR 26.9; 95% CI 2.38-305.9; p = 0.008), LV end-diastolic size (OR 10,24; 95% CI 1.36-77.14; p = 0.02), LV end-diastolic volume (OR 3.71; 95% CI 1.34-10.23; p = 0.01). According to the results of the multivariate Cox regression analysis it was found that with the excess of the optimal distribution point for MMP-9 (<11.19 ng/ml), the risk of developing a three-year mortality in ischemic CHF patients with preserved EF and renal dysfunction significantly increases (hazard ratio [HR] 11.58; 95% CI 21-110.39; p = 0.03), age>72 years (HR 4.55; 95% CI 1.02-20.21; p = 0.04), LV mass index > 144 g/m2 (HR 5.18; 95% CI 0.99-27.07; p = 0.05), RVPs >27.3 mm Hg (HR 7,82; 95% CI 0.91-67.9; p = 0.05).

Conclusions: The level of MMP-9, age, LV mass index and RVPs in patients with ischemic chronic heart failure with preserved EF and renal dysfunction are independent predictors of the risk of sudden cardiac death during long-term follow-up.

P974

Rationale, design and methodology of the APOLLON trial: A population-based, observational registry of heart failure with mid-range and preserved ejection fraction

B Bulent Ozlek[1]; E Ozlek[1]; M Biteker[1]

[1] Sitki Koçman Universty, School of Medicine, Cardiology, Mugla, Turkey

On behalf of: APOLLON investigators

Objective: Although almost half of patients with chronic heart failure (HF) have mid-range (HFmrEF) and preserved left-ventricular ejection fraction (HFpEF), there have been no studies carried out with these patients in our country. This study aims to determine the demographic characteristics and current status of the clinical background of HFmrEF and HFpEF patients in a large, multicenter nationwide trial.

Methods: The APOLLON trial (A POpuLation-based, ObservationaL Registry Of Heart Failure with Mid-range and Preserved EjectioN Fraction) will be an observational, multicenter, and non-interventional study conducted in Turkey. The study population will include 1065 patients from 10 sites in Turkey. All the data will be collected at one point in time and current clinical practice will be evaluated (ClinicalTrials.gov number NCT03026114).

Results: We will enroll all consecutive patients admitted to the cardiology clinics from January 30, 2018, through April 31, 2018, who were at least 18 years of age and had New York Heart Association class II, III, or IV HF, elevated natriuretic peptides within last 30 days, and an left ventricular ejection fraction (LVEF) of at least 40%. Patients will be stratified into two categories according to LVEF: mid-range EF (HFmrEF, LVEF 40-49%), and preserved EF (HFpEF, LVEF = 50%). Exclusion criteria included; an alternative probable cause of the patient's symptoms (e.g., significant pulmonary disease), any LVEF below 40%, a history of acute coronary syndrome, coronary revascularization, or stroke within the previous 3 months, primary hemodynamically significant uncorrected valvular heart disease,

percutaneous or surgically corrected valvular disease (e.g., mechanical or biological prosthetic valves), hypertrophic or restrictive cardiomyopathy, pericardial disease; cor pulmonale or other cause of isolated right heart failure, pregnancy, patients with congenital heart diseases and heart transplant recipients. Regional quota sampling will be performed to ensure that the sample was representative of the Turkish population. Demographic, lifestyle, medical and therapeutic data will be collected by this specific survey.
Conclusions: APOLLON registry will be the largest and most comprehensive study in Turkey evaluating HF patients with a LVEF= 40%, and also will be the first study specifically analysing recently designated HFmrEF category.

P975
What influences exercise capacity in male and female with heart failure and preserved ejection fraction of left ventricle?

KI Cherniaieva[1]
[1]*National O.O. Bohomolets Medical University, Department Internal Medicine, Kiev, Ukraine*

The evaluation of the ability of an individual to perform exercise appears to be one of the strongest criteria of patient's subjective and objective well-being. However, factors observed in patients with HFpEF that alter exercise capacity are not unified and can be different dependently on gender.
Purpose: To reveal the link between echocardiographic parameters or laboratory tests and the results of 6-minute walk test n male and female with HFpEF, paying the most attention at diastolic function of left ventricle (LV).
Materials and methods. We consequently enrolled 54 patients with signs and symptoms of chronic HF II and III class NYHA at the moment of admission. Transthoracic 2D Echocardiography and tissue Doppler were performed to confirm LV diastolic dysfunction (criteria: LV ejection fraction (LVEF)>45%, left atrium diameter (dLA)>40 mm, LVMI >115 g/m^2 , E/e'>13). Plasma NT-proBNP level was evaluated to establish HFpEF; arterial elastance (Ea) and ventricular elastance (Ees) were calculated. 6-minute walk test was performed according to "ATS Statement: Guidelines for the Six-Minute Walk Test". Patients with proven coronary artery diseases were not included.
Results: 28 women and 26 men were examined. Groups didn't differ in age (f-71 ± 7,6 vs m-67,3 ± 12,1) and body mass index (BMI) (f-31,5 ± 4,9 vs m-29,9 ± 5,4), all p>0,05. The correlation analysis revealed an inverse correlation between the LA volume index (LAVI) (f-40,9 ± 6,3; m-42,7 ± 6,9), E/e' (f-15,1 ± 2,4; m-14,9 ± 1,5), mean pulmonary artery pressure (MPAP) (f-44,6 ± 13,3; m-38,2 ± 11,7), plasma NT-proBNP (f-595,5 ± 430,6; m-673,9 ± 428,3) level and distance of 6MW (f-362,5 ± 65,2; m-433,1 ± 102,3) in both groups of patients; between the right ventricle diameter (dRV) (2,9 ± 0,6), Ea (2,1 ± 0,5) and the distance of 6MW in women; between the age and the distance of 6MW in male. Results are shown in the table.
Conclusions: Such parameters as LAVI, MPAP, E/e', NT-proBNP correlates significantly with the results of 6MW test independently on gender. Correlation between age and 6MW distance in men can probably be associated with multiple comorbidities that are added with age. In women, correlation between dRV and Ea can be determined by mechanisms that provide a female-specific cardiovascular aetiology in HFpEF, but still it has to be clarified.

Correlation with 6MW test results

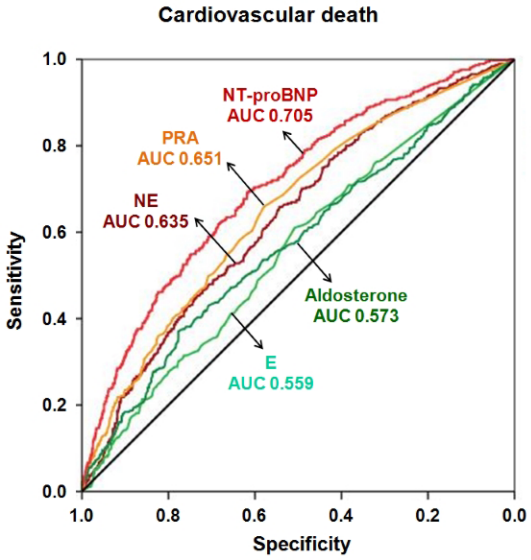
Groups	Parameters						
LAVI	E/e'	MPAP	NT-proBNP	dRV	Ea	Age	
Female (n = 28)	R=-0,541	R=-0,471	R=-0,684	R=-0,719	N/C	N/C	R=-0,479
Male (n = 26)	R=-0,687	R=-0,677	R=-0,637	R=-0,768	R=-0,524	R= -0,512	N/C

N/C - no correlation; in all cases p < 0,005

P976
Norepinephrine, plasma renin activity and prognosis in chronic systolic heart failure

A Alberto Aimo[1]; G Vergaro[2]; C Passino[1]; M Emdin[1]
[1]*Sant'Anna School of Advanced Studies, Pisa, Italy*; [2]*Gabriele Monasterio Foundation, Pisa, Italy*

Background: The demonstration of sympathetic and renin-angiotensin-aldosterone system activation in systolic heart failure (HF), and its negative prognostic impact, changed our understanding of HF pathophysiology and our therapeutic approach. Little is known on neurohormonal function in contemporary cohorts of HF patients.
Methods: Data from 1477 consecutive outpatients with systolic HF (LVEF < 50%) assessed from 1999 to 2016 were retrieved. Norepinephrine (NE), epinephrine (E), plasma renin activity (PRA), aldosterone, and N-terminal fraction of pro-B-type natriuretic peptide (NT-proBNP) were evaluated as predictors of cardiovascular death.
Results: Patients were aged 66 ± 13 years, 75% were men, and 44% had non-ischemic HF. Median
left ventricular ejection fraction (LVEF) was 32% (interquartile interval 25-38%). At the time of sampling, 69% of patients were on BB, 75% on ACEi/ARB, and 48% on MRA, versus 88%, 87%, and 66%, respectively, after therapy optimization during the same visit. Median values of NE, E, PRA, aldosterone, and NT-proBNP were 494 ng/L, 30 ng/L, 1.2 ng/mL/h, 130 ng/dL, and 1441 ng/L, respectively.
Over a median 4.8-year follow-up (2.4-8.2 years), 376 patients (26%) experienced cardiovascular death. The best cut-offs were 487 ng/L NE, 29 ng/L E, 1.2 ng/mL/h PRA, 200 ng/dL aldosterone, and 1645 ng/L NT-proBNP. The risk of cardiovascular death increased almost exponentially with the number of neurohormones equal or above cut-offs. All the neurohormones were univariate predictors of cardiovascular death. In prognostic model including age, ischemic etiology, estimated glomerular filtration rate (eGFR), LVEF, diabetes and chronic obstructive pulmonary disease, both NT-proBNP (hazard ratio - HR 1.36, 95% confidence interval - CI 1.25-1.49) and PRA (HR 1.22, 95% CI 1.14-1.31) were independent predictors of cardiovascular death. Also the 1.2 ng/mL/h PRA cut-off held independent prognostic value. Adding either absolute PRA levels or the PRA cut-off to a prognostic model including age, ischemic etiology, eGFR, LVEF, diabetes, chronic obstructive pulmonary disease, and NT-proBNP improved both discrimination and reclassification.
Conclusions: Circulating PRA and NE hold prognostic significance for cardiovascular death, although only PRA is independent predictor in a model including NT-proBNP. These assays deserve consideration as further tools for risk stratification in this patient population.



P977
Clinical outcome and prognosis in patient with acute heart failure

A Ashok Tahilyani[1]
[1]*Tan Tock Seng hospital, Cardiology , Singapore, Singapore*

Introduction: Acute pulmonary oedema (APO) is a potentially life-threatening condition, characterized by dyspnoea and is a frequent cause for recurrent hospitalisation. Many of the published series of patients with APO are historical and offer only descriptive data on highly selected patients following presentation with acute myocardial infarction. There is therefore an important paucity of data indicating the prognosis of this condition and limited data describing the spectrum of APO in the broader population. Moreover, little is known about the functional status of such patients and even less about their potential for rehabilitation.
Objective: To provide a description of clinical factors and outcomes in an unselected series of patients presenting with APO
Methods: A total of 921 patients were selected who were admitted under heart failure services in 2015 at Tan Tock Seng hospital, Singapore. All admissions with

primary cause of dyspnoea had their case records and chest radiograph/ TTE, and are identify as appropriate patients and were chosen for study.
Approval for this study was sought from our national health group domain specific review board Singapore.
Result: We followed these patient for 14 months +/- 8 months. The total mortality was 194 patients (21.06%) during the study period. Predictors for mortality were low EF (<35%) with high pulmonary artery systolic pressure (> 40mmHg) in the setting of AMI, sepsis and out of hospital collapse. Out of 921 patients enrolled in study, 38 died in 1 yr. Patient with EF of <25% have high mortality rate in year time. The commonest cause of admission for patient with pre-existing poor EF is non-compliance to fluid restriction and medication, Followed by Atrial fibrillation, IHD, Hypertensive urgency, and others.
Conclusion: The outlook of APO in the present era remains substantial but may have improved from historical series. According to previous studies published in acute medicine journal and EHJ on long term survival of acute of acute pulmonary oedema, the mortality rate has noted to be significantly lower in our study group. It is unclear as of now the exact cause of significantly improved mortality over period of time. However, its presumed to be the early revascularisation, increase awareness of fluid restriction and life style modification.

P978

Difference in n-terminal pro-b-type natriuretic peptide (NT-proBNP) levels in patients with heart failure with preserved ejection fraction (HFpEF) and non-cardiac comorbidity

KI Cherniaieva[1]
[1]*National O.O. Bohomolets Medical University, Department Internal Medicine, Kiev, Ukraine*

Multiple studies have already revealed a direct link between non-cardiac comorbidities and the development of HFpEF, emphasizing that it is challenging to assess how significant is a role of the comorbidities and their combinations in elevation of plasma NT-proBNP levels.
Purpose: To estimate the difference between NT-proBNP values in patients with HFpEF, who have one or more concomitant non-cardiac diseases diagnosed prior or during hospitalization, or doesn't have any of them.
Materials and methods. We enrolled 80 hemodynamically stable patients with HFpEF, confirmed clinically (signs and symptoms), instrumentally (echocardiography with careful evaluation of left ventricle diastolic function) and laboratory (elevated plasma NT-proBNP level). After additional examination (plasma levels of glucose and HbAc1, hemoglobin, ferritin, GFR, calculated by CKD-EPI and spirometry) patients were divided into 4 groups: with 1, 2 or 3 and more concomitant non-cardiac diseases, or without them.
Results: Non-cardiac comorbidity was present in 57 (71,25%) patients. Group 1 included 22 patients (27,5%), Group 2 - 12 (15%), Group 3 - 23 (28,75%) and Group 4 - 13 (16,25%). They didn't differ in age (63,2 ± 10,9 vs 63 ± 6,9 vs 69,9 ± 6,6 and 65 ± 7,7 years), gender (12 (54,5%) vs 7 (58,3%) vs 10 (43,5%) and 8 (61,5%) males) and body mass index (30,9 ± 4,3 vs 28,1 ± 1,9 vs 30,9 ± 4,1 and 28,8 ± 2,7); all p>0,05. Plasma NT-pro-BNP levels are demonstrated in the table. The revealed comorbidities distributed following way: type 1 diabetes mellitus – 23 (28,75%) patients, anemia - 16 (20%) patients, chronic renal impairment - 34 (42,5%), ventilation disorders (obstructive, restrictive and combined) - 29 (36,25%).
Conclusions: Benefits of using comorbidity-oriented approach to assessment of patients with HFpEF can be proven by statistically important difference in mean NT-proBNP levels between groups of patients with concomitant non-cardiac diseases and a group with none of them. Combination of non-cardiac comorbidities, when 3 or more are present, can cause higher levels of NT-proBNP.

NT-proBNP levels in groups of patients

	Gr1 (n = 22) M±m	Gr2 (n = 12) M±m	Gr3 (n = 23) M±m	Gr4 (n = 13) M±m
NT-proBNP	420,6±231,6*	615,4±323**	947,4±402,9***	287,4±132,2

*p < 0,001 compared to group 3; **p = 0,012 compared to group 4; ***p < 0,001 compared to group 4.

Chronic Heart Failure - Epidemiology, Prognosis, Outcome

P979

Association between resting heart rate, rhythm status and outcomes in patients with heart failure

Y Chia[1]; V Goh[2]; THK Teng[3]; WT Tay[3]; E Tan[4]; J Tromp[3]; C Chandramouli[3]; M Macdonald[5]; J Yap[6]; AM Richards[7]; IS Anand[8]; CSP Lam[9]
[1]*Duke-NUS Graduate Medical School Singapore, Singapore, Singapore*; [2]*Singapore General Hospital, Singapore, Singapore*; [3]*National Heart Centre Singapore, National Heart Research Institute, Singapore, Singapore*; [4]*National University Heart Centre, Singapore, Singapore*; [5]*Changi General Hospital, Singapore, Singapore*; [6]*National Heart Centre Singapore, Singapore, Singapore*; [7]*National University Health System, Cardiovascular Research Institute, Singapore, Singapore*; [8]*University of Minnesota, Veteran Affairs Medical Center, Minneapolis, United States of America*; [9]*National Heart Centre Singapore, University Medical Center Groningen, Duke NUS Medical School, Singapore, Singapore*

On behalf of: ASIAN-HF Investigators
Funding Acknowledgements: National Medical Research Council (Singapore); A*STAR Biomedical Research Council; Boston Scientific; Bayer

Background: Resting heart rate (HR) is an important prognostic marker for patients with heart failure (HF) and reduced ejection fraction (HFrEF) who are in sinus rhythm (SR). However, survival benefits in patients with preserved ejection fraction (HFpEF) or atrial fibrillation (AF) remain unclear.
Purpose: To determine if low resting HR reduced mortality or HF hospitalisations for patients with HF; and if ejection fraction (EF) or rhythm status modified this relationship.
Methods: We included patients with HFrEF (EF < 40%) or HFpEF (EF = 50%) from 11 Asian regions in the prospective multi-national ASIAN-HF study. Baseline clinical characteristics including resting HR (measured in beats per minute, bpm), comorbidities and usage of guideline recommended pharmacological agents were obtained. HR control was categorised into low (< 80 bpm) versus high (= 80 bpm). Patients with AF were identified from either a history of AF or baseline electrocardiography (ECG) showing AF rhythm. Patients in SR were defined as those without a history of AF and who were in SR on baseline ECG. Patients were followed for the primary composite outcome of all-cause mortality or first HF hospitalisation.
Results: A total of 6405 patients (mean age 62 ± 13 years, 73% male, 82% HFrEF) were studied. Majority had ischaemic aetiology of HF (54%) and were in New York Heart Association (NYHA) classes I-II (60%). Mean baseline HR was 79 ± 16 bpm, with 3542 (55%) and 2863 (45%) patients having low and high resting HR respectively. A total of 4076 (64%) patients were in SR while 1370 (21%) had AF; with similar HR control between both groups (SR vs AF, 79 ± 15 bpm vs 79 ± 18 bpm, p = 0.431). Patients with low resting HR were more likely to be older (63 vs 60 years, p < 0.001), have HFpEF (vs HFrEF, 21% vs 15%, p < 0.001), lower NYHA class (I-II vs III-IV, 72% vs 60%, p < 0.001) and on beta-blockers (80% vs 70%, p < 0.001). The primary outcome occurred in 1613 (25%) patients over a median follow-up period of 392 days. When adjusted for baseline clinical characteristics, comorbidities and HF medication (including beta-blocker) usage, a high (vs low) resting HR was associated with worse outcomes (adjusted HR = 1.18, 95% CI 1.06-1.31). This was irrespective of aetiology of HR (ischemic vs non-ischemic, p-interaction = 0.937), EF (reduced vs preserved, p-interaction = 0.107) or beta-blocker usage (p-interaction = 0.515). However, low (vs high) resting HR control conferred survival benefits mainly for patients in SR (adjusted HR = 0.78, 98% CI 0.68-0.90) but not for patients in AF (adjusted HR = 1.10, 95% CI 0.88 - 1.37) (p-interaction = 0.001) (Figure 1). Beta-blockers reduced the primary outcome (adjusted HR = 0.83, 95% CI 0.72-0.95) regardless of rhythm status (AF vs SR, p-interaction = 0.617).
Conclusions: Low resting HR reduced mortality or HF hospitalisation in patients with HF regardless of EF or beta-blocker usage. However, it was associated with better prognosis only for patients in SR and not for patients with AF.

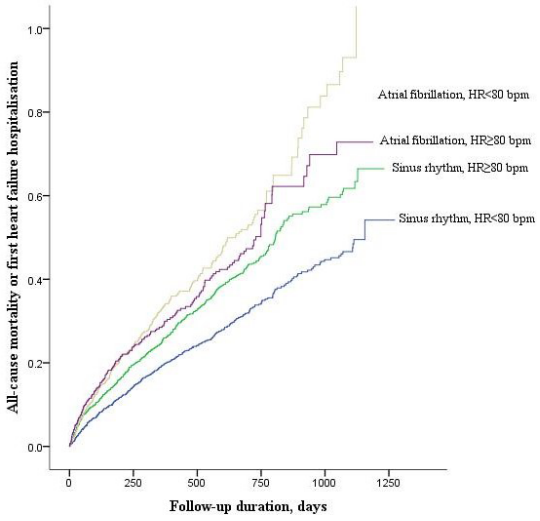


Figure 1

P980

Long-term and clinical profile of patients with heart failure with recovered ejection fraction followed in a non-tertiary hospital heart failure unit.

V Martinez Mateo[1]; MJ Fernandez Anguita[1]; L Cejudo Del Campo[1]; AJ Paule[1]
[1]Hospital Mancha Centro, Cardiology, Alcázar De San Juan, Ciudad Real, Spain, Spain

Introduction and objetives: Recovered heart failure (HF) with reduced ejection fraction (EF) is emerging as a different HF subtype. Information about his clinical profile and evolution in hospitals that are not reference in advanced HF is not described.
Purpose/Methods: We analyzed characteristics and prognosis of patients with recovered HF followed prospectively in the HF Unit of a non-tertiary hospital.
Results: Since the begin of Unit in 2010 until 2017, 431 patients with HF with reduced EF have been followed (median 50 months, 79.3% men, mean age 70.3 ± 12.2 years [median 73]). 26,9% patients (N 116) recovered EF, mainly in the first year of follow-up (76.7%). Compared with patients that did not recovered EF in the follow-up, they are younger (64.,3 vs 68,0 years, p 0.006), rate of ischemic origin of cardiomyopathy is less frequent (31.3% vs 51.4%, p 0.000) and presented less comorbidity (chronic renal failure 19.0 vs 27.9%, p 0.05; peripheral arterial disease 15.1 vs 26.1%, p 0.07; and chronic obstructive pulmonary disease 23 vs 33.7%, p 0.04). Rate of treatment with beta blockers/ivabradine, angiotensin converting enzyme inhibitors/angiotensin receptor blockers/sacubitril-valsartan and aldosterone antagonists were 93.1%, 95.7% and 57.1% respectively without significant differences between both groups. Implantable electronic devices (ICD/CRT) were more frequently used in patients without recovered EF (23.8 vs 10.4%, p 0.000). Younger age of 68 years (odds ratio [OR] 0.98, 95% confidence interval [CI] 0,96-0,99; p 0,025), ischemic origin (OR 1,12, CI 1,01-1,21; p 0,003) and use of aldosterone antagonists (OR 1,89, CI 1,09-3,26; p 0,023) were the variables independently associated to normalization of EF. Regarding the prognosis, mortality was lower in patients with recovered HF (survival median of 85,2 +/- 2,1 vs 74,2 +/- 1,9 months respectively; Logrank 11.5, p 0.001) with etiology of deaths mainly not secondary to HF (73.4 vs 46.0%, p 0.000). Chronic renal failure was the only variable independently associated to higher mortality (hazard ratio [HR] 0.42, CI 022-0.79; p 0.008) while age less than 68 years (HR 1,03, CI 95% 1,01-1,10; p 0,018) and treatment with beta blokers (HR 2,74, CC 95% 1,34-5.58; p 0,005) and sacubitril/valsartan (HR 11,97, CI 95% 3,26-43.9; p 0,000) with lower mortality.
Conclusion: Recovered HF is a frequent phenomenon in patients with HF with reduced EF. It has a more favorable clinical course, prognosis and basal characteristics than HF with persistent reduced EF. Further studies are needed to identify natural history and optimal medications for HF-recovered patients.

P981

Gender differences in the characteristics and outcomes of heart failure: the israel heart failure disease management study (IHF-DMS)

A Avishay Grupper[1]; D Freimark[1]; H Murad[2]; L Olmer[2]; M Benderly[2]; LS Freedman[2]; A Ziv[2]; N Friedman[3]; G Kaufman[3]; H Silver[3]; O Kalter-Leibovici[2]
[1]Sheba Medical Center, Leviev Heart Center, Ramat Gan, Israel; [2]The Gertner Institute for Epidemiology & Health Policy Research, Ramat Gan, Israel; [3]Maccabi Health Services, Tel Aviv, Israel

Background: Heart failure (HF) incidence is increasing in both men and women, and becoming a major and growing problem globally. Approximately half of all HF patients are women, and there are significant sex related differences in disease etiology, expression, patient's characteristics, outcomes and response to therapy.
Purpose: To study the effect of sex on HF characteristics and outcomes.
Methods: This is a sub-analysis of a randomized controlled prospective trial on HF disease management (DM) in which patients with HF (N = 1,360; 27.5% women) were randomly assigned to DM (N = 682) or usual care (UC) (N = 678). The study intervention did not significantly affect the rate of hospital admissions or mortality. The association between sex and hospital admissions and mortality during follow-up was tested in multivariable models adjusted for the patients' baseline characteristics.
Results: Compared to men, women recruited in this study were, on average, 3 years older and presented with worse functional capacity, quality of life and depression symptoms (p <0.001). Women were more likely than men to have HF with preserved EF (LVEF = 50%) and less likely to have HF due to ischemic heart disease (p <0.001). At recruitment, there were no sex-related differences with respect to treatment with HF medications (ACE-I/ARBs, beta adrenergic blockers, aldosterone antagonists and loop diuretics), but women were less likely than men to be treated with statins and anti-aggregates. During a median follow-up of 2.7 years (range: 0-5), 557 (56.5%) men and 218 (58.3%) women had a primary composite endpoint event (HF hospitalization or death from any cause). In multivariable analysis adjusted for study group, baseline demographic, EF, morbidity-related characteristics and medical treatment during follow-up, women were significantly less likely than men to experience the primary outcome [adjusted hazard ratio (HR) = 0.835, 95% confidence interval (CI): 0.699, 0.998)] or to die from any cause [adjusted HR = 0.712; 95%CI: 0.560, 0.901]. Women also had lower rates of all-cause hospital admissions and in-hospital days during follow-up compared to men [rate ratio (95%CI): 0.798; (0.705, 0.904), and 0.801 (0.661, 0.970), respectively].
Conclusions: Women with HF have 30% lower risk of all caused mortality as well as lower rates of all-cause hospital admissions and in-hospital stay compared to men. These sex differences were not explained by HF characteristics, comorbidities or medical treatment.

P982

Repeated echocardiography in chronic heart failure patients for personalized risk assessment

V J Victor Joharran Van Den Berg[1]; M Strachinaru[2]; KM Akkerhuis[2]; VAWM Umans[3]; M Brankovic[1]; N Van Boven[2]; OC Manintveld[2]; JH Cornel[3]; JJ Brugts[2]; K Caliskan[2]; AA Constantinescu[2]; ML Geleijnse[2]; E Boersma[1]; BM Van Dalen[2]; I Kardys[1]
[1]Erasmus Medical Center, Clinical epidemiology of Cardiology, Rotterdam, Netherlands; [2]Erasmus Medical Center, Cardiology, Rotterdam, Netherlands; [3]Northwest clinics, Cardiology, Alkmaar, Netherlands

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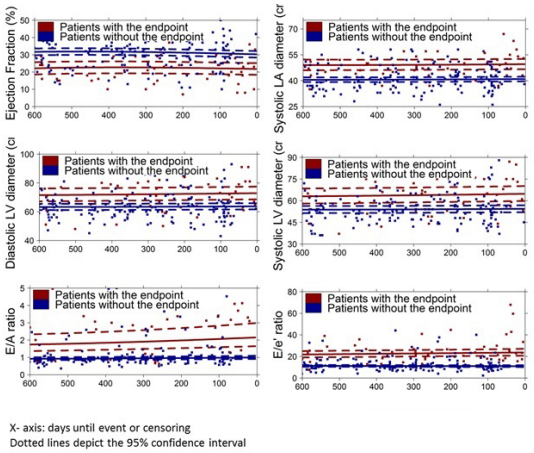
Background: Single, 'baseline' measurements of systolic and diastolic left ventricular function are predictive of adverse clinical outcomes in patient with chronic heart failure (CHF). However, the temporal evolution of these measurements preceding adverse outcomes has not yet been investigated in detail.
Purpose: To investigate temporal evolution of echocardiographic measurements and their associations with adverse clinical outcomes in CHF patients with reduced ejection fraction.
Methods: This prospective, observational study comprised of 106 CHF patients, in whom repeated, 6-monthly echocardiographs were performed. The following parameters with known high feasibility and reproducibility, were assessed using TOMTEC software: ejection fraction, end-diastolic and end-systolic left ventricle diameter, end-systolic left atrium diameter and Doppler E, e' and A wave velocities. The endpoint was a composite of HF hospitalization, cardiovascular death, left-ventricular assist device or heart transplantation, whichever occurred first. Data were analyzed using joint models, which combine mixed models for subject-specific evolution of the echocardiographic measurements and Cox regression for occurrence of the composite endpoint.
Results: Mean age was 58 years, 78% were man and 13 were in a NYHA-class >II at baseline. During a median (IQR) follow-up of 2.3 (1.7-2.7) years, a total 331

echocardiographs were made (median (IQR) per patient 3 (2-4)); 25 patients had the study endpoint. Overall, in endpoint cases, dimensions and diastolic ratios were larger and ejection fraction was lower(Table). None of the parameters revealed significant worsening on the echocardiographs before the study endpoint(Figure).
Conclusion: Although the echo measurements were associated with adverse cardiovascular outcomes, serial measurements during a 2.3 year time window did not capture echocardiographic worsening prior to the outcomes. It thus seems that regular monitoring of the systolic or diastolic function with echocardiography within the short time frame of several years does not carry incremental prognostic information over a single measurement.

Results joint models

Variable	-1 SD	Mean	+1 SD	Estimate (95%CI)	P-value
Left ventricle Ejection fraction#	20	29	38	2.86 (1.77 - 5.08)	<0.001
Diastolic left ventricle diameter$	55	65	77	2.25 (1.52 - 3.45)	<0.001
Systolic left ventricle diameter$	45	56	69	2.33 (1.49 - 3.62)	0.001
Systolic left atrial diameter$	35	42	51	4.18 (2.24 - 8.76)	<0.001
E/A-ratio$	0.65	1.02	1.98	5.72 (2.75 - 12.40)	<0.001
E/e'-ratio$	7.37	12.89	22.53	3.64 (2.35 - 6.08)	<0.001

Hazard per 1 SD decrease$ Hazard per 1 SD increase on the log2 scale



Average temporal trajectories

P983

Impact of a structured follow-up in a HF clinic after a HF hospitalization: a propensity score analysis

E Eva Cabrera Romero[1]; D Fernandez Vazquez[1]; DJ Vazquez Andres[1]; M Gomez Molina[1]; A Ferrero-Gregori[2]; I Gomez-Otero[3]; R Vazquez[4]; J Delgado Jimenez[5]; J Alvarez-Garcia[2]; MIRIAM Martinez-Selles[6]; A Bardaji[7]; P Garcia-Pavia[8]; JR Gonzalez-Juanatey[3]; JR Cinca[2]; DJ Pascual Figal[1]
[1]Hospital Clínico Univeristario Virgen de la Arrixaca, Servicio de Cardiologia, Murcia, Spain; *[2]Hospital de la Santa Creu i Sant Pau, Servicio de Cardiologia, Barcelona, Spain*; *[3]University Hospital of Santiago de Compostela, Servicio de Cardiologia y Unidad Coronaria, Santiago de Compostela, Spain*; *[4]University Hospital Puerta del Mar, Servicio de Cardiologia, Cadiz, Spain*; *[5]University Hospital 12 de Octubre, Servicio de Cardiologia, Madrid, Spain*; *[6]University Hospital Gregorio Maranon, Servicio de Cardiologia, Madrid, Spain*; *[7]Hospital Universitario Joan XXIII, Servicio de Cardiologia, Tarragona, Spain*; *[8]University Hospital Puerta de Hierro Majadahonda, Servicio de Cardiologia, Madrid, Spain*

On behalf of: REDINSCOR II research groups

Background: Heart failure (HF) re-hospitalizations remain as an unsolved problem in the management of the disease. The transition after discharge represents a relevant intervention in order to prevent re-hospitalizations. We aimed to study the impact in clinical practice of a specialized follow-up in the transition period after discharge.
Methods. The study population consisted of 1,831 patients hospitalized with acute HF from a national multicenter prospective registry (REDINSCOR II), which included data from 18 Spanish hospitals of varying complexity. Patients were consecutively recruited between October 2013 and December 2014. Data were collected using specifically designed web forms (http://www.redinscor2.org/), and quality controls were undertaken periodically. Patients were included in the analysis only if they had available data on "long term control after discharge", resulting in a study population of 1530 patients (83.6% of the total). Only 30 patients (1.6%) were lost to follow-up. Patients were classified according to the presence of a structured follow-up in a HF unit or not. Readmission was defined as any hospital readmission within the first year after discharge due to HF causes, or readmission due to any cause. Due to the nonrandomized nature of the study we performed a propensity score matching (statistical package "MatchIt" from the R project) analysis aimed to minimize potential biases that might influence the prognosis.
Results: Of 1500 patients, a total of 439 (29.3%) had access to a structured follow-up in a HF clinic. Among other characteristics, these patients had a higher rate of prior HF admissions (1.06 ± 1.50 vs. 0.74 ± 1.38, p <0.001) and lower left ventricular ejection fraction (44.5 ± 17.4 vs. 49.1 ± 18.1%, p <0.001). At 1 year, a structured transition in a HF clinic was associated with lower rate of HF readmissions (26.2% vs. 32.0%, p = 0.027) and all-cause readmissions (51.3% vs. 57.0%, p = 0.041), as well as lower number of HF readmissions (0.38 ± 0.78, p = 0.017) and all-cause readmissions (0.96 ± 1.46 vs. 1.25 ± 1.66, p = 0.003). After propensity score matching, a balanced population without differences in clinical characteristics was obtained (415 vs. 415); the transition in a HF unit had a significant effect on reducing the number of HF readmissions (RR 0.71 (CI95 0.54-0.93, p = 0.0136) and all-cause readmissions (RR 0.83 CI95% 0.68-0.99, 0.0487). No interactions were observed regarding clinical characteristics.
Conclusions. In the transition of care after a HF hospitalization, a structured follow-up in a HF clinic was associated with a lower risk of readmissions at 1-year, which was driven by a reduction in the risk of HF readmissions.

P984

What main concerns do patients with chronic heart failure report? A textual analysis of the opening question of the (Integrated) Palliative care Outcome Scale POS and IPOS

A Anna Oriani[1]; P Guo[2]; A Gadoud[3]; L Dunleavy[3]; M Brice[4]; P Kane[2]; FEM Murtagh[5]
[1]Hospital of San Giovanni, Oncological Institute of Southern Switzerland, Bellinzona, Switzerland; *[2]King's College London, Cicely Saunders Institute , London, United Kingdom*; *[3]Lancaster University, International Observatory on End of Life Care, Lancaster, United Kingdom*; *[4]St Christopher's Hospice, London, United Kingdom*; *[5]Hull York Medical School, Wolfson Palliative Care Research Centre, York, United Kingdom*

Background: Chronic heart failure has a significant impact on physical, psychological and social wellbeing. The Palliative care Outcome Scale and Integrated Palliative care Outcome Scale (POS and IPOS) are part of a family of tools specifically designed to measure physical symptoms, psychosocial, spiritual, and information and support needs of people severely affected by advanced chronic disease. POS and IPOS start with an open question for patients to report their main concerns, with subsequent closed questions about multi-dimensional needs.
Purpose: To explore the main concerns self-reported by patients with chronic heart failure in the open question of POS and IPOS.
Methods: A secondary textual analysis of the opening question of the POS and IPOS collected in three previous longitudinal studies with patients with chronic heart failure. Each participant contributed only one survey to this secondary analysis. Thematic analysis is used to search for and identify themes which are then used to compare with the subsequent closed questions.
Results: Data came from 102 participants in three studies: i) 40 participants with advanced heart failure, receiving a palliative care intervention, ii) 37 participants with end-stage kidney and chronic heart disease managed conservatively, and iii) 25 participants with advanced heart failure. The participants' mean age was 80 years (range 52-98), 62% male and 87% white. The baseline NYHA score was available for only 65 patients: 19 patients were classified NYHA I, 37 patients were classified NYHA II, and nine patients were classified NYHA III. 88/102 (86%) completed the IPOS or POS questionnaire, with 19 patients providing three responses to the open question, 18 providing two, 26 providing one and 25 patients providing no concerns. Of those 88 participants, 21 (24%, 95%C.I. 16%-32%) reported poor mobility, 14 (16%, 95% C.I. 10%-22%) breathlessness, 12 (14%) fatigue, 9 (10%, 95%C.I. 8%-20%) general concerns caused by co-morbidities , 9 (10%, 95% C.I. 4%-16%) pain, 8 (9%, 95% C.I. 4%-15%) practical problems not addressed, and 7 (8%, 95%C.I. 3%-11%) anxiety. There were other self-reported concerns including decrease of quality of life, fluid retention, depression, bowel problems, drowsiness, itch, cough, and insomnia. A total of 107 concerns were reported in the open questions problems. Of these 83 (77%) were reflected in the subsequent IPOS/POS closed questions.The high correspondence between the free-text responses and the

closed questions, indicates that most issues are included in the closed POS/IPOS items.
Conclusion: Patients affected by chronic heart failure are characterised by high symptom burden. IPOS and POS questionnaires reflect comprehensively main problems and concerns of these patients and the open question is able to capture the remaining unique concerns. IPOS and POS are useful questionnaires for advanced CHF, but further psychometric validation is needed in this population.

P985
Beta blocker doses and heart rate in patients with heart failure

M Grundtvig[1]; T Eriksen-Volnes[1]; LL Gullestad[2]
[1]St Olavs Hospital, Fagenheten, Trondheim, Norway; [2]Oslo University Hospital, Department of Cardiology and University of Oslo, Oslo, Norway

Background: It is an IA recommendation by the European Society of Cardiology to treat patients with heart failure (HF) and reduced left ventricular ejection fraction (HFrEF) with the highest tolerated dose of a beta blocker. The ESC Guidelines for HF recommend (IIa) additional treatment to reduce heart rate (HR) in patients with HFrEF and sinus rhythm and HR above 70 bpm. Our aim of the present study was to examine HR in relation to the use of beta blockers in these patients.
Method All the patients (N = 1762) with sinus rhythm at stable follow-up who had left ventricular ejection fraction (EF) < 40% at the first visit to the specialised heart failure hospital outpatient clinics and recorded in our registry were included.
Results: Two thirds of the patients had a resting HR < 70 bpm. Of those, 19.9 % used = 100 % of the target beta blocker dose, while 32.3 % of those with HR = 70 bpm used = 100 % of the dose . One third of the patients had a HR = 70bpm (Table 1) and these patients were younger, had higher NYHA functional class, higher NT-proBNP, lower blood pressure, lower serum sodium, lower eGFR, more obstructive lung disease and used much more diuretics than patients with HR < 70/min. One year mortality for the 1011 patients who were observed for a minimum of 365 days after stable follow-up were 5.8, 7.5, 11.0 and 14.7 % among the patients with a HR < 70, 70-79, 80-89 and > 89 bpm, respectively. Ivabradine was only used in one patient.
Conclusions: A high HR in patients with sinus rhythm and EF < 40 % is associated with worse clinical variables and worse outcome. A very high proportion of the patients with a HR = 70 bpm were not treated with/do not tolerate the target dose of a beta blocker suggesting increased effort to increase the beta blocker dose should be done or treatment with ivabradine should be considered. However, more studies to examine actions to reduce HR in these patients are in great need.

Table 1

Heart ratebpm	Beta blocker in % of target dose	Total N			
0-24%	25-49%	50-99%	≥100%		
<70	179	325	439	234	1177
70-79	35	94	135	127	391
80-89	16	22	62	45	145
>89	14	11	7	17	49
Total N	244	452	643	423	1762

Number of patients with sinus rhythm and EF < 40 % receiving defined doses of beta blocker

P986
Prevalence of iron studies during admission of heart failure patients to leeds teaching hospitals

R Khatib[1]; S Winsor[1]
[1]Leeds Teaching Hospitals NHS Trust, Department of Cardiology, Leeds, United Kingdom

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Background and Aim: Around 900,000 people in the United Kingdom are living with heart failure (HF), a life-limiting condition marked by frequent hospital admissions. Iron Deficiency (ID) and Iron Deficiency Anaemia (IDA) are known co-morbidities of HF, with research consistently showing an overall prevalence of around 50%. ESC guidelines recommend that patients with HF should be screened for ID and the simple treatment, iron therapy, be prescribed where appropriate. We audited the prevalence of iron studies during the admission of patients with HF to our hospital (LTHT) to inform practice.
Methodology: We reviewed the records of 1,000 patients to assess how many of those patients in a one year period anaemia had and how many had any iron studies done during their acute admission with HF. We assessed findings against the following standards:
- All patients admitted with HF need to have their haemoglobin levels measured
- All patients admitted with HF should have iron studies carried out during admission
- All patients admitted with HF and identified to have anaemia need iron studies
Results: From April 2016 - February 2017, 1,000 patients were admitted to LTHT, of whom 527 (53%) were men and 473 (47%) were women, with an average age of 77 (minimum 22 - maximum 101).
- Almost all patients (99.7%) had their haemoglobin (Hb) measured during admission, consequently 60% were found to be anaemic (n = 601).
- Only 12.9% of patients received a Hospital Episode Statistics (HES) code for secondary anaemia or ID suggesting the condition is under-reported.
- Only 18.5% of the overall sample and 24% of the anaemic patients received Ferritin testing.
- When iron studies were conducted, Ferritin was the predominant test requested, with only 1.1% and 0.4% of patients undergoing serum iron and transferrin saturations (TSAT) measurements, respectively.
Conclusion: Whilst standards for Hb testing are well adhered to, iron studies are not conducted as frequently as advised by guidance. Despite ESC and other international guidelines, clinicians are not screening enough for ID in both anaemic and non-anaemic patients admitted with HF. We need to raise awareness about the growing evidence in this area and improve protocols.

P987
Improvement of pulmonary hypertension is significantly correlated with better long-term prognosis in patients with pulmonary hypertension associated with heart failure with reduced ejection fraction

HJ Heejin Kwon[1]; JH Park[1]; SW Seong[1]; BJ Sun[1]; JH Lee[1]; IW Seong[1]
[1]Chungnam National University Hospital, cardiology, Daejeon, Korea Republic of

Background: The presence of pulmonary hypertension (PH) was associated with increased mortality and morbidity in heart failure with reduced ejection fraction (HFrEF) patients. However, there is little data on prognosis about the changes of LVEF and/or improvement of PH in these patients. We evaluated long-term survival of patients with PH associated with left ventricular systolic dysfunction (LVSD), especially according to the improvement of PH and/or LVSD.
Methods: We screened all consecutive patients with PH with HFrEF from September 2011 to March 2017. PH was defined maximal tricuspid regurgitation velocity (TR Vmax) more than 3.0m/sec and the presence of HFrEF was decided LVEF less than 45% with reasonable symptoms. We included only patients with follow-up echocardiographic study within 12 months.
Results: We screened total 1237 consecutive patients with PH and LVSD. Of them, 271 patients (167 males, mean 65 ± 14 years old) were enrolled in this analysis. In the baseline echocardiography, LVEF was 28 ± 8% and TR Vmax was 3.4 ± 0.4m/sec. In the follow-up echocardiography, 183 (68%) showed improvement of LVEF more than 15% and 165 (61%) demonstrated disappearance of PH (TR Vmax < 3.0m/s). According to the improvement of PH and/or LVSD, we classified the study group into 4 groups; group 1 with both improvement (134 patients), group 2 with PH and improvement of LVEF (49 patients), group 3 with disappearance of PH and LVSD (31 patients) and group 4 with sustained PH and LVSD (57 patients). Group 4 had older age and higher incidence of MI and aggravation of pre-existing HF. Study patients were followed total 31 ± 20 months. During the period, 97 patients had more than 1 episode of major cardiocerebrovascular accidents (MACCE, 52 deaths, 65 admissions for HF, and 17 strokes). The 5-year survival rate was 72.3% and MACCE-free survival rate was 50.2%. Group 4 showed worst survival rate and MACCE-free survival rate. Group 3 showed better MACCE-free survival rate than group 2 after the adjustment of age and gender (Figure 1, P = 0.001).
Conclusion: In patients with PH associated with HFrEF, the improvement of PH was associated with more favorable MACCE-free survival.

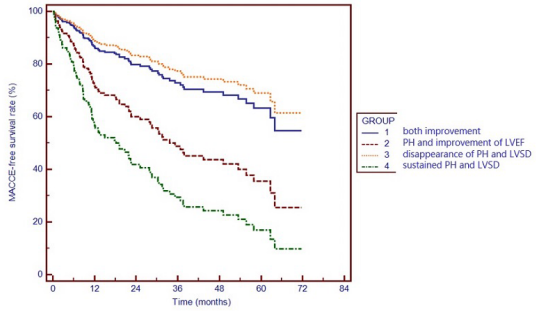


Figure 1. MACCE-free survival rate

P988

Health-related quality of life in heart failure: findings from a systematic literature review

L Giles[1]; CL Freeman[1]; P Field[1]; G Osei-Assibey[2]; E Sorstadius[3]; B Kartman[3]
[1]PharmaGenesis Oxford Central, Oxford, United Kingdom; *[2]Oxford PharmaGenesis, Oxford, United Kingdom*; *[3]AstraZeneca Gothenburg, Mölndal, Sweden*

Funding Acknowledgements: Systematic review and medical writing support were provided by PharmaGenesis Oxford Central, Oxford, UK, and funded by AstraZeneca.

Background: The physical and mental limitations of heart failure (HF) may have a significant effect on the health-related quality of life (HRQoL) of patients with the condition.
Purpose: To assess the impact of HF on HRQoL, using findings from a systematic literature review (SLR).
Methods: Electronic databases (Embase, MEDLINE and the Cochrane Library) were searched in May 2017 for observational studies reporting HRQoL in 200 patients or more, published between 2007 and 2017. The search was focused by HRQoL as measured using the 12- or 36-item Short Form Health Surveys (SF-12/36), the EuroQol Group 5-dimensions measure of health status (EQ-5D), Minnesota Living with Heart Failure Questionnaire (MLHFQ) and Kansas City Cardiomyopathy Questionnaire (KCCQ).
Results: In total, 54 studies were identified (Europe: 25; North America: 24; rest of the world/multinational: 5). Relatively few of these studies examined HRQoL in patients with HF in comparison with individuals without HF or patients with other chronic diseases. In a Dutch study, patients with HF (New York Heart Association [NYHA] class II–IV) reported worse scores across all individual domains of the SF-36 instrument compared with a population of age- and sex-matched community controls. In a cohort survey conducted in the UK, patients with HF reported lower baseline EQ-5D scores (both index value and visual analogue scale [VAS]) than patients with asthma, chronic obstructive pulmonary disease, diabetes mellitus, epilepsy or stroke. In this survey, the only significant change found for EQ-5D between baseline and 1-year follow-up was for VAS scores in HF. A total of four studies across the three geographical regions assessed HRQoL by NYHA class, all of which reported worse HRQoL (measured by MLHFQ and KCCQ) as NYHA class increased; in particular between NYHA class I and II, and between class II and III, with a smaller HRQoL reduction between class III and IV. An additional study reported that HRQoL declined with increasing disease severity, but did not report data for separate NYHA classes.
Conclusions: The evidence identified in this SLR indicates that HF is associated with worse HRQoL compared with both the general population and patients with other chronic diseases. Furthermore, there is evidence that HRQoL deteriorates as disease severity increases, in particular between NYHA class I and II, and between class II and III.

P989

30-days hospital readmission does not depend solely on clinical features of elderly heart failure patients discharged from Internal Medicine Units

V Verdiani[1]; P Francesconi[2]; F Profili[2]; G Panigada[3]; I Chiti[3]; R Laureano[4]; C Lusini[4]; F Bacci[4]; A Fortini[4]; G Landini[4]; L Masotti[5]
[1]Internal Medicine, Grosseto, Italy; *[2]Tuscany Regional Agency of Health, Florence, Italy*; *[3]Internal Medicine, Pescia, Italy*; *[4]Internal Medicine, Florence, Italy*; *[5]Internal Medicine, Empoli, Italy*

On behalf of: POST-SMIT Study Group

Background: Approximately 20% of Heart Failure (HF) patients who have been hospitalized are readmitted within 30 days. Although some different models have been studied, the preventability of readmission remains unclear, particularly in real world of Internal Medicine.
Methods: We enrolled patients who were discharged by 23 Internal Medical Units of Tuscany, an Italian region of 3,7 million inhabitants, in a period of 30 days with the main diagnosis of HF. We recorded epidemiological, instrumental and clinical data and patients were followed over a 1 month period. We considered 6 comorbidities: diabetes mellitus, hypertension, chronic renal failure (CRF), chronic obstructive pulmonary disease (COPD), atrial fibrillation (AF), anemia, NYHA class, LVEF during hospitalization. We compared 30-days readmission group respect not 30-days readmission group to identify potential correlations between features of patients and early rehospitalisation.
Results: We recruited 451 patients (M= 44.3%) with a mean age of 83 + 8.4 years. In 1 month follow-up 83 patients (18.4%) were readmissed for medical causes. In multivariate analysis, early readmission were not significantly correlated with: age (RR 0.99; P = 0.50), sex (F vs M RR 0.87; P = 0.54), diabetes (RR 1.11; P = 0.65), hypertension (RR 1.04; P = 0.88), CRF (RR 1.23; P = 0.11), COPD (RR1.38; P = 0.16), AF (RR 0.93; P = 0.76), anemia (RR 1.40; P = 0.15), NYHA class (RR 1.19; P = 0.46), LVEF < 40% (RR 1.20; P = 0.51), number of comorbidity (RR 1.01; P = 0.93). Only previous hospitalization (< 1 year) was significantly correlated with 30-days readmission (RR 1.38, P = 0.02).
Conclusions: The only clinical features are not able to indicate which of HF patients discharged from Internal medicine units are at major risk of early readmission, but patients with previous hospitalization are more likely to be readmissed. Particularly for elderly patients, future study should assess the relative contributions of different data (eg. caregiver presence, disability, psychological, environmental, social factors) to early readmission risk prediction.

P990

Overweight/obesity paradox in coronary patients with heart failure; the sociodemographic hypothesis. Hellenic Heart Failure study.

C Christina Chrysohoou[1]; M Kouvari[2]; M Kouvari[2]; P Aggelopoulos[1]; P Aggelopoulos[1]; C Pitsavos[1]; I Haritou Kotsopoulou[1]; D Tousoulis[1]; C Pitsavos[1]; D Tousoulis[1]
[1]University of Athens, Athens, Greece; *[2]Harokopio University, Nutrition Science - Dietetics, Athens, Greece*

Background/Introduction: Overweight/obese patients are to have a survival advantage in a wide range of chronic diseases during the rehabilitation procedure. This is also the case in established acute coronary syndrome (ACS) with major complications (i.e. heart failure), yet to what extend this is irrespective to other characteristics, remains inconclusive.
Purpose: to evaluate the role of body mass index (BMI) in ACS prognosis and to investigate potential interactions with patients' age and gender.
Methods: in 2006-2009, 1,000 consecutive patients, hospitalized at a Cardiologic Clinic in Athens with ACS diagnosis were enrolled in the study. In 2016, 10y follow-up was performed (75% participation rate). Overweight was defined as 25 = BMI = 29.9 kg/m2 while obesity as BMI>29.9 kg/m2.
Results: BMI status and 10y ACS prognosis followed a J-shape association (p = 0.009). In multivariate logistic regression analysis, overweight patients had significantly better ACS prognosis compared with their normalweight counterparts (OR = 0.45, 95%CI (0.23, 0.90)), whilst obese patients did not have significant differences compared with the reference group. Significant interactions were observed between sociodemographic parameters (i.e. age, gender) and BMI on 10y ACS prognosis (all ps for interaction = 5%). Stratified analysis was performed using gender (males vs. females) and age (= 65 vs. >65 years) as strata. In this context, the aforementioned paradoxical association was retained only in patients being females (OR = 0.37, 95%CI (0.16, 0.82)) and = 65 years (OR = 0.25, 95%CI (0.09, 0.69)).
Conclusions: overweight paradox was highlighted in 10 year ACS prognosis of heart failure patients. Nonetheless, certain prerequisites were indicatively stated, implying that this paradoxical association is not a case for all; with this relation being more evident in females and younger patients.

P991

Prognostic value of right and left heart functional parameters and levels of biomarkers in chronic heart failure patients with preserved, mid-ranged and reduced ejection fraction

LR Liana Tumasyan[1]; KG Adamyan[1]
[1]Institute of Cardiology, Yerevan, Armenia

The aim of study was to assess predictive power of right and left heart functional parameters and levels of NT-pro-BNP and high sensitivity C-reactive protein (hsCRP)

in prediction of survival in patients (pts) with chronic heart failure in relation to reduced (HFrEF), mid-ranged (HFmEF) or preserved (HFpEF) ejection fraction (EF).
Methods. Left (LV) and right ventricular (RV), left (LA) and right atrial (RA) functional parameters by Doppler and tissue echocardiography, NT-pro-BNP (pg/ml) and hsCRP (ng/ml) levels were prospectively studied in 186 pts (age 59.8) with HFrEF (EF < 0.4), 133 pts (age 60.1) with HFmEF (0.4 = EF < 0.5) and 128 pts (age 63.2) with HFpEF (EF = 0.5) in III-IV NYHA functional class CHF.
Results: During 37 ± 0.7 months from cardiac causes died total 157 (35.1%) pts, 68 (36.6%) with HFrEF, 46 (34.6%) with HFmEF and 43 (33.6%) with PEP. In HFpEF probability of death was predicted (p < 0.01 for all) by levels of hsCRP, tricuspid annulus plane systolic excursion (TAPSE), tissue Doppler-derived tricuspid lateral annular systolic velocity (s') and a mean e' septal and lateral wall and level of NT-proBNP (p < 0.05). Kaplan-Mayer analysis survival rate (%) was 62 in pts with CRP = 15, 61 with TAPSE < 15, 63 with s' < 8.5 and e' = 16 (63), 65 with NT-pro-BNP = 1500, and 86 with CRP < 15, 87 with TAPSE = 15, 86 with s' = 8.5, and 87 with e' < 16 and 80 with NT-pro-BNP < 1500. In HFrEF Kaplan-Mayer analysis (p < 0.01 for all) revealed survival of 62 for NT-proBNP = 3500, 62 with RA functional index (RA FI < 0.18) and 64 with LA FI < 0.19, 65.5 with pulmonary vein (PV) systolic contribution (SC) < 30, 62.5 with PV S/D < 0.25, and 88 with NT-pro-BNP < 3500, 86 with RA FI = 0.18 and 87 with LA FI = 0.19, 82 with PVSC = 30 and 87 with S/D = 0.25. In HFmEF independent prognosticators of death (p < 0.05) were levels of parameters with survival rate of 62 for NT-pro-BNP = 2500, 60 for hsCRP = 25, 64 for TAPSE < 14, and 62 for s' < 7, 63 and 66 for RAFI and LAFI < 0.3, and 88 in pts with NT-pro-BNP < 2500, 85 with CRP < 25, 83 for TAPSE = 14 and 87 for s' = 7, 86 and 85 with RAFI and LAFI = 0.3, respectively. Distribution of pts with HFrEF, HFmEF and HFrEF according to cut-off values NT-pro-BNP < 3500, 2500, 1500 and NT-pro-BNP = 3500, = 2500, = 1500 respectively, allowed to identify low (20.5, 19.6 and 18.7) and high risk (49.1, 46.1 and 42.7) of cardiac death (p < 0.01 for HFrEF, p < 0.05 for HFmEF and HFpEF).
Conclusions: 1) In pts with severe HFrEF, HFmEF and HFpEF revealed almost similar mortality. 2) NT-pro-BNP levels were the strong prognosticators in CHF, irrespective of LV EF, but with different threshold and significance. 3) Levels of hsCRP, RV systolic and LV diastolic dysfunction were the most powerful predictor of death in HFpEF. 4) LA and RA functional parameters were the strong prognosticators in HFrEF. 5) RV systolic and LV diastolic dysfunction, LA and RA parameters were strong predictor of death in HFmEF, but with low significance (p < 0.05) of parameters compare to HFpEF and HFrEF.

P992

Prevalence, incidence and long-term prognosis of patients with heart failure in the Czech Republic: data from national health registers 2012-2016

J Jiri Parenica[1]; JJ Jarkovsky[2]; JS Spinar[1]; MP Pavlusova[1]; RM Miklik[1]; SL Littnerova[2]; K Benesova[2]; J Belohlavek[3]; F Malek[4]; V Melenovsky[5]
[1]Faculty Hospital, Brno, Czech Republic; [2]Institute of Biostatistics and Analyses of Masaryk University, Brno, Czech Republic; [3]General University Hospital, Prague, Czech Republic; [4]Na Homolce Hospital, Prague, Czech Republic; [5]Institute for Clinical and Experimental Medicine (IKEM), Prague, Czech Republic

Data about the prevalence/incidence and prognosis of patients with heart failure are based on relatively small studies/registries. The aim of the work is to provide this important information on the basis of extensive data from Czech National Register of Hospitalizations and the Database of Deaths. Patients with heart failure were identified on the basis of the international classification of disease, used data were mainly from the period 2012-2016. Data since 1994 were used to estimate the number of surviving heart failure patients.
In total, 36-40 thousand patients with newly dignosed heart failure (as a first or other diagnosis according to DRG coding) are hospitalized annualy in the Czech Republic. In total, 60-65 thousand of the patients with diagnosis of heart failure (600 patients/100 thousand inhabitantts/year) are hospitalized annualy. The total number of hospitalizations for heart failure is 95-98 thousand /year (920 hospitalizations/100 thousand inhabitants/year). The average age of admitted men is 71 years, women 74 years. There is 52% of men. Hospitalization mortality is 16,2%. 5-year standardized survival is only 36.8%.
There are about 216,000 patients in the Czech Republic with a history of heart failure, which represents 2.7% of the adult population.

P993

What is the prevalence of heart failure with preserved ejection fraction (HFpEF) in patients referred for sleep apnoea assessment?

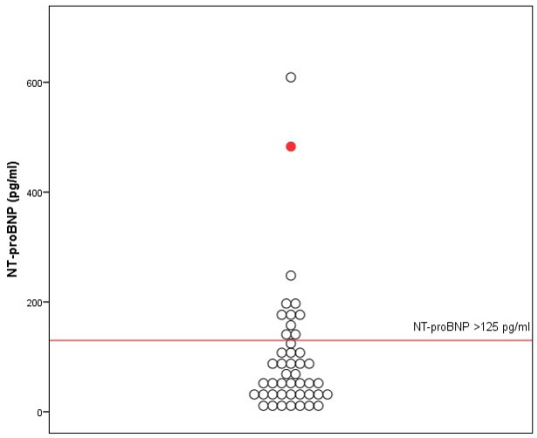
A Gallagher[1]; A Simonds[2]; MR Cowie[1]
[1]Imperial College London, London, United Kingdom; [2]Royal Brompton Hospital, London, United Kingdom

Background: Breathlessness and fatigue are common, but non-specific, presenting symptoms. Hence different diagnostic pathways can be followed, including testing for sleep apnoea. Patients diagnosed with obstructive sleep apnoea typically share similar phenotypic characteristics with heart failure patients with preserved ejection fraction (HFpEF). Current guidelines indicate the use of natriuretic peptide measurements and echocardiography, in symptomatic patients, for diagnostic work-up of heart failure.
Purpose: We aimed to determine the prevalence of HFpEF in patients with suspected sleep apnoea.
Methods: Patients scheduled for a diagnostic respiratory polygraphy were recruited as part of an ongoing observational study. Exclusion criteria included age < 40 years, previous heart failure diagnosis or treated sleep apnoea. Each patient was assessed with a cardiovascular examination, electrocardiogram, N-terminal-pro B-type natriuretic peptide (NT-proBNP) measurement and transthoracic echocardiogram.
Results: Preliminary data for 45 patients are presented. Hypertension (56%), diabetes (20%) and obesity (67%) were highly prevalent. Sleep apnoea was identified (apnoea-hypopnoea index >5) in 30 patients (67%). 64% were breathless and 34% reported peripheral oedema. All were in sinus rhythm. NT-proBNP levels ranged between 5-609pg/ml. 11 patients (24%) had NT-proBNP levels above 125pg/ml, the ESC recommended threshold for echocardiography referral. Of these 11 patients, all had normal left ventricular ejection fraction and one patient had definite diastolic dysfunction, but no associated heart failure symptoms or signs. Another patient had severe septal left ventricular hypertrophy. No significant correlation between NT-proBNP and sleep apnoea severity was seen (r = -0.39, p = 0.81).
Conclusion: Cardiovascular risk factors are highly prevalent in patients referred for sleep apnoea assessment. However, in this population HFpEF appears uncommon, with no cases identified according to standard criteria. Given the considerable proportion of false positive NT-proBNP levels, biomarker screening in these patients may be of limited benefit. The value of echocardiography, however, remains to be determined.

Patients (n = 45)	
Age (Mean ± SD)	59 ± 10.5
Male	23 (51%)
Body Mass Index (Mean ± SD)	32.8 ± 3.5
NT-proBNP (Median (IQR))	60 (32-119)
LVEF (Mean ± SD)	61.8 ± 3.6
Epworth Sleepiness Score (Median (IQR))	10 (6-14)

Table 1: Baseline Characteristics

Figure 1: NT-proBNP levels in patients tested for Sleep Apnoea



One patient with echocardiographic diastolic dysfunction highlighted in red

P994

Trends in one-year mortality following first-time heart failure hospitalization from 2010 to 2015 in Silesia. The SILCARD database

J T Niedziela[1]; Z Parma[2]; T Pawlowski[3]; P Rozentryt[4]; M Gasior[1]; W Wojakowski[2]
[1]Medical University of Silesia, SMDZ in Zabrze, 3rd Department of Cardiology, Silesian Centre for Heart Disease in Zabrze, Katowice, Poland; [2]Medical University of Silesia, Department of Cardiology and Structural Heart Diseases, School of Medicine in Katowice, Katowice, Poland; [3]Upper Silesian Medical Centre, 3rd Division of Cardiology, Katowice, Poland; [4]Medical University of Silesia, Department of Social Medicine and Prevention, School of Public Health in Bytom, Katowice, Poland

P994 One-year mortality

	2010 2011	2012 2013	2014 2015	p
Number of patients, n	10,741 10,954	10.202 9,682	9,909 10,008	0.07
Number of patients per 100,000 population, n 280	286 266	253 260	263 0.07	
Overall one-year mortality *, % 34.5	31.8 33.2	33.1 32.1	33.1 0.45	
Mortality < 65 years *, % 24.8	22.7 22.3	22.1 19.9	20.4 0.02	
Mortality ≥ 65 years *, % 36.8	34.1 36.1	36.0 35.4	36.4 1	
One-year mortality in women *, % 35.4	32.6 35.0	34.1 35.1	35.5 0.45	
One-year mortaity in men *, % 33.5	30.9 31.3	32.1 29.2	30.8 0.26	
One-year mortality andjusted for age and sex, % 39.3	35.8 33.7	30.9 29.6	29.7 0.02	

* - unadjusted

Background: Heart failure (HF) is a leading epidemic problem worldwide. The data on the outcomes including mortality rates in patients with HF is of great epidemic and clinical importance.
Purpose: The purpose of the study was to analyse the secular trends in one-year mortality in patients hospitalized for the first time with principal diagnosis of HF in Silesia, Poland between 2010 and 2015.
Methods: Data on the patients hospitalized each year for the first time with the primary HF diagnosis, and their one-year mortality was obtained from National Health Fund in Katowice. One-year mortality from the hospital admission was presented as crude, by sex and age groups (< 65 and = 65 years old) and after adjustment for age and sex. The trends were analysed using Mann Kendall trend test. P-value of < 0.05 was considered significant.
Results: The study included 61,496 patients admitted to hospital for the first time with principal diagnosis of HF between 2010 and 2015. There was no significant trend in crude one-year all-cause mortality. After adjustment for age and sex, the decreasing trend became significant. Similar trend was found among patients < 65 years old.
Conclusion: In large population of patients hospitalized for the first time with principal diagnosis of HF, decreasing trend in one-year mortality adjusted for age and sex was found between 2010 and 2015.

P995

Echo-derived peak cardiac power output-to-left ventricular mass with cardiopulmonary exercise testing predicts outcome in patients with heart failure and depressed systolic function

N Pugliese[1]; I Fabiani[1]; G Galeotti[1]; G Mandoli[1]; L Conte[1]; A Lombardo[1]; A Simioniuc[1]; G Bigalli[1]; V Di Bello[1]; F Dini[1]
[1]*Azienda Ospedaliero-Universitaria Pisana, Cardiothoracic Department, Pisa, Italy*

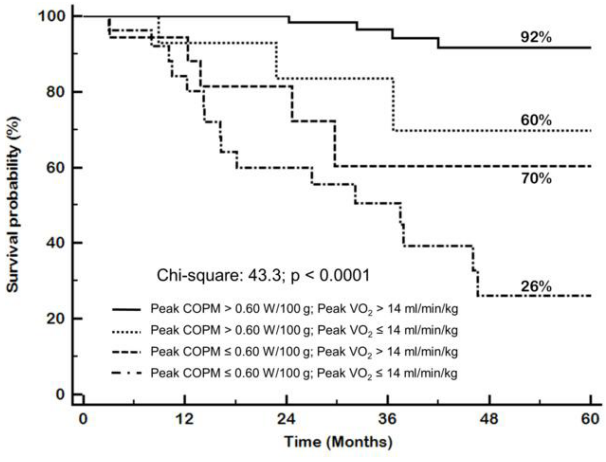


Fig.1

Background: Peak cardiac power output-to-mass (CPOM) represents a measure of the rate at which cardiac work is delivered with respect to the potential energy stored in left ventricle (LV) mass.
Aim: To investigate the value of peak CPOM and cardiopulmonary exercise test (CPET) in risk stratification of patients with chronic heart failure (HF).
Materials and methods. We studied 137 patients with chronic HF (mean LV ejection fraction 30%) undergoing CPET and exercise stress echocardiography. CPOM was calculated as the product of a constant (K = 2.22 × 10-1) with cardiac output (CO) and the mean arterial pressure (MAP), divided by LV mass (M), and expressed in the unit of W/100 g: CPOM = [K × CO (l/min) × MAP (mmHg)] / M(g). Patients were followed-up for the primary end-point, that included all-cause death and VAD implantation and the composite end-point that comprised hospitalization for HF.
Results: In multivariate Cox regression analyses, peak COPM was selected as the most powerful independent predictor of the end points (HR: 0.043, 95% CI: 0.004-0.044, p = 0.008; HR: 0.011, 95% CI: 0.02-0.66, p = 0.016). 5-year survival free from all-cause death or VAD implantation was 92% in those exhibiting VO2 >14 ml/min/kg and peak COPM >0.6 W/100 g. Peak VO2 = 14 ml/min/kg provided incremental prognostic value over demographic and clinical variables, BNP and resting echocardiographic parameters (chi-square: from 34.2 to 46.1; p = 0.005), that was further increased by peak COPM = 0.6 W/100 g (chi square: 52.2; p = 0.026).
Conclusion: Peak COPM and peak VO2 showed independent and incremental prognostic values in patients with chronic HF.

P996

Low T3, it is not the same.

SM Mettini[1]; DA Fernandez[1]; CA Biglia[1]; C Cejas[1]; M Taboada[1]; IL Ramella[1]; L Secco[1]; SM Pereiro Gonzalez[1]
[1]*Hospital Center Churruca-Visca, Buenos Aires, Argentina*

Objective: To establish the difference between patients (p) hospitalized with decompensating heart failure (DHF) according to T3 values (normal or diminished).
Method: It is a retrospective analysis of 524 patients admitted for decompensated heart failure, consecutively, in our Cardiology Department, from June 2012 to November 2017. Median follows up: 39 months (Q1 24 - Q3 54). We divided 2 groups (G) according to admission T3 values: G1: normal T3 (260 p) and G2: low T3 (173 p). Quantitative variables were expressed with median (m) and quartiles (analyzed by Mann Whitney's Test). Dichotomous variables were analyzed by Chi^2. It had been made a survival curve (Kaplan-Meier and Cox-Mantel test) for mortality and rehospitalization. It had been evaluated variables'impact on endpoints for uni and multivariable analysis.
Results: Median age was G1 69 years old (yo) (Q1 61-Q3 78) vs 79 yo (Q1 68-Q3 85), with differences statistically significant (DSS). There were less p older than 75 yo at G1 (46.2 vs 65.3% p < 0.001), and shorter stay (4 vs 5 days, p = 0.011), but more smokers (49 vs 34.7%, p = 0.003). Prevalent etiology was coronary disease but the DSS were of unknown etiology and valvular at G2 (p < 0,05 and p = 0.009 respectively). Inadequate treatment and arrhythmias were the 2 more prevalent decompensating cause, without DDS, but diet was higher at G1 (p < 0.001). G1 p had wider intraventricular diameters with DSS and lower ejection fraction (EF). Both G had predominantly p with EF < 40%. Presence of HFpEF was bigger at G2, also the number of p with a pacemaker (p = 0.001). At admission, G2 had DSS in higher values of BNP, BUN, creatinine and glomerular filtration rate (GFR), and lower values of proteins and albumin, and at hospital discharge, as higher values of creatinine and BUN. Normal T3 was associated with higher diminished in the GFR during the stay. Low T3 had more atrial fibrillation (p < 0.05). More patients in G2 needed non-invasive ventilation and inotropic agents (p = 0.005 and p = 0.02, respectively).

The multivariate analysis showed that age, albumin, GFR, cardiac rhythm and elderly patients were independent predictors to low T3 ($p < 0.001$, OR 1.08; $p < 0.001$, OR 0.3; $p < 0.05$, OR 0.98; $p < 0.05$, OR 0.55 y $p < 0.05$, OR 0.43 respectively). Patients with low T3 had higher hospital mortality (5.8 vs 1.5% $p = 0.01$) but not at the follow up (40.3% vs 64% $p < 0.001$). In the multivariate analysis, T3 value, maximum furosemide dose, patients older than 75 yo, cardiac rhythm and inotropic use, were hospital mortality independent predictors. T3 values were associated with rehospitalization (OR 0.99).
Conclusions: Patients with low T3 showed a subgroup with more serious heart failure. T3 values also were associated with worst hospital evolution and rehospitalization. We believe it is very important to detect this sort of patients in admission to adjust treatment. Hormonal replace treatment is still controversial.

P997
Is there a real difference in age between patients with heart failure with reduced or preserved left ventricular ejection fraction?

A Abdallah Al-Mohammad[1]; D Rogers[1]; NT Lewis[1]; A Charalampopoulos[1]
[1]*Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, United Kingdom*

Introduction and Purpose: The majority of those with Heart failure (HF) are old people. Patients with HF associated with reduced left ventricular ejection fraction (HFREF) are believed to be younger than those with other types of HF. We investigated whether age varies according to the type of HF diagnosed in an incident HF clinic.
Methods: Patients in our city suspected of having new onset HF are referred to our incident HF clinic if their NTproBNP is > 400 ng/l. Our clinic is the only provider of the service for a population of 550,000 people. All patients undergo detailed echocardiography and are assessed by a HF consultant cardiologist. We collected data on consecutive patients between 13th of April 2012 and 31st of December 2016. The age, the NTproBNP levels and the type of HF were recorded. Comparisons were made between those with HFREF and those with heart failure with preserved left ventricular ejection fraction (HFPEF), using independent t test statistics, with significance at $p < 0.05$.
Results: A total of 3939 patients were seen in this period with a median age of 80 years. HFREF was diagnosed in 1209 patients (30.7%), with median age of 80 years and mean NTproBNP of 3243 ng/L. The patients with HFPEF were 1354 patients (34%) with a median age of 81 years and a mean NTproBNP of 1684 ng/L ($p < 0.0002$). The remaining patients were 846 patients with HF related to pulmonary hypertension [median age of 82 years and a mean NTproBNP of 2004 ng/L (p NS)]; and 950 patients (24%) who did not have HF. Those latter group had a median age of 78 years and a mean NTproBNP level of 969 ng/L. The NTproBNP ranges were overlapping.
Conclusions: Patients with HFREF and HF due to pulmonary hypertension tend to have similar mean NTproBNP levels, that are significantly higher than those with HFPEF. Contrary to common assertions, the median age for patients with different types of heart failure appear to be similar, and thus can not help differentiating HFREF from HFPEF.

P998
Lower left ventricular ejection fraction can independently predict the poor response to immunosuppressive treatment in patients with cardiac sarcoidosis

K Kisho Ohtani[1]; K Takesue[1]; K Hiasa[1]; T Fujino[1]; T Higo[1]; T Ide[1]; H Tsutsui[1]
[1]*Kyushu University Graduate School of Medical Sciences, Fukuoka, Japan*

Immunosuppressive agents including corticosteroid are mainstay of initial treatment for cardiac sarcoidosis (CS), however, a subset of patients with CS fail to respond to these treatments. This study aimed to identify the predictors for non-responders to immunosuppressive treatments. Non-responders were defined as those in whom cardiac death, hospitalization due to worsening heart failure, marked decrease in left ventricular ejection fraction (< 15%), life-threatening ventricular arrhythmias occurred within 5 years after immunosuppressive treatments. We analyzed 39 consecutive patients (58 ± 14 years, 27 women) who were definitely diagnosed as CS and treated with immunosuppressive agents. Eight patients received a single second-line immunosuppressive agent such as methotrexate or a combination of this agent and corticosteroid. During a mean follow-up of 7.4 years, 12 patients (30.8%) were identified as non-responders. The estimated 10-year survival from cardiovascular death was 28.8% in non-responders, as compared with 77.4% in responders (hazard ratio [HR] for cardiovascular death as compared with responders, 9.8; 95% confidence interval [CI], 2.4 to 40.2; $P = 0.0015$). Univariate analysis showed presence of basal thinning in interventricular septum (100% vs 63%, $P = 0.017$), lower left ventricular ejection fraction (LVEF, 34.9 ± 15.2% vs 48.9 ± 19.0%, $P = 0.03$), and higher BNP (543 ± 368pg/ml vs 233 ± 308pg/ml, $P = 0.023$) before the immunosuppressive treatments were associated with non-responders. Multivariate Cox hazard analysis showed lower LVEF (HR, 1.08; 95% confidence interval, 1.02-1.16; $P = 0.0062$) was the only independent predictors of the non-responders. In conclusion, lower LVEF is a predictor of poor response to immunosuppressive therapy in patients with CS.

P999
The rehospitalisation rates among patients with preserved, mid-range and reduced ejection fraction: databased analysis

R Pancheva[1]; N Runev[1]; E Manov[1]; E Dimchovski[2]; D Vassilev[3]
[1]*University Hospital Alexandrovska, Cardiology Clinic, Department of Propaedeutics of Internal Diseases, Sofia, Bulgaria*; [2]*Medical Institute of Ministry of Interior, Department Cardiology, Sofia, Bulgaria*; [3]*University Hospital Alexandrovska, Department Cardiology, Sofia, Bulgaria*

Background: The hospital readmissions due to worsening of heart failure (HF) remain huge medical, social and financial burden.
Purpose: The aim of this study was to compare the frequency of rehospitalization rates among patients with preserved, mid-range and reduced ejection fraction (EF).
Methods: An observational analysis of patients, hospitalized due to congestive HF from our department between January 2012 and June 2013, was conducted to assess readmission rates for decompensated HF.
Results: A total of 1028 patients were included with an age of 67.5 ± 11.3 years; 49.8% were women, the mean EF was 57 ± 11.2% (66.1% with preserved EF (<50%), 13% with mid-range EF (40-50%) and 7.6% with reduced EF (< 50%)). A total of 290 patients (28.2%) were aged = 75 years, and 737 (71.7%) were aged < 75 years. The demographic characteristics of our population are as follows: 94.8% of HF patients had hypertension (HT) (1.8% I stage; 64.1% II stage; 28.9% III stage); 26.97% diabetics (DM); 47.2% had coronary artery disease (CAD) and 32.6% of whom experienced myocardial infarction; 32% had valvular heart disease (VHD), 15.5% had thyroid gland disorders (3.4% hyperthyroidism vs. 12.1% hypothyroidism). Atrial fibrillation (AF) was present in 61.7% of the patients with HF; 29.8% had elevated pulmonary artery systolic pressure (PASP) (<40 mmHg). The length of hospitalization for HF was typically between 5 and 10 days, mean 6 days. All patients received guideline-directed medical therapy for HF. During the 3-year follow-up 14% experienced hospital readmissions because of an exacerbation of congestive HF. The patients with EF < 50% had more frequent readmissions due to increasing severity HF than those with preserved EF (2.5% of the patients with more than two hospitalizations had preserved EF, 5.2% had mid-range EF and 6.4% had reduced EF) ($p < 0.05$).
Conclusions: Our data showed that EF predict the frequency of rehospitalization for HF. The patients with mid-range and reduced EF experienced significantly high readmission rates, then those with preserved EF.

P1000
sST2 adds to the prognostic value of Gal-3 and BNP in chronic heart failure, independent of Mineralocorticoid Receptor Antagonists treatment.

M Barutaut[1]; P Fournier[1]; WF Peacock[2]; C Dambrin[1]; C Caubere[1]; C Servoz[1]; F Koukoui[1]; M Galinier[1]; F Smih[1]; P Rouet[1]
[1]*UMR UT3 CNRS 5288, Evol. Medicine, Obesity and heart failure: molecular and clinical investigations, Toulouse, France*; [2]*Baylor College of Medicine, Emargency Medicine, Houston, United States of America*

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Aims: The soluble form of the IL-33 receptor (sST2) and Galectin-3 (Gal-3) are fibrosis biomarkers with prognostic value in heart failure (HF). We investigated the prognostic capacity of sST2 when combined with Gal-3, and determined if the prognostic utility of sST2 is affected by mineral corticoid receptor antagonist (MRA) therapy.
Methods and Results: sST-2 and Gal-3 were measured in 100 stable chronic HF (CHF) patients receiving MRA therapy and compared to 97 BNP and cardiovascular risk factor matched patients not treated with MRA. sST2 and Gal-3 levels were measured to determine the relationship with all-cause mortality at 6 year follow up. ROC curve cut-off points were defined as sST2 = 36.3 ng/ml, Gal-3 = 17.8 ng/ml, and BNP = 500 pg/ml, and had 6-years mortality hazard ratios (HR) of 7.3, 6.6 and 4.4, respectively. The combination of an elevated sST2 and Gal-3 had a HR = 4.4 [95% CI 1.9-8.9]. Adding BNP decreased the HR to 2.1 [95% CI 1.2-4.8]. Combining sST2 and Gal-3 to a clinical model relevant for CHF prognosis allowed a significant reclassification of 1-year adverse outcome risk, even when BNP was included. Finally, prognostic prediction by sST2 was unaffected by MRA treatment.

Conclusion: Simultaneous sST2 and Galectin-3 elevation is associated with poorer prognosis compared to either alone, regardless of BNP levels, and the prognostic capacity of sST2 is independent of MRA therapy.

P1001

Managements and outcomes of heart failure patients with paroxysmal vs. non-paroxysmal atrial fibrillation in Taiwan: Data from Taiwan Society of Cardiology-Heart Failure with reduced Ejection Fraction

H-Y Hung-Yu Chang[1]; M-C Fong[1]; A-N Feng[1]; W-T Lai[1]; C-W Hsueh[1]; Z-C Chiang[1]; W-H Yin[1]
[1]*Cheng-Hsin General Hospital, Taipei, Taiwan ROC*

Background: The prognostic significance and treatment strategy of atrial fibrillation (AF) in patients with heart failure remains controversial. We aimed to evaluate the characteristics, managements and outcomes of AF patients in the Taiwan Society of Cardiology-Heart Failure with reduced Ejection Fraction (HFrEF) registry.
Methods: We collected the clinical data of 1509 patients hospitalized for acute heart failure with left ventricular ejection fraction less than 40% from 21 hospitals between 2013 and 2014 in Taiwan. Baseline characteristics, AF status, medications, and one-year outcomes were analyzed.
Results: At baseline, 393 (26%) patients had AF, including 117 (29.8%) patients with paroxysmal AF (PAF) and 276 (70.2%) with non-paroxysmal AF (N-PAF). Age, gender, CHADS2-VASc score, and history of stroke were similar in both groups. PAF patients more frequently had ischemic cardiomyopathy (47.3% vs. 29.7%, p = 0.021) compared with N-PAF patients, while N-PAF patients had larger left atrial diameter (50.5mm vs. 47.3mm, p = 0.004) compared with PAF patients.
PAF patients were more likely to receive amiodarone (31.6% vs. 13.8%, p <0.001) and anti-platelet agents (54.1% vs. 42.5%, p = 0.041) but less likely to received renin-angiotensin system blockers (52.3% vs. 64.9%, p = 0.021), digoxin (26.1% vs. 46.6%, p <0.001), diuretics (80.6% vs. 88.4%, p = 0.058) and anti-coagulants (33.3% vs. 50%, p = 0.003) compared with N-PAF patients at discharge. Discharge heart rate, systolic blood pressure, and beta-blocker prescription rates were similar in both groups. One-year mortality (25.9% vs. 16.5%, p = 0.038) and non-cardiovascular death rates (13% vs. 5%, p = 0.008) were significantly higher in PAF patients.
Conclusions: In this observational, real-world registry, patients with PAF and HFrEF were less likely to receive guideline-recommended therapy, more likely to receive anti-arrhythmic agents and had worse one-year outcome. Our findings further emphasize the importance of optimized medication in HFrEF patients.

P1002

The time of presentation to the emergency department defines two different phenotypes of acute heart failure

C Lombardi[1]; A Ravera[1]; A Roncolato[1]; V Carubelli[1]; Al Castrini[1]; E Sciatti[1]; I Bonadei[1]; E Gorga[1]; E Vizzardi[1]; M Metra[1]
[1]*University of Brescia, Cardiology, Department of Medical and Surgical Specialties, Radiological Sciences, and Public Health, Brescia, Italy*

Background: Acute Heart Failure (AHF) is a potentially life-threatening condition characterized by different clinical presentations.
Purpose: The aim of the study is to evaluate if the time of presentation to the Emergency Room can influence different clinical characteristics and treatments of patients (pts) with AHF.
Methods: we retrospective analysed 426 pts admitted to the Emergency and Urgency Department and hospitalized for clinical and instrumental evidence of AHF. Pts admitted to the Emergency Department were divided in two groups according to the time of presentations: daytime pts from 8 am to 20 pm, and night-time pts from 20 pm to 8 am. Medical and clinical data at time to presentation were collected. We have also analysed the echocardiographic parameters obtained at the Emergency Department. The therapeutic pathway during hospitalization has been analysed according to the time of presentation.
Results: 329 pts arrived at the hospital during the day (8 am - 20 pm), 97 pts during the night (20 pm - 8 am). No differences were found in age, sex, weight, comorbidities and baseline therapies between the two groups. Pts admitted during the night were characterized by significantly higher systolic and diastolic blood pressure compared with pts admitted during the day (systolic blood pressure 142 ± 34 mmHg vs 127 ± 28 mmHg, p < 0.0001; diastolic blood pressure 82 ± 19 mmHg vs 73 ± 15 mmHg p < 0.001). Peripheral oxygen saturation was significantly worse in pts hospitalized during the night (92 ± 7% vs 94 ± 5%, p 0.03). Echocardiographic parameters showed an increase of vena cava congestion in daytime pts (87% vs 76%, p < 0.01). Pts admitted during the night required higher use of vasodilators (15% vs 6%, p 0.005) and higher average doses of furosemide (125 ± 118, p.0.04 vs 100 ± 11 mg, p < 0.01) compared with daytime pts. NT-proBNP and Troponin values were inferior in patients admitted during the night without statistical significance. During hospitalization death for cardiovascular causes occurred in 5% of daytime pts and in 6% of night-time pts (ns).
Conclusion: the time of presentation to the Emergency Department characterizes a specific phenothipe of Acute Heart Failure. During the night patients with elevated blood pressure, desaturation and no congestion of vena cava are significantly more frequent. This clinical picture, typically characterized by acute pulmonary edema, required higher doses of vasodilators and diuretics compared with daytime patients.

P1003

Predictors of cardiac death due to progression of chronic heart failure in patients after myocardial infarction

I A Leonova[1]; S Boldueva[1]; E Bykova[1]
[1]*North-Western Sate Medical University named I.I. Mechnikov, St-Petersburg, Russian Federation*

Despite the achievements of recent years in the management of patients with myocardial infarction (MI), patients continue to die from progression of chronic heart failure (CHF).
Objective: to identify predictors of cardiac death due to the progression of CHF in patients after MI.
Methods: 772 patients with acute MI were examined, prospective follow-up was carried out at the time from 1 to 7 years. The average age of patients was 58.2 ± 8.9 years.
Results: One of the leading causes of death of patients was the progression of CHF (in 26% of all cases
of death). Based on the results of multifactorial regression Cox analysis among independent risk factors of development of non-sudden cardiac death were age, aneurysm and left ventricular ejection fraction (LVEF).
With augment of age, every year increased the risk is of cardiac death due to the progression of CHF almost in 2.5 (RR = 2.46, p = 0.01). It seems interesting the fact that the average age of survivors and suddenly patients did not differ, while patients who died as a result of progression of CHF, were older than survivors: 63.8 ± 9.0 years vs 57.9 ± 9.5 years, p = 0.002. The results of most of the studies conducted also consider age as an independent prognostic factor affecting the mortality of patients with CHF for 5 years. In 21.9% of all cases MI was complicated by the development of aneurysm of LV, however among patients, who died due to progression of CHF, LV aneurysm was noted in 50% of cases.
Based on the results of multivariate regression analysis of Cox the absence of LV aneurysm resulted in a reduction in the risk of non-sudden cardiac death by 4.3 times (RR = 4.32, p = 0.003). Average LV EF among patients who died due to the progression of CHF was authentically (p = 0.000004) lower (45.59% ± 11.27%) than in survivors (56.51% ± 10.67%). It should be noted that the number of person with LVEF less than 40% in the group of CHF died patients was significantly more (22,7% p = 0.001) then among the survivors (5.6% of cases). As a results of multivariate regression analysis Cox increase of EF LV for each unit of measurement made it possible to reduce the risk of death in 2.4 (RR = 2.43, p = 0.006).
Conclusion: the main risk factors of cardiac death after MI were age, systolic dysfunction and LV aneurism

P1004

Training general practitioners to improve treatment of patients with heart failure: a cluster randomized trial

F H Frans Hendrik Rutten[1]; MJM Valk[1]; AW Mosterd[1]; MA Landman[1]; DDL Broekhuizen[1]; NPA Zuithoff[1]; AW Hoes[1]
[1]*University Medical Center Utrecht, Julius Centre for Health Sciences and Primary Care, Utrecht, Netherlands*

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Background: Drug treatment of patients with heart failure (HF) can be improved and we wanted to assess whether a single training session of general practitioners improved evidence-based drug treatment of heart failure patients.
Methods: A cluster randomized controlled trial in established heart failure patients. Primary care practices (PCPs) were randomized to care-as-usual (control) group, or to the intervention group in which GPs received a half-day training on HF management, and a leaflet on HF drug uptitration. Changes in HF medication, health status, hospitalization, and survival were compared between the two groups.
Results: 15 PCPs with 200 HF patients were randomized to the intervention group, and 15 PCPs with 198 HF patients to the control group. Mean age was 76.9 (SD 10.8) years, 52.5% were female. On average the patients were diagnosed with HF 3.0 (SD 3.0) years ago. In total, 204 had HFrEF and 194 HF with preserved ejection fraction (HFpEF). In participants with HFrEF, the use of angiotensin converting enzyme inhibitors/angiotensin receptor blockers (ACEI/ARB) decreased in six months in both groups (5.2% (95% confidence interval (CI) 2.0-10.0) and 5.6% (95%CI 2.8-13.4)),

respectively (baseline-corrected odds ratio (OR) 1.07 (95%CI 0.55-2.08), while beta-blocker use increased in both groups with 5.2% (95%CI 2.0-10.0) and 1.1% (95%CI 0.2-6.3), respectively (baseline-corrected OR 0.82 (95%CI 0.42-1.61). Also for health status, hospitalizations, or survival after 12 to 28 months there were no significant differences between the two groups, also not when separately analysed for HFrEF and HFpEF.
Conclusion: A half-day training of GPs does not improve HF drug treatment of patients with established HF.

P1005
Clinical profile and management of octogenarian patients admitted for acute heart failure

EK Egle Kavaliunaite[1]; I Navickaite[1]; I Kaminskaite[1]; R Salkevic[2]; J Motiejunaite[3]; I Jonauskiene[3]; V Juknevicius[4]; D Rimkeviciute[3]; A Mebazaa[5]; A Kavoliuniene[3]; J Celutkiene[4]
[1]Hospital of Lithuanian University of Health Sciences, Kaunas, Lithuania; *[2]Vilnius University, Faculty of Medicine, Vilnius, Lithuania*; *[3]Hospital of Lithuanian University of Health Sciences, Dept of Cardiology, Kaunas, Lithuania*; *[4]University Hospital Santariskiu Klinikos, Clinic of Cardiac and Vascular Diseases, Centre of Cardiology and Angiology, Vilnius, Lithuania*; *[5]Inserm UMR-S 942, Inserm, Hospital Lariboisiére, Université Paris Diderot, Paris, France*

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Introduction: Acute heart failure (AHF) is the most common cause of hospitalization in elderly patients. (1) More than 25% of AHF patients are octogenarians. (2) Previous studies have demonstrated substantial differences in presentation and management of AHF according to age. (3, 4) Therefore, the aim of our study was to describe the clinical profile and management of elderly AHF patients presenting to emergency department.
Purpose: We aimed to evaluate whether the clinical profile and management of octogenarian patients admitted for AHF differ from their younger counterparts.
Design and Methods: A prospective two-centre observational cohort study enrolled 1433 dyspnoeic patients consecutively admitted to the emergency department. AHF was the cause of acute dyspnoea in 725 patients (50%). Patients were classified as octogenarians when being = 80 years old. Data were analyzed with One-way ANOVA.
Results: 171 (24%) of all AHF patients were octogenarians. The more common comorbidities in the octogenarian patient group differ (see table). Clinical signs at admission were similar in both patient groups. Diuretics and beta-blockers were more often prescribed to younger patients compared to octogenarians, while other medical treatment at discharge did not differ between the two groups.
Conclusions: Octogenarians presented with more comorbidities than younger AHF patients. Clinical profile at admission was similar in octogenarians compared to younger AHF patients. Basic medical treatment at discharge did not differ between octogenarians and younger AHF patients, except diuretics and beta-blockers

>= 80 vs. < 80 year old AHF patients

	≥80 years old	<80 years old	p value
Peripheral vascular disease including carotid artery disease (%)	11	6	p = 0.013
Pacemaker (%)	25	16	p = 0.006
Chronic liver disease (%)	1	7	p = 0.002
Chronic renal disease (%)	33	23	p = 0.010
Beta-blockers at discharge (%)	65	74	p = 0.027
Mineralocorticoid antagonists at discharge (%)	36	42	p = 0.127
ACEIs/ARBs at discharge (%)	61	63	p = 0.700
Diuretics at discharge (%)	72	81	p = 0.013
Systolic blood pressure (mmHg)	148 ±34	143±36	p = 0.299
Diastolic blood pressure (mmHg)	82±22	84±22	p = 0.375
Heart rate (bpm)	85±28	90 ± 30	p = 0.066
SpO2 (%)	91±3	90±4	p = 0.296

P1006
A gradient of frequency of rehospitalization of heart failure patients between different types atrial fibrillation and correlation with left atrial diameter

R Pancheva[1]; N Runev[1]; E Manov[1]; B Stoimenov[1]; E Dimchovski[2]; D Vassilev[3]
[1]University Hospital Alexandrovska, Cardiology Clinic, Department of Propaedeutics of Internal Diseases , Sofia, Bulgaria; *[2]Medical Institute of Ministry of Interior, Department Cardiology, Sofia, Bulgaria*; *[3]University Hospital Alexandrovska, Department Cardiology, Sofia, Bulgaria*

Background: The atrial fibrillation (AF) and heart failure (HF) have emerged as new cardiovascular epidemics over the last decade. The fact that either AF or HF alone can predispose a patient to repeated hospitalization, and that prognosis of both together is worse than either alone, makes this interplay even more interesting.
Purpose: To assess the frequency of rehospitalization of HF patients with the different types AF.
Methods: An observational analysis of patients hospitalized due to congestive HF (with preserved EF (<50%), mid-range EF (40-50%) and reduced EF (< 50%)) from our depatment, between January 2012 and June 2013, was conducted to assess the gradient of frequency of rehospitalization between the different types AF and correlation with left atrial (LA) diameter.
Results: A total of 1029 patients were included with an age of 67.5 ± 11.3 years; 49.8% were women, mean EF was 57 ± 11%, 634 of whom had AF (61.7%) (3.9% new onset AF; paroxysmal 20%; persistent 5.6%; permanent 31.6%). The demographic characteristics of our population are as follows: 94.8% had arterial hypertension (HT) (1.8% I stage; 64.1% II stage; 28.9% III stage); 26.97% had diabetes mellitus (DM); 47.2% had coronary artery disease (CAD) and 32.6% of whom had previous myocardial infarction (MI); 32% had valvular heart disease (VHD), 15.5% had thyroid gland disorders (3.4% hyperthyroidism; 12.1% hypothyroidism). The patients with AF had greater risk of rehospitalization due to more severe congestive HF than those without AF (1.3% vs. 11.4%, respectively; $p < 0.01$). The different types AF were associated with difference in the readmission rates (5.0% had new onset AF, 20.3% had paroxysmal AF, 15.8% had persistent AF and 17.8% had permanent AF ($p < 0.01$). The patients with LA diameter >55mm experienced more frequent rehospitalization (8.6% vs. 2.8%, respectively; $p < 0.01$). The readmission rates were not influenced by management of AF - 27.2% had rhythm control strategy and 72.8% had rate control strategy ($p = 0.671$). Anticoagulation therapy didn't affect the rehospitalization rates, but antiplatelet therapy was associated with increased readmission rates: 1% for monotherapy and 6,8% for dual antiplatelet therapy ($p < 0.01$). On multivariate logistic regression analysis the independent predictors of readmissions due to decompensated HF were: de novo AF (OR 0.298; 95% CI, 0.146-0.605; $p < 0.01$), LA diameter > 55 mm (OR 0.457; 95% CI, 0.233-0.897; $p < 0.05$), rate control strategy ($p < 0.05$) with digoxin (OR 0.205; 95% CI, 0.053-0.794; $p < 0.05$), beta blocker (OR 0.099; 95% CI, 0.020-0.560; $p < 0.01$) and Ca-antagonist (OR 0.298; 95% CI, 0.146-0.605; $p < 0.01$).
Conclusions: Our data showed that the different types AF are associated with difference in readmission rates due to decompensated HF and LA diameter more than 55 mm is independently associated with higher readmission rates.

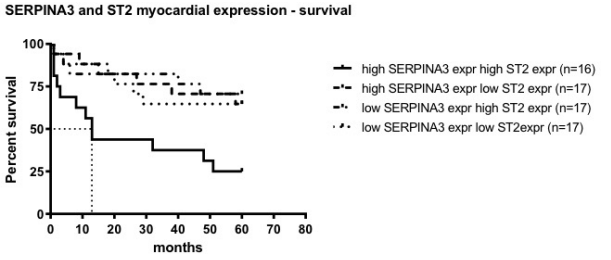
P1007
Prognostic role of myocardial SERPINA3 and ST2 transcripts in predicting mortality in patients with heart failure due to idiopathic cardiomyopathy

L Delrue[1]; K Dierickx[1]; W Heggermont[1]; R Dierckx[1]; S Verstreken[1]; M Goethals[1]; M Marc Vanderheyden[1]; J Bartunek[1]
[1]OLV Hospital Aalst, Cardiovascular Center, Aalst, Belgium

Background: Prognostic stratification in heart failure (HF) remains challenging. Myocardial serine peptidase inhibitor class 3A gene expression has recently been shown to be upregulated in pts with non-ischemic cardiomyopathy and a significant positive correlation between myocardial LV SERPINA3 and length of hospitalization was found in LVAD patients. Similarly, clinical trials revealed that serum sST2 levels predict outcome in pts with chronic heart failure and that ablation of ST2 causes exaggerated cardiac remodelling in non-ischemic HF.
Aim: To evaluate the prognostic role of myocardial LV SERPINA3 and ST2 transcripts as markers of remodeling/inflammation with respect to mortality in patients with CCMP.
Methods: LV message levels (qRT-PCR, rel units) were investigated in non-surviving HF patients due to CCMP with LV ejection fraction (EF) < 45% and < 75 years (n = 35). All patients died within 5 years after LV biopsy procurement taken at the time of routine cardiac catheterization. LV message levels were compared to those in CCMP survivors (n = 39) matched for age and hemodynamic phenotype including volumes, filling pressure and ejection fraction. The impact of myocardial expression on survival was analyzed by Kaplan-Meier curves dichotomized according to the median value of the transcripts levels.
Results: Significant up-regulation of LV ST2 (10.99 ± 24.22, $p < 0.01$) and SERPINA3 (2.44 ± 3.80, $p < 0.001$) transcripts was seen in non-survivors vs survivors

(0.72 ± 0.81 and 0.36 ± 0.22, resp.). CCMP patients with a higher than median expression of one of the 2 factors showed survival rates of resp 39 and 43 % at 5 years vs 71-63% in patients with a low expression. When combining both factors, survival rate dropped to 11% in HF patients with both high SERPINA3 and ST2 expression or 50% survival at 10 months (log-rank test, p = 0.0103)(Fig.1). Note, no significant difference was seen in the mean proBNP and ST2 serum levels in the four groups.

Conclusion: Combined myocardial upregulation of SERPINA3 and ST2 is associated with poor survival in CCMP patients irrespective of circulating BNP and ST2 serum levels. Further prospective studies should determine whether tissue myocardial profiling may be of added value in prognostic stratification in heart failure in addition to conventional analysis of circulating biomarkers.



P1008

Clinical outcomes at 5 to 9 years following Transcatheter Aortic Valve Replacement

E Munoz-Garcia[1]; M Munoz-Garcia[1]; A J Antonio Jesus Munoz Garcia[1]; JM Garcia-Pinilla[1]; F Carrasco-Chinchilla[1]; AJ Dominguez-Franco[1]; JH Alonso-Briales[1]; JM Hernandez-Garcia[1]; MF Jimenez-Navarro[1]; E De Teresa-Galvan[1]

[1]University Hospital Virgen de la Victoria, Department of Cardiology, Malaga, Spain

The durability of transcatheter heart valves and long-term clinical outcomes are unknown. The aim of this study was to evaluate clinical and hemodynamic outcomes between 5 to 9 years after Transcatheter Aortic Valve Replacement (TAVR).

Methods: Between April 2008 and December 2012, 305 patients underwent TAVR for the treatment of severe symptomatic aortic stenosis with the auto-expandable prosthesis

Results: the mean age, logistic EuroSCORE and STS score were 79.3 ± 6.5 years, 19.4 ± 12% and 6.6 ± 4% respectively. Mean aortic valve gradient decreased from 48.7 ± 15 mm Hg to 8.9 ± 4.3 mmHg after TAVI, to 11.1 ± 9 mm Hg at 4 years, and 22.7 ± 12 mmHg at 5 years (p for post-TAVI trend 0.03). Mean aortic valve area increased from 0.63 ± 0.16 cm2 to 1.57 ± 0.3cm2 after TAVI to 1.48 ± 0.2 at 4 years and 0.97 ± 0.3 cm2 at 5 years (p for post-TAVI trend 0.01). Mean left ventricular ejection fraction increased from 61.1 ± 15 % to 65.5 ± 11% after TAVI, to 58.2 ± 17% at 4 years and 60.7 ± 8% at 5 years (p for post-TAVI trend 0.001) Late mortality after a mean of 4.15 ± 2.4 years 58% and in only 34.1% patients was cardiovascular mortality. Survival rates at 1 to 9 years were at 87.5%, 79%, 73.1%, 65.6%, 55.4%, 48.2%, 41.9%, 37.3% and 35.1% respectively. At 5 years, 3 patients had severe prosthetic valve dysfunction (severe stenosis and moderate transvalvular regurgitation). Median survival time after TAVI was 6 years (95% confidence interval [CI]: 5.89 to 6.28), and the risk of death was significantly increased in patients with frailty (adjusted hazard ratio [HR]: 1.864; 95% CI: 1.204 to 2.886),p = 0.001, Charlson index [HR= 1.243 (95% CI 1.148-1.346), p < 0.001], and left ventricular ejection fraction [HR= 1.012;(95% CI 1.001-1.024)p = 0.044].

Conclusions: Our study demonstrated favorable long-term outcomes after TAVR. Signs of prosthetic valve failure were observed in 0.97% of patients.

P1009

Role of emergency medical system and early intervention by specialist cardiologist/heart failure expert in influencing the clinical outcomes in Manipal Heart Failure Registry [MHFR] patients

A Ajit Singh[1]; T Devasia[1]; H Kareem[1]; YR Karkala[2]; S Chauhan[2]; PN Shetty[1]; S Rao[1]; P Ganesh[1]; D Uppunda[1]; KK Shetty[3]

[1]Kasturba Medical College and Hospital, Cardiology, Manipal, India; *[2]Melaka Manipal Medical College, Pharmacology, Manipal, India*; *[3]Vinaya Hospital, Medicine/Cardiology, Kundapur, India*

On behalf of: MHFR

Background/Introduction: Optimal utilization of emergency services in emergency department (ED) is necessary/ important for better patient outcome and cost-effectiveness. Visit by an HF specialist delineates further treatment plans who decide on admission to ward/ICCU or discharge.

Purpose: To evaluate the time consumption of emergency medical facilities for HF care and to assess the impact of factors on patient outcome

Method: Manipal heart failure registry is an observational cohort study conducted in a tertiary care referral hospital in South India. The study recruited all patients who came to the emergency department with acute HF or exacerbation of chronic HF from September 2015 to December 2016. Arriving modalities and exercises including first evaluation by ED physician, admission, assessment by HF expert at ED, and shifting to HF special care unit were analysed. Clinical outcomes upto one year were evaluated.

Results: A total of 764 patients were included in this study. Mean age was 59 ± 10.7 years. 527 (69%) patients were males. 397 (52%) patients arrived by public transport, and 92 (12%) patients came by ambulance. After the initial evaluation, 99 (13%) patients were found to have only mild symptoms, these were managed with IV diuretics and sent back. 665 (87%) patients were admitted to HF special care unit from ED.

Preliminary tests including ECG, ECHO, troponin T and NT- proBNP were done at ED to confirm HF. Majority of the patients (n = 636; 83.2%) were diagnosed to have HF with reduced ejection fraction and remaining 128 (16.8%) had HF with preserved EF.

In-hospital mortality was 9.02% during an average stay of 5.2 ± 2.9 days. Post-discharge cumulative one month, 6 month and 12-month mortality were 4.9%, 13.2% and 16.9% respectively.

Arrival by ambulance was significantly associated with in-hospital mortality, whereas arrival by public transport was positively associated with 6-month mortality (p < 0.05).

First evaluation by HF expert in ED was done 41 minutes (average gap) after patient's arrival to ED. The average time between arrival at ED to admission, first evaluation by HF expert in ED to transfer to HF care unit and emergency arrival to HF care unit were 85 minutes, 102 minutes and 121 minutes respectively.

Time from patient's emergency arrival to reach HF care unit is statistically associated (p < 0.01) with in-hospital mortality. Delayed first evaluation by HF expert at ED to HF care unit transfer is associated (p < 0.05) with higher in-hospital mortality. Increased time delay between patient's emergency arrival and first evaluation by HF expert at ED is associated (p < 0.05) with 1 month mortality.

Conclusion(s): HF patient may present to ED with acute decompensation. Early evaluation by HF expert with ECG, ECHO, troponin T and NT-proBNP play a vital role in both short and long-term mortality and morbidity. Emergency management of acute decompensation play a pivotal role in the management of HF patients.

Chronic Heart Failure - Diagnostic Methods

P1010

Diastolic dysfunction as a prognosticator in patients with heart failure with preserved ejection fraction

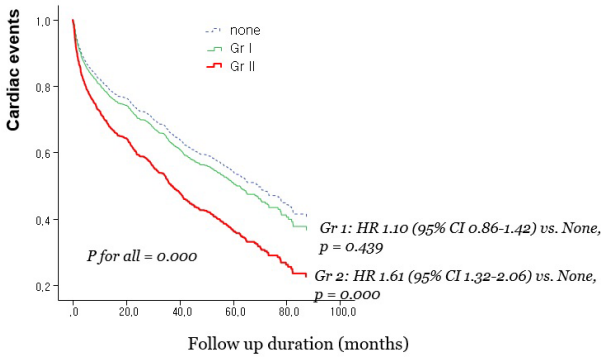
GY Goo-Yeong Cho[1]; JJ Park[1]; JB Park[2]; JH Park[3]

[1]Seoul National University Bundang Hospital, Seongnam, Korea Republic of; *[2]Seoul National University Hospital, Seoul, Korea Republic of*; *[3]Chungnam National University Hospital, Cardiolgoy, Daejon, Korea Republic of*

Background: Echocardiographic Doppler parameters were used for assessment of diastolic dysfunction. Heart failure with preserved ejection fraction (HFpEF) is usually associated with diastolic dysfunction. However, not all patients had diastolic dysfunction in HFpEF.

Purpose: We evaluated whether how many patients had diastolic dysfunction and whether this dysfunction was associated with adverse cardiac outcome.

Methods. Total 1,132 consecutive patients (age 73, female 61%) were admitted for acute decompensated heart failure. All patients had EF = 50%. Diastolic dysfunction was graded based on diastolic annular tissue velocity (e') and E/e' (Non: E/e' = 14 and e' = 7 cm/sec, Gr I: E/e' > 14 or e' < 7, Gr II: E/e' > 14 and e' < 7). Cardiac events were defined as all-cause death and heart failure admission.



diastolic grading for events

Results: Diastolic dysfunction was detected in 78% (grade 1: 31%, grade 2: 47%). During a median follow-up of 28.6 months (IQR 8.9-52.1), 569 patients (50.3%) were developed cardiac events. Patients with cardiac events showed older age, higher incidence of atrial fibrillation, lower EF, higher E/e', and lower e' than patients without events. By cox-regression survival analysis, progression of diastolic dysfunction was associated with higher cardiac events in both univariate and multivariate analysis. However, event free survival between Non and Gr I dysfunction was not statistically significant (HR 0.91, p = 0.439) (Figure).
Conclusions: Among patients with HFpEF, 22% of patients did not have a diastolic dysfunction. Although the degree of diastolic dysfunction was closely related with cardiac events, patients with Gr I dysfunction were not different from Non.

P1011

Prognostic value of NT-ProBNP/BNP ratio in patients with heart failure and reduced ejection fraction using sacubitril-valsartan: systematic review and post hoc analysis of PARADIGM-HF Trial

E Eduardo Pitthan[1]; VN Hirakata[1]; JN Barbisan[1]; CG Rodrigues[1]
[1]*Institute of Cardiology of Rio Grande do Sul, Porto Alegre, Brazil*

Background: The PARADIGM-HF trial showed that Sacubitril–Valsartan (SV) was superior to Enalapril in reducing the rates of morbimortality among patients with heart failure and reduced ejection fraction (HFrEF). SV increases B-type natriuretic peptide (BNP) and decreases NT-proBNP levels. The NT-proBNP/BNP ratio might be a valuable prognostic biomarker in HFrEF patients in treatment with SV and indirectly discriminated "responder" and "no responder" patients.
Purpose: To assess the relationship between NT-proBNP/BNP ratio and clinical outcomes in patients with HFrEF undergoing treatment with SV.
Methods: A systematic review (SR) was conducted in accordance with PRISMA. We included studies evolving HFrEF patients undergoing treatment with SV which had the levels of NT-proBNP and BNP and morbimortality outcomes measured. We reviewed PubMed, EMBASE and Web of Science. Data from PARADIGM-HF trial publications was extracted and reanalyzed for the purpose of this study. Associations between NT-proBNP/BNP ratio and cardiovascular death (SD) or HF hospitalization (HFH) were examined, among others, as was the effect of SV vs Enalapril on the NT-proBNP/BNP ratio.
Results: 180 publications were screened and 8 included. Decreased NT-proBNP/BNP ratio when compared to baseline before randomization (6.39) was associated with good prognosis: patients alive (6.33) and event-free (6,14) at the end of the study. In contrast, increased NT-proBNP/BNP ratio when compared to baseline was associated with poor prognosis: sudden death (6.49), death due to progression of HF (7.35), cardiovascular death (CD) (6.65), non-CD (6.62), HF hospitalization (6.48), emergency visits (6.53) and worsening of cardiac function (6.72). In the Enalapril arm, the NT-proBNP/BNP ratio was not associated with good or poor prognosis outcomes. The ratio was indirectly associated with the efficacy of SV in the treatment of HFrEF. The MAGGIC Score predicts mortality in HF, the applicability of the NT-proBNP / BNP rate was linearly associated with risk of HFrFE mortality. The Score EMPHASIS was linearly associated with worsening of quality of life and the applicability of the index can be a predictor or guide for quality of life evaluation.
Conclusions: When compared to baseline, reduced NT-proBNP/BNP ratio is associated with better outcomes and increased ratio with worse outcomes. More studies will be conducted to clarify the prognostic value of NT-proBNP/BNP ratio in HFrEF patients in treatment with SV.

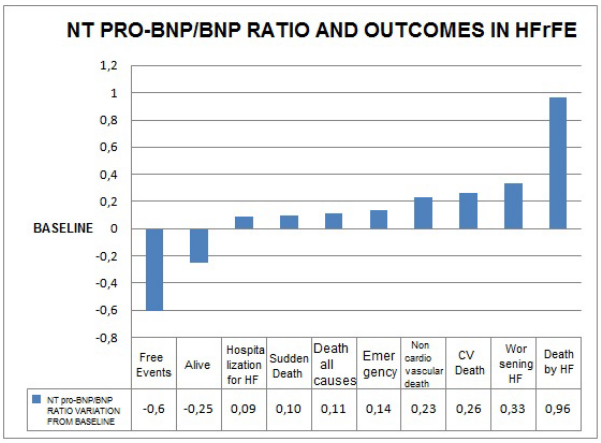


Figure 1

P1012

Relationship between aldosterone level and comorbidities in chronic heart failure with preserved ejection fraction

A Shevelyok[1]; N Vatutin[2]; N Vatutin[3]; V Venzheha[1]; V Venzheha[2]
[1]*Donetsk national medical university, Donetsk, Ukraine*; [2]*M. Gorkiy Donetsk national medical university, V. K. Gusak Institute of Urgent and Recovery Surgery, Donetsk, Ukraine*; [3]*V. K. Gusak Institute of Urgent and Recovery Surgery, Donetsk, Ukraine*

Background: Plasma aldosterone level has been shown to be an independent determinant of cardiovascular complication in chronic heart failure (CHF), but whether it's associated with comorbidities is unknown.
Purpose: The study aims to investigate the relationship between plasma aldosterone level and comorbidities in CHF with preserved ejection fraction (CHFpEF).
Methods: The study included 158 patients (58 men and 100 women, mean age 62.3 ± 7.4 years) with CHFpEF (< 50%). All patients had no history of primary aldosteronism and did not use the mineralocorticoid receptor antagonists during the last 6 weeks. Aldosterone plasma level was measured and comorbidities were assessed. For statistical purpose, patients were divided into two groups according to whether their median value of plasma aldosterone was high (< 160 pg/ml) or normal (< 160 pg/ml). The predictive capacity of comorbid burden for explaining variance in aldosterone level was assessed after standardization for any other differences.
Results: According to laboratory results 99 patients (67.1%, 95% confidence interval (CI) 59.6-74.2%) had normal aldosterone level (nAld) and 59 patients (37.3%, 95% CI 30.0-45.0%) had high aldosterone level (hAld). hAld patients were significantly younger (57.75 ± 7.5 vs. 65.02 ± 7.1 years, p < 0.001), severe (NYHA III-IV) CHF majority (62.7% vs. 33.3%, p < 0.001) compared with nAld patients. They more often had a history of myocardial infarction (59.3% vs. 41.4%, p = 0.044), atrial fibrillation (33.9% vs. 17.2%, p = 0.027), long-term (<10 years) history of arterial hypertension (57.6% vs. 25.3%, p < 0.001), chronic obstructive pulmonary disease (COPD) (27.1% vs. 7.1%, p = 0.001), diabetes mellitus (39.0% vs. 19.2%, p = 0.011), obesity (64.4% vs. 29.3%, p < 0.001) and renal dysfunction (88.1% vs. 50.5%, p < 0.001). Multiple regression analysis showed that after standartization for age and severity of CHF only long-term arterial hypertension (odds ratio (OR) 2.67, 95% CI 1.58-5.59), COPD (OR 4.62, 95% CI 2.00-8.53), obesity (OR 3.15, 95% CI 1.96-6.24) and renal dysfunction (OR 4.82, 95% CI 2.12-10.61) remained the independent risk factors of high aldosterone level.
Conclusion: In patients with CHFpEF plasma aldosterone level is closely associated with comorbidities. Long-term history of arterial hypertension, COPD, obesity and renal dysfunction are the independent risk factors of secondary hyperaldosteronemism.

P1013

Predictive models of mortality and readmission in patients with chronic heart failure and preserved ejection fraction

A Ana Belen Mendez Fernandez[1]; A Ferrero Gregori[1]; J Ordonez Llanos[2]; MJ Pirla Buxo[1]; A Garcia Osuna[2]; M Grau Agramunt[2]; S Mirabet Perez[1]; J Alvarez Garcia[1]; J Cinca Cuscullola[1]; E Roig Minguell[1]
[1]*Hospital de la Santa Creu i Sant Pau, Department of Cardiology , Barcelona, Spain*; [2]*Hospital de la Santa Creu i Sant Pau, Department of Biochemistry, Barcelona, Spain*

Introduction: Heart failure with preserved ejection fraction (HFpEF) is an increasingly common diagnosis and responsible for a high number of consultations as well as hospital admissions and readmissions. The pathophysiological pathways leading to the disease are not clear, which makes it difficult to find specific treatments.
The knowledge of predictors of mortality and re-entry would allow early identification of higher risk patients. Different metabolic markers have been introduced in the usual clinical practice, being undoubtedly the natriuretic peptides the reference ones.
Objective: The aim of the study was to evaluate the value of new biomarkers, which involve different pathophysiological pathways, to assess the prognosis of patients with HFpEF or mid-range ejection fraction (HFmrEF).
Methods: From May 2009 to May 2015,HFpEF and HFmrEF patients assessed for the first time in the Heart Failure Unit were included in the study.
Blood samples were taken by peripheral venipuncture and frozen, for later evaluation of a multi-marker panel with NTproBNP, GDF15, hs-TnT and Galectina 3.
Results: A total of 315 patients were included. 70% had LVEF> 50%, and 30% had LVEF between 40-49%. Mean age was 68 years (32% were women). The ethiology was ischemic (34%), followed by idiopathic (24%).
The values of the biomarkers were: Galectin 326 ± 20 ng/ml; hs-TnT 61 ± 405 ng/L; GDF-15 3809 ± 3521 pg/ml; NTproBNP 2867 ± 4909 pg/ml. There were no significant differences in the mean value of the biomarkers under study (GDF15, Galectina 3, hsTnT, NTproBNP) between patients with HFpEF and HFmrEF. The mean follow-up in the HFpEF group was 24 ± 20.6 months and in the HFmrEF group 21.6 ± 19.8 months (no significant differences). There were also no differences in the re-admission rate in both groups, which was 10.9% during the first month and 48.9% during the follow-up in the HFpEF group, and 10% during the first month and 43.3% during the follow-up of HFmrEF
Mortality during follow-up was 35% in the HFpEF group and 22% (p 0.02) in the HFmrEF group.
Multivariate analysis identified NYHA FC 3-4 (p 0.04); Systolic blood pressure (p 0.01); Left atrium size (p 0.03) and Age (p 0.0001) as independent predictors of mortality. When the biomarkers were added to the model, only GDF15 was statistically significant (p 0.01).
The IDI after the inclusion of GDF15 in the model with established mortality risk factors was 0.0279, which increases the ability to precede death by 2.8% (p 0.0118). The NRI, which represents the quantification of the improvement in the classification for events (mortality), discounting what worsens for non-events, was 0.271, which means a 27.1% improvement in the reclassification (p 0.024).
Conclusions: In patients with HFpEF and HFmrEF, the addition of GDF-15 values to the current clinical model could add prognostic information beyond that of current methods.

P1014

Cardiovascular biomarkers predict post-discharge rehospitalization risk and mortality among swedish heart failure patients

J Molvin[1]; E Bachus[2]; W Gallo[2]; G Tasevska-Dinevska[1]; H Holm[2]; A Jujic[2]; O Melander[2]; A Fedorowski[2]; M Magnusson[1]
[1]Lund University, Department of Cardiology, Skåne University Hospital, Malmö, Lund, Sweden; *[2]Department of Clinical Sciences, Lund University, Skåne University Hospital, Malmö, Sweden*

On behalf of: HARVEST
Funding Acknowledgements: The Swedish Heart and Lung foundation [2015-0322] and Wallenberg Center for Molecular Medicine, Lund University.

Background/Purpose: Here we aimed to analyse biomarkers related with neuroendocrine responses and cardiovascular stress (mid-regional pro-adrenomedullin (MR-proADM), copeptin, C-terminal pro-endothelin-1 (CT-pro-ET1) and N-terminal pro-brain natriuretic peptide (NT-proBNP)) and renal function (cystatin C) to test their predictive role in regard to mortality and risk of rehospitalization in a Swedish prospective heart failure (HF) patient cohort.
Methods: Two-hundred-and-sixty-eight patients hospitalized for HF (mean age: 75 years; 29% women) had complete data on all variables used in the analyses. Relations between baseline biomarker plasma concentrations and death as well as rehospitalization risk due to cardiac causes were assessed using multivariable Cox regression analysis adjusting for age, sex, body-mass index, systolic blood pressure, NYHA-class at hospitalisation, diabetes, total cholesterol, high-density lipoprotein, prevalent atrial fibrillation and smoking. A two-sided Bonferroni-corrected p-value of 0.05/5 = 0.010 was considered statistically significant;
Results: During follow-up period (mean time, 17 ± 12 months), a total of 57 patients died. In the multivariable-adjusted Cox regression analysis, all the biomarkers except CT-pro-ET1 (hazard ratio (HR) per 1SD: 1.42, 95% confidence interval (CI), 1.03-1.95; p = 0.034) were significantly associated with increased risk of death; NT-proBNP (HR, 1.85; CI, 1.17-2.17; p = 4.0x10-4), MR-proADM (HR, 1.72; CI, 1.22-2.41; p = 2.2x10-4), copeptin (HR, 1.70; CI, 1.22-2.36; p = 0.0002), and cystatin C (HR, 2.11; CI, 1.56-2.86; p = 1.0x10-6). A total of 178 patients were rehospitalized (mean follow-up time, 9 ± 8 months) due to cardiac causes. NT-proBNP was the only biomarker that showed significant association with risk of 1st rehospitalization due to cardiac causes ((HR, 1.47; CI, 1.13-1.91; p = 0.005).
Conclusion: Among patients hospitalised for HF, elevated plasma levels of NT-proBNP, MR-proADM, copeptin and cystatin C are significantly associated with increased risk of death after discharge, whereas NT-proBNP is the only biomarker that independently predicts the risk of rehospitalization.

P1015

Exhaled acetone in the differential diagnostics of heart failure

A A Alexandra Bykova[1]; L K Malinovskaya[1]; PH YU Kopylov[1]; P SH Chomahidze[1]; V B Betelin[2]; A L Syrkin[1]
[1]I.M. Sechenov First Moscow State Medical University, Moscow, Russian Federation; *[2]Scientific Research Institute for System Analysis of the Russian Academy of Science, Moskow, Russian Federation*

Background: Heart failure (HF) had certain symptoms, most of them has high sensitivity and low specificity. To verify the diagnosis of HF various laboratory and instrumental testing had to be done. According a few recent studies exhaled acetone increase in patients (pts) with HF.
Purpose: The aim of this study was to evaluate exhaled acetone in the differential diagnostics of HF.
Methods: From October 2014 to April 2016 78 pts with symptoms of HF such as breathlessness, fatigue, reduced exercise tolerance and ankle swelling was enrolled. Fasting exhaled breath samples were collected during the first 24h of hospitalization in 1L Tedlar bags. Exhaled breath was analyzed using PTR-MS (Compact PTR-MS, Ionicon, Austria). Diagnosis of HF was confirmed by echocardiography (in all pts) and NTproBNP (in pts with left ventricle ejection fraction (LV EF) more than 40%).
Results: The baseline characteristics of pts are in the Table 1. Exhaled acetone was significantly higher in pts with HF (916 [433; 2474] vs 383 [313; 665] ppb, p = 0,012). Receiver operator characteristic (ROC) analyses was performed to assess optimal cutoff points for this biomarker and to calculate sensitivity and specificity. The area under the ROC curve for acetone was 0,722 (95% CI 0,603 - 0,842, p = 0,012). The optimal cutoff concentration for acetone was 340 ppb, corresponding to sensitivity of 84% and specificity of 61%. The positive predictive value of the elevated exhaled acetone was 81%. The negative predictive value of the elevated exhaled acetone was 33%.
Some significant correlation of exhaled acetone also has been found with LV EF (r= - 0,244, p = 0,009), mean pulmonary artery pressure (r = 0,649, p < 0,0001), NTproBNP (r = 0,546, p < 0,0001).
Conclusion: Exhaled breath analysis is a novel non-invasive method of diagnostic of HF. It could be performed in real-time manner and detection of exhaled acetone might be used in the differential diagnostics of pts with symptoms of HF. The relatively few participants is the main limitation of this study.

P1016

Measurement of multiple cytokines for discrimination and risk stratification in patients with chagas disease and idiopathic dilated cardiomyopathy

A Adnan Khan[1]; Y Wang[1]; N Wessel[2]; HP Schultheiss[3]; MDA C Moreira[4]; T Walther[5]
[1]Hannover Medical School, Department of Cardiology and Angiology, Hannover, Germany; *[2]Humboldt University Berlin, Department of Physics, Berlin, Germany*; *[3]Charite - Campus Benjamin Franklin, Department of Cardiology, Berlin, Germany*; *[4]Federal University of Minas Gerais, Department of Internal Medicine, Belo Horizonte, Brazil*; *[5]School of Medicine and School of Pharmacy, University College Cork, Department of Pharmacology and Therapeutics, Cork, Ireland*

On behalf of: Excellence Cluster Cardio-Pulmonary System (ECCPS)
Funding Acknowledgements: DAAD and CAPES Grant (415-br-probral/po-D/08/11632)

Introduction: Chagas' disease (CD), caused by the hemoflagellate protozoan, Trypanosoma cruzi, is endemic in most countries of South and Central America, where it continues to be a major source of social, health, and financial burden. Heart failure (HF) is often a late manifestation of chronic CD, and is associated with high morbidity and mortality. Early identification of patients with CD, therefore, would be desirable as early intervention may help to improve the prognosis.
Purpose: Keeping in view the inflammatory nature of CD, this study investigated the possible role of 21 different inflammatory cytokines as biomarkers for prediction and prognosis of CD.
Methods: The plasma concentration of each of these cytokines was measured in a group of patients with CD (n = 94), and then compared with those measured in patients with dilated cardiomyopathy (DCM) from idiopathic causes (n = 48), and with control subjects (n = 25).
Results: Using monovariate analysis, plasma levels of cytokines such as stem cell growth factor beta (SCGF beta), hepatocyte growth factor (HGF), monokine induced by interferon gamma (MIG), and macrophage inhibitory factor (MIF) were significantly increased in CD patients with advanced HF compared to control group. Although, none of the cytokines could demonstrate any prognostic potency in patients with

CD, MIG was however, able to show a clear trend in predicting mortality and necessity for heart transplant in patients with DCM. Further, multivariate analysis was able to prognosticate a large proportion of CD and DCM patients, but it could not discriminate CD from idiopathic DCM. In CD patients, HGF and Interleukin-12p40 (IL-12p40) together were able to separate 81.9% of 3-year survivors from the deceased, while in DCM, stromal derived factor-1 alpha (SDF-1alpha), stem cell factor (SCF), and MIG together discriminated 77.1% of survivors from the deceased.

Fig 1

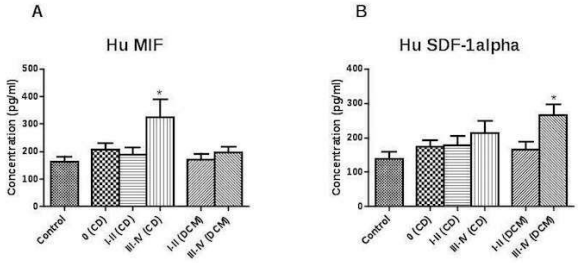


Fig 1A. Plasma concentration of MIF in controls (n = 25); in patients with CD distributed in asymptomatic (0) (n = 46), NYHA classes I-II (n = 24), and NYHA classes III-IV (n = 23); and in patients with DCM divided in NYHA classes I-II (n = 22) and NYHA classes III-IV (n = 26). Data is given as mean ± SEM. * $p < 0.05$ vs control.

Fig 1B. Plasma concentration of SDF-1alpha in controls (n = 21); in patients with CD distributed in asymptomatic (0) (n = 44), NYHA classes I-II (n = 25), and NYHA classes III-IV (n = 23); and in patients with DCM divided in NYHA classes I-II (n = 22) and NYHA classes III-IV (n = 26). Data is given as mean ± SEM. * $p < 0.05$ vs control.

Plasma concentration of MIF & SDF-1alpha

Conclusion: The significant increase in plasma concentrations of cytokines such as HGF and MIG in CD patients with advanced heart failure compared to controls, and the ability of these cytokines to prognosticate a large proportion of patients with CD and DCM using multivariate analysis, encourages further studies to clarify the diagnostic and prognostic potential of cytokines in these patients.

P1017

How much does right ventricular dysfunction influence the elevation of NT-proBNP in patients with acute heart failure?

R Raquel Lopez Vilella[1]; I Sanchez Lazaro[1]; I Husillos Tamarit[1]; L Martinez Dolz[1]; L Almenar Bonet[1]
[1]*Hospital Universitario y Politécnico La Fe, Heart Failure and Transplant Unit. Cardiology Department, Valencia, Spain*

Background and Objective: Acute heart failure (AHF) is associated with an elevation of brain natriuretic peptides due to myocardial stress caused by ventricular wall tension. If right ventricular dysfunction (RVD) would significantly increase peptide values is not clear. Our purpose was to analyze whether in patients with left-sided heart failure (HF) with preserved ejection fraction (HFpEF) and reduced ejection fraction (HFrEF) right dysfunction increases NT-ProBNP levels.
Methods: We included 1140 consecutive patients admitted for AHF in a cardiac acute hospitalization area of a reference hospital. We excluded patients with a poor acoustic window in the echocardiographic study, lack of determination of NT-ProBNP at admission, values of this peptide below 1,000 pg / mL and severe renal dysfunction (creatinine clearance < 30 ml/min). The total number of patients recruited was 602. Patients were classified into 6 groups depending on the left ventricular ejection fraction (LVEF) in good (LVEF > 45% (G)) and poor (LVEF < 45% (P)) ejection fraction, and right ventricular function (good > 50% (G), intermediate 40-50% (I) and poor < 40%(P)).
Results: The majority of patients were male (54%), age 73 ± 12 years. Etiology: Hypertension: 11%, Ischemic heart disease: 28%, Idiopathic dilated cardiomyopathy: 11%, Valvular: 17%, other: 33%. The values of NT-ProBNP were increasing as the degree of dysfunction increased (p: 0.0001). In patients with HFpEF and good right ventricular function, the NT-ProBNP value was 6477 ± 7382 pg / mL. In patients with HFpEF and poor right ventricular function, the NT-ProBNP value was 8946 ± 7730 (p: 0.9). Similarly, the levels of NT-ProBNP in patients with HFrEF was 10119 ± 9417 pg / mL, and 11954 ± 10236 when RVD was associated (p: 0.85).
Conclusions: In patients with AHF, NT-ProBNP values are higher when right ventricular dysfunction is associated. This occurs in both HFpEF and HFrEF. In our study, these differences were not statistically significant because of the large dispersion of NT-ProBNP levels.

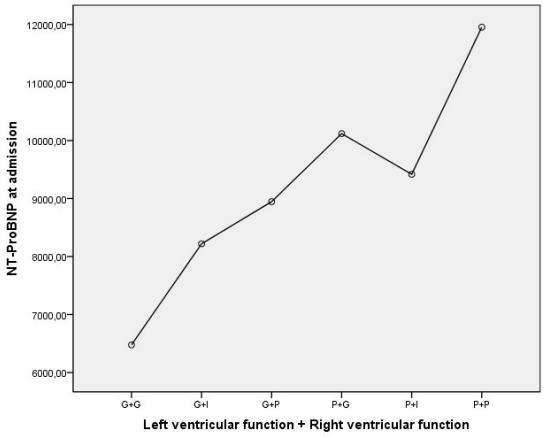


Image 1

P1018

The level of natriuretic peptide at the diagnosis of heart failure in comorbidal patients with thyrotoxicosis

Al Chesnikova[1]; EV Pashchenko[1]; VI Kudinov[1]; VP Terentev[1]; O Olga Kolomatskaya[1]; VA Safronenko[1]; NS Skarzhinskaya[1]
[1]*State Medical University of Rostov-on-Don, Rostov-on-Don, Russian Federation*

Background: It's necessary to take into account a frequent combination of ischemic heart disease (IHD) with thyroid pathology, as well as their combined effect on CHF markers level (such as brain natriuretic peptide (BNP) and N-terminal pro-B-type natriuretic peptide (NT-proBNP).
Purpose: To estimate the clinical significance of NT-proBNP level analysis for the diagnosis of CHF in patients with IHD and thyrotoxicosis, to determine the cut-off index for a combination of these diseases.
Methods: 111 patients were divided into 4 groups. Mean age was 58,3 ± 5,6 years. The main group consisted of 25 patients with IHD, CHF II-III FC and thyrotoxicosis; the 1st group of comparison - 30 patients with IHD and CHF II-III FC, normal finding of thyroid gland; the 2nd group - 30 patients with thyrotoxicosis without IHD, the 3rd group - 26 patients with thyrotoxicosis and IHD, with no signs of CHF. The levels of free triiodothyronine (fT3), free tetraiodothyronine (fT4), thyroid-stimulating hormone (TSH) were determined. The level of NT-proBNP was evaluated by the method of enzyme immunoassay. A new cut-off NT-proBNP for the diagnosis of CHF in comorbid patients was calculated by using ROC analysis and ROC-curve making (Receiver Operator Characteristic Curve).
Results: In all patients the concentration of NT-proBNP exceeded the set level of 125 pg/ml. The lowest index was obtained in the 2nd group - 225.5 (180.1, 376.1) pg/ml. The NT-proBNP values in the patients of the 1st and 3rd groups did not differ significantly (326.6 (253.7, 456.7) pg/ml and 345.3 (263.8, 420.6) pg/ml; p = 0.88), but exceeded the result in patients of the 2nd group by 27.8% and 35.2% respectively (p <0.05). The highest level of NT-proBNP was detected in the main group - 712.1 (434.3, 893.9) pg/ml. Accounting for the initial elevated level of NT-proBNP in patients with thyrotoxicosis, a cut-off of this marker for screening CHF in comorbid patients with IHD and thyrotoxicosis was calculated by using ROC analysis - 556.4 pg/ml. Thus, in our study, NT-proBNP values below 556.4 pg/ml make it possible to exclude CHF in this group of patients with a sensitivity of 72%, a specificity of 100%, an accuracy of 87.2% (p <0.001). The Area Under Curve (AUC) was 0.942 ± 0.0298 (p <0.001), which indicates an excellent quality of the model and the possibility of its application in clinical practice.
Conclusions: The highest level of NT-proBNP was observed in the group of patients with CHF by IHD and thyrotoxicosis, which is probably due to the combined influence of the volume load on the heart and thyroid hyperfunction. There were no significant differences in the concentration of NT-proBNP in patients with IHD and CHF without thyrotoxicosis and in patients with thyrotoxicosis and IHD without CHF. Consequently, a new cut-off of this biochemical marker is to be calculated for the diagnosis of heart failure in comorbid patients with thyrotoxicosis.

P1019

Serum N-terminal pro-BNP levels predicts the progression of arterial stiffness in Japanese healthy men

H Hirofumi Tomiyama[1]; KT Shiina[1]; T Chikamori[1]; A Yamashina[1]
[1]*Tokyo Medical University, Tokyo, Japan*

Funding Acknowledgements: Omron Health Care company

Backgrounds: Although several prospective observational studies have demonstrated that the serum N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels is a marker for future cardiovascular events including heart failure, the underlying mechanisms of this association has not been fully clarified. On the other hand, arterial stiffness and abnormal central hemodynamics have been much focused as independent risks for cardiovascular disease.
Purpose: The present prospective study was conducted to examine whether the serum NT-proBNP levels predict the progression of arterial stiffness and/or worsening central hemodynamics in healthy Japanese men.
Methods: In 1972 Japanese healthy men (43 ± 8 years old; the subjects with cardiovascular disease and/or whose serum NT-proBNP levels >100 pg/mL were excluded), serum NT-proBNT levels, radial augmentation index (rAI) and brachial-ankle pulse wave velocity (baPWV) were measured at the baseline of study period, and 6 years later baPWV and rAI were measured again.
Results: During the study period, baPWV was increased significantly (from 1278 ± 170 to 1333 ± 197 cm/sec) and rAI was also increased (from 69 ± 12 to 72 ± 12 %)($p < 0.01$). The delta change of baPWV, but not rAI, during the study period was higher in subjects whose NT-proBNP >10 pg/mL (n = 628, 62 ± 128 cm/sec) than in those whose NT-proBNP < 10 pg/mL (n = 1344, 41 ± 112 cm/sec), even after the adjustment of covariates ($p < 0.05$).
Conclusion: In Japanese healthy men, mild elevation of serum NT-proBNP levels is a risk for the progression of arterial stiffness rather than worsening central hemodynamics. Thus, increased arterial stiffness may be one of underlying mechanisms of increased cardiovascular risk related with elevated serum NT-proBNP levels.

P1020

Association of plasma Fischer ratio (FR) and atrial fibrillation (AF) in Patients with Idiopathic Dilated Cardiomyopathy (DCM)

M Wakasa[1]; H Aoki[1]; K Hujibayashi[1]; H Akao[1]; Y Kawai[1]; K Kajinami[1]
[1]*Kanazawa Medical University, Ishikawa, Japan*

Backgrounds: FR is the molar ratio of branched-chain AAs (BCAAs: leucine, valine, isoleucine) to aromatic AAs (phenylalanine, tyrosine) and
Decreased level of BCAA has been reported in AF rats. However, the relation between its levels and AF remains unclear in human. To explore potential role of FR or BCAA in AF of human failing heart, we measured plasma FR in patients with biopsy-proven DCM and evaluated association between its levels and the clinical parameters.
Methods: Consecutive 70 patients with DCM (M/F: 54/16, mean age: 62 years) were enrolled. Subjects showing abnormal liver enzyme level or chronic hepatitis viral infection were excluded. We measured plasma FR in peripheral blood samples, washout rate of Tc-99m Sestamibi (WOR) as function of mitochondria and LVEF as LV function parameters. The planer imaging was obtained 30 min and 180 min after injection of MIBI and WOR was calculated.
Results: Mean plasma FR of AF group (n = 14) were significantly lower than those of without AF (n = 56) (2.87 ± 0.40 vs 3.28 ± 0.55, $p < 0.05$). In AF group, plasma FR showed a significant and positive association with LVEF ($r = 0.658$, $p < 0.05$). Furthermore the WOR showed significant negative association with FR (r=-0.749, $p < 0.05$).
Conclusions: BCAA might have a protective role in AF development in DCM patients through maintain mitochondrial function.

P1021

Association of heart and vessels remodeling with biological markers level: transforming growth factor and e-selectin, in patients with heart failure.

M Maria Kozhevnikova[1]; GA Shakaryants[1]; VYU Kaplunova[1]; AA Shchendrygina[1]; EV Babayan[1]; EA Zheleznykh[1]; YUA Danilogorskaya[1]; FM Bogatyreva[1]; IS Ilgisonis[1]; AO Iusupova[1]; EV Privalova[1]; YUN Belenkov[1]; YUF Shumskaya[1]; LD Morozova[1]; VYU Zektser[1]
[1]*I.M. Sechenov First Moscow State Medical University, Moscow, Russian Federation*

Purpose: to reveal association between hemodynamic parameters estimated by using echocardiography (ECO) and remodeling of large and small vessels measured by photoplethysmography (PPG) and nail fold computer videocapillaroscopy (VC) and transforming growth factor ß2 (TGF-ß2) level in patients with heart failure (HF).
Methods: 34 patients (18 men, average age 65,82 ± 10) with HF: fifteen patients (44,1%) with preserved ejection fraction (HFpEF) and 19 (55,9%) patients with mid-range ejection fraction (HFmrEF) comparable to age, sex, presence of diabetes mellitus type 2 (DM) and hyperlipidemia were included in the study. All patients underwent ECO (ejection fraction (EF), interceptall wall thickness (IWT), left ventricle posteriori wall (LVPW). Remodeling of small vessels was assessed by VC (capillary densities (CD, cap/sq.mm), CD after reactive hyperemia test (CDrh, cap/sq.mm) and CD after venous occlusion (CDvo, cap/sq.mm)) and by PPG (index of refractionRI). Remodeling of large vessels (stiffness index-aSI, in\s) were evaluated by PPG. TGF-ß2 level was measured by IFA.
Results: It was found that TGF-ß2 level was increased (23305 pg/ml [1259; 65087] (reference level = 5222 - 13731 pg/ml)) in patients with HF. The E-selectin level was higher (39,4 ng/ml [27,62;51,17]) in patients with HFpEF than in patients with HFmrEF (56,53 ng/ml [43,63;69,43]), ? < 0,076. There was not significant differences of E-selectin level in patients with and without DM. LVPW was significantly thicker ($p < 0.028$) in patients with HFpEF (1,04 sm. [0,96;1,12]) compared to the patients with HFmrEF (1,18 sm. [1,10;1,27]), as well as IWT 1,04 [0,94;1,16]; 1,2 [1,08;1,31] respectively $p < 0.03$). Significant negative correlation was found in both groups between CD($r=-0.51$; $p < 0.05$), CDrh ($r=-0.55$; $p < 0.05$), CDvo ($r=-0.59$; $p < 0.05$) and E-selectin level. TGF-ß2 has been correlated with CD. There was not any correlation between E-selectin level and RI, aSI.
Conclusion: 1. This data revealed, that patients with HF had high levels of TGF-ß2. There was no significant difference in TGF-ß2 and E-selectin parameters between groups of patients with HF associated with diabetes mellitus type 2 and in patients with isolated HF. 2. Significant negative correlation was found in both groups between TGF-ß2 level and parameters of microvascular remodeling. 3. Patients with HFpEF and HFmrEF had different levels of E-selectin. 4. The negative correlation of E-selectin level with capillary densities after reactive hyperemia test and after venous occlusion was revealed.

P1022

Cardiorenal relationships in patients with heart failure of ischemic etiology

N Shilyaeva[1]; ? Ryabov[1]; A Germanov[1]; Y Shchukin[1]
[1]*Samara State Medical University, Cardiology, Samara, Russian Federation*

Purpose: To investigate the association of biomarkers of renal dysfunction with other biochemical and instrumental indicators in patients with CHF of ischemic etiology.
Methods. 133 patients (the average age of 55.3 ± 7.7 years) with chronic heart failure (CHF), previous myocardial infarction (MI) and percutaneous intervention were enrolled in the study. Patients grouped by type of MI: Q-wave and non-Q wave. NGAL, cystatin C, galectin-3 and NT-proBNP were measured by immunoassay analysis. eGFR was calculated using the CKD-EPI equation. Descriptive data are presented as frequencies (percent), median (25th-75th percentile). Comparison between two groups was made using Mann-Whitney test. Rank correlation coefficients were calculated according to Spearman (r). $P < 0.05$ was considered statistically significant.
Results: Patients with MI with Q-wave had lower LVEF and higher levels of NT-proBNP, but there had not differences in levels of biomarkers of renal dysfunction and Syntax score between groups (table). Correlation analysis revealed the weak and moderate positive correlations in pairs: NGAL-galectin-3 ($r = 0,210$, $p < 0,05$), NGAL-NT-proBNP ($r = 0,314$, $p < 0,01$), NT-proBNP-index of violation of local LV contractility ($r = 0.404$, $p < 0.01$) and NT-proBNP-Syntax score ($r = 0.324$, $p < 0.01$) for 1 group; cystatin C-pulmonary artery pressure (PAP) ($r = 0,402$, $p < 0,05$), cystatin C-Syntax score ($r = 0,413$, $p < 0,05$) for 2 group. eGFR decreased significantly with increasing levels of NT-proBNP and PAP (r=-0,210, -0,219, accordingly, for all $p < 0,05$) in 1 group and with decreasing LVEF ($r = 0,330$, $p < 0,05$) in 2 group.
Conclusion: Biomarkers of renal dysfunction are significantly correlated with echocardiographic and coronary angiographic measures in CHF patients with previous MI. Cystatin C, NGAL and eGFR are associated with biomarkers of myocardial stress and fibrosis in patients with MI with Q-wave.

Baseline characteristics of CHF patients

Characteristics	1 group (n = 94)	2 group (n = 39)	p
Male, n (%)	86 (91,5)	29 (74,4)	0,009
NYHA (I/II/III FC), %	5/88/7	5/90/5	1,000
LVEF, %	52 (45,5-60)	59 (53-63)	0,003
Syntax score, points	16,5 (10-24,75)	16,5 (8-27)	0,998
NT-proBNP, pg/ml	316,8 (147,9-734,3)	86,7 (53,7-151,8)	<0,001
Galectin-3, ng/ml	12,8 (8,8-17)	13,3 (10-22)	0,167
Cystatin ?, pg/ml	986,8 (858,3-1192)	1026,4 (830,9-1170,1)	0,972
NGAL, ng/ml	17,3 (14,5-22,6)	17,8 (14-23,3)	0,789
eGFR, ml/min/1,73m^2	77 (67,5-87,5)	75 (67-90)	0,848

P1023

Characteristics of right ventricular dysfunction in various causes of acute dyspnea

D Dovydas Verikas[1]; R Norvilaite[1]; G Ziubryte[1]; J Bugaite[2]; D Gabartaite[2]; A Krivickiene[3]; J Motiejunaite[3]; D Zaliaduonyte-Peksiene[3]; R Jurgaitiene[4]; K Cerlinskaite[4]; G Balciunaite[4]; D Zakarkaite[4]; A Kavoliuniene[3]; J Celutkiene[4]; A Mebazaa[5]

[1]*Lithuanian University of Health Sciences, Kaunas, Lithuania*; [2]*Vilnius University, Faculty of Medicine, Vilnius, Lithuania*; [3]*Lithuanian University of Health Sciences, Department of Cardiology, Kaunas, Lithuania*; [4]*Vilnius University, Clinic of Cardiac and Vascular diseases, Center of Cardiology and Angiology, Vilnius, Lithuania*; [5]*Hospital Lariboisiere, Paris, France*

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Introduction: Right ventricular (RV) systolic dysfunction (RVSD) can clinically manifest as dyspnoea. Echocardiography may provide information about the mechanisms of RVSD. However, knowledge on RV dysfunction is scarce.
Purpose: To characterize echocardiographic parameters of RVSD in patients presenting with acute dyspnea to the emergency department (ED).
Methods: Prospective observational cohort study enrolled consecutive patients admitted to the EDs of two university hospitals with acute dyspnea due to various causes. Echocardiography was performed in 482 patients during the first 48 hours of admission. It included the following parameters: RV basal diameter, tricuspid annular plane systolic excursion (TAPSE), velocity of the tricuspid annular systolic motion (RV S'), fractional area change (FAC), pulmonary artery systolic pressure (PASP) and RV longitudinal strain of free wall and entire RV. The current study included 347 (72%) patients with demographic, clinical and RV echocardiographic parameters. All patients were divided into five groups: acute heart failure (AHF), n = 206 (60%); pulmonary embolism (PE); n = 42 (12%); pulmonary disease (pneumonia and COPD) n = 26 (8%); acute coronary syndromes (ACS) n = 30 (9%); and other diagnoses, n = 43 (13%). Data were analyzed using One-way ANOVA.
Results: The distribution of RV echocardiographic parameters is presented in Table 1. Parameters of prominent RV dysfunction were comparable in AHF and PE groups: only RV S' was significantly lower in AHF group (p = 0.02). Dilatation and impaired RV deformation was observed in pulmonary diseases. Both AHF and PE showed significantly reduced longitudinal strain of free wall and entire RV compared to ACS and other diagnoses (p = 0.02). PASP was significantly increased in PE compared to other diagnoses (p = 0.04). Normal RV free wall strain was found only in ACS and other diagnoses.
Conclusions: RV function was much more impaired in AHF and PE than other causes of dyspnea. Reduced RV deformation was found in the majority of acute dyspnea patients.

ECHO parameters of RV in acute dyspnea

	AHF	PE	Pulmonary disease	ACS	Other diagnoses
RV basal diameter (mm)	46.8±9.7[a]	46.5±9.3[b]	42.2±7.2	38.0±7.3*§	38.8±9.2*§
TAPSE (mm)	15.5±5.4[a]	16.8±4.9[b]	18.7±6.2*	18.0±4.8*	19.3±5.9*§
RV S' (cm/s)	9.6±3.4[a]	11.1±3.5*	11.9±3.6*	10.7±2.7	12.6±4.2 *
FAC (%)	34.5±13.6[a]	35.6±11.7[b]	41.1±10.6	43.2±10.6*	43.6±13.2*§
Strain ofRV free wall	-15±6[a]	-12±6[b]	-16±7	-22±7*§	-19±7*§
Strain of entire RV	-11±5[a]	-10±5[b]	-13±6	-16±5*§	-15±6*§
PASP (mmHg)	42.1±14.9[a]	46.2±13.3[b]	38.2±14.4	37.6±13.8	36.3±13.7§

a- reference * p < 0.05 b- reference §p < 0.05

P1024

Lessons learned during an echo certification process in heart failure trials

A K Radha Krishnan[1]; DA Morris[1]; E Belyavskiy[1]; A Frydas[1]; F Huang[1]; M Kropf[1]; S Marandi[1]; B Pieske[1]; E Pieske-Kraigher[1]

[1]*Charité - Universitätsmedizin Berlin, Department of Internal Medicine and Cardiology, Berlin, Germany*

Background: Echo certification process is designed to improve the standard echo image quality in clinical trials.
Aim: The aim of the present study was to analyze the prevalence and reasons of echocardiograms with poor imaging quality in heart failure (HF) clinical trials.
Methods: We evaluated the quality of the echo acquisitions for three contemporaneous HF clinical trials that used echocardiographic parameters as clinical end-point. We analyzed 428 echocardiograms from 214 different centers from Australia, America, Canada, Europe, Japan, Singapore, South Korea, and Taiwan in an Echo Core Lab. The optimal echo acquisitions were determined according to the recommendations for chamber quantification and diastolic function of the European Association of Cardiovascular Imaging.
Results: Seventy-seven (18%) out of 428 echocardiograms did not pass the certification process. The reasons of the echocardiograms that did not pass the certification process were: poor endocardial border definition or dropout in > 2 LV segments (30%); poor imaging quality of mitral spectral Doppler measurements (15%); poor imaging quality of mitral tissue Doppler measurements (18%); incorrect number of cardiac cycles [< 3 in sinus rhythm or < 10 in atrial fibrillation] (25%); and technical or incorrect saved format (12%) see Figure 1.

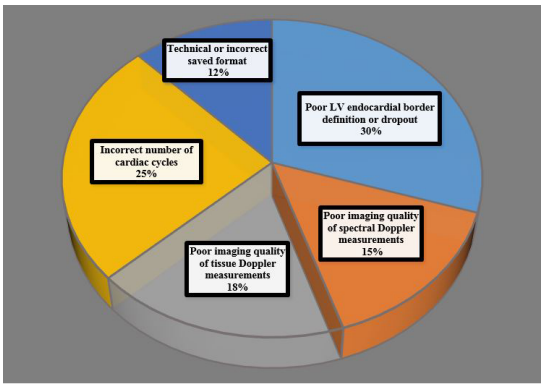


Figure 1.Reasons for failing

Conclusion: In spite of the advances in modern echocardiographic technologies, echocardiograms remain operators' and patients' dependent, which could represent up to 18% of dropout in HF clinical trials. In addition, the findings from this study suggest that a certification process before the initiation of a trial could reduce the dropout due to operators' mistakes and thereby, improve significantly the quality of the echocardiograms in clinical trials.

P1025

Multiparametric evaluation of the right ventricle systolic function after cardiac surgery

G Giovanni Tilocca[1]; L Lazzari[1]; A Crocetti[1]; G Khoury[1]; D Bovelli[1]; E Boschetti[1]; G Ambrosio[1]

[1]*Az. Osp. "S. Maria", Cardiology Department, Terni, Italy*

Background: the evaluation of right ventricular systolic function (RVSF) is essential to the management of patients undergoing cardiac surgery (CS) as it is a strong prognostic predictor in follow-up. Nevertheless, correct assessment of RVSF is challenging, as tricuspid annular plane systolic excursion (TAPSE) is often reduced despite normal value of other parameters.
Purpose: different echocardiographic indices express different characteristics of RVSF; so a correct evaluation requires a multiparametric assessment. We evaluate diagnostic power and correlation among parameters of three different echocardiographic indices in evaluation of RVSF after CS.
Methods: 265 consecutive patients (70.56% males, age 69.89 ± 9.87 years) with normal RVSF, undergoing CS, were re-evaluated before discharge using three echocardiographic parameters: TAPSE, Fractional Area Change (FAC) and the Tissue Doppler TEI index. The cut-off reported by the ESC position paper on the evaluation of cardiac chambers (European Heart Journal - Cardiovascular Imaging 2015 16; 233-271), were used for definition of right ventricular systolic dysfunction (RVSD): TAPSE < 17 mm, FAC < 35%, TEI index > 0.54.
Results: incidence of RVSD was 30.93% according to TEI index and 23.02% according to FAC, while it raises up to 84.89% using TAPSE. We also evaluated whether two of the three different methods, alternately, were in agreement or not expressing normal right ventricular function or dysfunction: TAPSE showed poor results, with an assessment agreement of only 36.95% compared to FAC (absence

of correlation: r = 0.164; = 0.059) and 42.02% compared to TEI (mild correlation: r = -0.180; p = 0.036). On the other hand, FAC and TEI agreed in 74.64% (moderate correlation r = -0.356; p = 0.000). Compared to post-CS RVSD identified by the TEI (assumed as the most reliable parameter), TAPSE was very sensitive (92.9%) but poorly specific (16.8%), p NS, - AUC 0.653, p < 0.05 - while FAC was not very sensitive (44.2%) but very specific (86.3%), p 0.000, - AUC 0.723, p 0.000 - . Different types of CS did not show different incidences of RVSD.
Conclusion: if used alone, TAPSE is an unreliable parameter in the detection of post-CS RVSD: it is not specific and has little correlation with other evaluation parameters. This study strengthen the recommendation of a multiparametric evaluation using FAC and, where possible, TEI index.

P1026
Comprehensive structural and functional integrated imaging for prediction of left ventricular reverse remodeling in non-ischemic cardiomyopathy

M Merlo[1]; M Mase[1]; G Vitrella[1]; M Belgrano[2]; G Faganello[1]; M Gobbo[1]; M Gigli[1]; A Altinier[1]; G Barbati[3]; F Ramani[1]; A De Luca[1]; G Morea[1]; MA Cova[2]; D Stolfo[1]; G Sinagra[1]
[1]Ospedale Cattinara, Cardiovascular Department, Trieste, Italy; *[2]Ospedale Cattinara, Radiological Department, Trieste, Italy*; *[3]University of Trieste, Biostatistics Unit, Department of Medical Sciences, Trieste, Italy*

Background: Defining short-term prognosis in NICM is challenging in clinical practice. Even though Left Ventricular Reverse Remodeling (LVRR) is a key prognostic marker in NICM there are few parameters able to predict it.
Purpose: To investigate whether a complete structural and functional Cardiac Magnetic Resonance Imaging (cMRI) evaluation is incremental to the classic clinical-echocardiographic approach in predicting Left Ventricular Reverse Remodeling (LVRR) in a large cohort of Non-Ischemic Dilated Cardiomyopathy (NICM) receiving evidence-based treatment.
Methods: Patients with a recent diagnosis of NICM (<3 months) who underwent complete clinical, echocardiographic and cMRI assessment were consecutively enrolled from 2008 to 2016. LVRR was defined as an increase = 10 points or normalization of Left Ventricular Ejection Fraction, associated with a = 10% reduction or normalization of Left Ventricular End-Diastolic Diameter at mid-term (median time 20 months) echocardiographic follow-up.
Results: Among 80 NICM patients included in the study, LVRR was observed in 43 (54%). At multivariate analysis, the clinical-echocardiographic evaluation failed to identify independent predictors of LVRR. However, absence of Late Gadolinium Enhancement (Odds Ratio [OR] 9.07; Confidence Interval [CI] 2.7-13.1; p-value 0.0003), Left Ventricular Mass (OR 1.018; CI 1.001-1.036; p-value 0.045) and Peak Circumferential Strain (OR 1.213; CI 1.011-1.470; p-value 0.049) assessed by cMRI were independently associated with LVRR. A model for LVRR prediction consisting of cMRI and clinical-echocardiographic parameters performed significantly better than the clinical-echocardiographic model alone (AUC 0.84 Vs 0.72; p-value 0.023). Conclusions. An integrated imaging approach with the addition of a structural and functional cMRI study to the standard-of-care evaluation improved the prediction of LVRR in a large cohort of patients with recently diagnosed NICM receiving evidence-based treatment.

P1027
Subclinical LV systolic dysfunction in patients with Left Bundle Branch Block and preserved ejection fraction: a 2D speckle tracking study

K Kalliopi Keramida[1]; V Kostopoulos[1]; L Markos[1]; P Kostakou[1]; CD Olympios[1]; N Kouris[1]
[1]Thriassio General Hospital, Athens, Greece

2D-speckle tracking echocardiography (2D-STE) is a method of quantitative assessment of myocardial systolic function, evaluating different pathophysiological properties of the myocardium from the ones expressed by ejection fraction (EF). 2D-STE has been used so far in patients (pts) with heart failure and Left Bundle Branch Block (LBBB), who are candidates for CRT. The aim of this study is to assess deformation mechanics in pts with LBBB and normal EF.
Our study population comprised of 62 consecutive pts with LBBB without history of heart disease. Of them we excluded 12 pts due to the presence of valvular disease and CAD proven from the diagnostic work up, so finally we included 50 pts with LBBB (39% men, with mean age 68 ± 10 years) and normal LVEF and 50 healthy controls (54% men with mean age 65 ± 10 years). All pts underwent a full echocardiographic study and additionally, global longitudinal and circumferential strain of the LV (LVGLS and LVGCS) were estimated off-line from the three apical views and from the parasternal short axis mid-LV view (at the papillary muscles level) using EchoPac 110 workstation (GE Vingmed Ultrasound).
There was no statistical difference between the two groups neither in EF (58.85 ± 3.48 vs 60.69 ± 5.47%), nor in LV end-diastolic diameter (46.84 ± 2.57 vs 48.15 ± 3.87mm). However, pts with LBBB had significantly impaired LVGLS (-12.7 ± 3.6 vs -19.6 ± 1.33%, p < 0.001) and LVGCS (-11.38 ± 4.11 vs -22 ± 2%, p < 0.001) compared to controls. The controls and 29 of pts with LBBB (58%) demonstrated normal diastolic function, while 21 pts had grade 1 diastolic dysfunction (DD), according to the latest ASE/EACVI criteria (2016). The presence of DD in pts with LBBB was not correlated to LVGLS (- 11.4 ± 4.4% in pts with DD vs -13.5 ± 3.2% in pts without DD, p = 0.22).
Consequently, the presence of LBBB, even without or before affecting EF, is not benign, as it impairs longitudinal and circumferential deformation of the left ventricle, independently of DD.

P1028
Iron deposition in the heart does not completely predict cardiac structural or fuctional impairement in patients with beta-thalassemia major

MD Maria Dimova-Mileva[1]; BK Kanazirev[1]; VK Kaleva[1]; KP Petrova[1]; VZ Zlateva[1]; SN Nikolova[1]; YB Bocheva[1]
[1]Medical University of Varna, Varna, Bulgaria

Cardiovascular complications and especially the heart failure are the leading cause of morbidity and mortality in transfusion dependent Thalassemia Major. The main pathophysiological mechanism is considered to be iron deposition in the myocardium.
Aim: to investigate the impact of cardiac iron load in transfusion dependent thalassemia on structural and functional cardiac parameters as early signs of heart failure.
Patients and Methods: we studied 37 thalassemic patients, mean age 32,35 ± 10,93 yrs, 54% female, with echocardiography, CMR (T2*) and NT-proBNP
Results: Mean value of T2* is 24,7 ± 11,8, median 27,17; 6 pts have T2* < 10, 3 pts 10-20, and 24 pts>20. There is a correlation between iron deposition and E/e' ratio: T2* value decreases in the upper tertile of E/e' while its maximum is in the middle range. In multifactor linear regression analysis with stepwise selection of the variables we find that the only significant echocardiographic predictor of myocardial iron load is E/e'. Increase of E/e' with 1 unit is related to decrease of the value of T2* with 3,46 (95% CI= -6,45 -0,465, p = 0,026), after adjusting for sex, lnBNP, age, EF, LAVi, LVMMi, TDISm, strain, and mean SBP. We find no other significant correlations between T2* and other cardiac and hemodynamic parameters and NT-proBNP.
Conclusions: The relation between iron deposition and E/e' shows early deterioration of diastolic function. Myocardial iron overload is not the only cause of cardiac complication and fibrosis and chronic ischemic condition are also important pathogenethic factors for the development of heart failure in patients with thalassemia major.

P1029
Right ventricular outflow tract tissue doppler in congestive heart failure

M Mikheil Tsverava[1]
[1]Tbilisi Medical Academy, Tbilisi, Georgia Republic of

Right ventricle (RV) plays important role in Heart Failure. Inflow and outflow tracts of this chamber are functionally and morphologically different. The inflow tract of RV (RV in) was actively studied by different EchoCG methods in normal and pathologic state, but there is little information about RV outflow tract.
Aim: To investigate RV outflow tract (RVout) pulsed wave TDI qualitative and quantitative parameters in patients with congestive heart failure (HF).
Material and Methods: We studied 125 healthy volunteers and 100 patients with HF. RVout pulsed wave TDI was registered from subcostal position with sample volume on RV lateral wall, near the pulmonary valve. RVin TDI was registered in apical 4 camber view with the sample volume positioned at lateral wall near the tricuspid valve.
Results: The pattern of TDI from RVout was quite different from pattern of TDI of RVin. It was characterized by prominent positive wave in isovolumic contraction period (Sict), high positive wave et the beginning of systole (S) with sharp decrease of velocity, prominent negative and positive waves during isovolumic relaxation period (Eict1 and Eict2) and two negative waves in diastole (E and A). The TDI waves of RVin where significantly greater and isovolumic relaxation time shorter then corresponding waves on RVout TDI. The Sict (4.0 ± 1.4 versus 6.4 ± 1.9 cm/sec), S (7.9 ± 1.8 versus 9.2 ± 2.4 cm/sec), Eist1 (-3.9 ± 1.9 versus -9.2 ± 2.4 cm/sec) and E (4.4 ± 1.3 versus 7.4 ± 1.8 cm/sec) on TDI from RVout where significantly slower in HF group compared with normal persons (p < 0.001).

Conclusion: In normal persons the TDI pattern of RV inflow and outflow tract is qualitatively and quantitatively different. In patients with HF the systolic and diastolic wave velocities where significantly lower compared to the normal persons.

P1030

Myocardial fibrosis assessment in left bundle branch block patients for prediction of response to cardiac resynchronization therapy

M Madina Utsumueva[1]; S Kashtanova[1]; O Stukalova[1]; V Shitov[1]; E Gupalo[1]; G Tarasovsky[1]; V Kiktev[1]; N Mironova[1]; S Golitsyn[1]
[1]National medical research center of cardiology, Moscow, Russian Federation

Introduction: Cardiac resynchronization therapy (CRT) is an established treatment for symptomatic patients with heart failure, severe left ventricular (LV) systolic dysfunction and prolonged QRS duration, preferably with left bundle branch (LBBB) morphology. However, up to 30% of patients do not benefit from this invasive and costly intervention. Presence, location and extent of myocardial fibrosis may influence the effects of CRT.
Purpose: To assess the impact of replacement myocardial fibrosis on the response to CRT in patients with LBBB.
Methods. The study included 25 patients with heart failure (mean age 61,6 years (SD = 8,3), 48% females and 52% males) due to ischemic (36%) or non-ischemic cardiomyopathy (64%), LV ejection fraction < 35%, QRS = 130 ms, LBBB and sinus rhythm. Late-gadolinium enhancement-cardiovascular magnetic resonance (LGE-CMR) was used to evaluate myocardial fibrosis prior to CRT devices implantation. Transmurality and location of fibrosis were estimated by LGE images using a 17-segment model, according to American Heart Assossiation. The semiquantitative analysis was performed using the fibrosis index (FI), which was calculated by the formula: FI = (1x?n1) + (2x?n2) + (3x?n3) + (4x?n4), where 1, 2, 3, 4 - fibrosis transmurality coefficient (1 - 0-25% wall thickness, 2 - 26-50%, 3 - 51-75%, 4 - 76-100%), ?n1-n4 - the number of segments affected by fibrosis. Response was defined as decrease in LV end-systolic volume by > 15% during 6 months follow-up period.
Results: Myocardial fibrosis was not found in 10 of 25 patients (40%), 7 of whom (70%) were responders to CRT. The presence of myocardial fibrosis was detected in 15 patients, 7 of whom (46,7%) responded to CRT. The average number of segments affected by fibrosis was greater in responders than in non-responders (4,1 vs 7, p < 0,05). The mean FI was significantly lower in responders than in non-responders (11 vs 23, p < 0,05).
Conclusions. The myocardial fibrosis extent was significantly greater in non-responders to CRT. The semiquantitative assessment of myocardial fibrosis is a perspective technique to improve selection of candidates for CRT. These **Conclusions:** need to be further tested in large studies.

P1031

Pharmacological stress echocardiogram: a predictor of prognosis in patients with dilated cardiomyopathy?

B Bebiana Faria[1]; M Oliveira[1]; L Calvo[1]; V Hafe[1]; O Azevedo[1]; S Ribeiro[1]; M Fernandes[1]; G Dias[1]; A Lourenco[1]
[1]Hospital Guimaraes, Guimaraes, Portugal

Introduction: The importance of pharmacological stress echocardiography (SE) has been widely documented, especially in patients with ischemic heart disease, both in the evaluation of ischemia and in the detection of viability. In recent years, there have been studies on the use of this technique in patients with dilated cardiomyopathy (DCM) based mainly on the evaluation of left ventricular inotropic reserve.
Objective: Evaluate in patients with MCD the ejection fraction and volume in SE, at baseline and peak stress, and its relation to the occurrence of cardiovascular events and the degree of recovery of left ventricular systolic function (LVSF).
Methods: A retrospective, unicentric study, included 34 consecutive patients diagnosed with MDC undergoing SE. The parameters of systolic and diastolic function were evaluated in the basal state and the ejection fraction and volume also at the peak of stress. The presence of death, dysrhythmias, hospitalizations, and emergency room visits for heart failure was determined as a combined endpoint of events.
Results: A total of 34 patients (P) with DCM were included, 55.9% of the male gender, with a mean age of 61.4 +/- 12.9 years. About 30% had a history of atrial fibrillation. Of the total of P 93.8% were medicated with ACE inhibitors, 84.4% with beta-blocker and 78.1% with aldosterone antagonist. They had cardiac resynchronization system (CRT) 17.6% of the P and 38.2% had cardioverter defibrillator (ICD). The SE was performed with dipyridamole in 82.4% of the P. At the time of the examination, 32.4% of the P had LVSF slightly depressed, 29.4% had moderate dysfunction and 38.2% had severe dysfunction, and the mean ejection fraction (EF) at baseline was 35.7 +/- 11%. At the peak of stress, there was a significant improvement of the LVSF with an increase in ejection volume (EV) of more than 20% in 50% of the P and an average value of EF at the peak of 45.8 +/- 12%.
The mean follow-up time was 25.8 +/- 27 months, with events occurring in 17.6% of the P, and in 18% of the cases there was an improvement in the LVSF from the SE until the last echocardiographic evaluation.
There was an association between the improvement of the LVSF and the presence of CRT (p = 0.022), lower baseline ejection fraction (p = 0.029) and lower s' septal value (p = 0.014). Increased age, increased QRS interval on ECG (p = 0.019), increased mean E/e' value (p = 0.002), a lower ejection fraction at peak stress (p = 0.009), increased baseline LV end-diastolic volume (p = 0.05), and a lower ejection volume in SE (p = 0.048) were associated with the presence of events.
Conclusion: SE in patients with DCM can stratify the prognosis, we observed that a lower value of EF in the peak of stress and a smaller increase in ejection volume in the subgroup of patients with events compared to the subgroup of patients with no events.

P1032

The real-world need for magnetic resonance imaging in patients with implanted pacemaker

N Radovanovic[1]; B Kircanski[1]; SU Pavlovic[1]; G Nikcevic[1]; M Zivkovic[1]; V Jovanovic[1]; A Milasinovic[1]; G Milasinovic[1]
[1]Clinical center of Serbia, Pacemaker Center, Belgrade, Serbia

Introduction: During the lifetime 50-75% of patients with cardiac implantable electronic devices are predicted to have an indication for a magnetic resonance imaging (MRI). The question is whether this assessment coincides with data from practice in all geographies.
Purpose: We aimed to assess the need for MRI in unselected patients with implanted MRI protected pacemakers in our institution in four year follow-up period.
Methods: We included patients in whom magnetic resonance-conditional pacemaker system was implanted during multicentre clinical study (CapSureFix® Novus Model 5076 Lead MRI Study, 2013.). In all, the CapSureFix® Novus Model 5076 leads were used for atrial and/ or ventricular stimulation. Four year follow-up was done in order to determine how many patients underwent MRI scan for any indication during that period.
Results: We included 27 patients. One patient was lost to follow-up. At implantation, mean age was 68.4 ± 9.3 years and 19 (70.4%) were male. The test-MRI was performed 9-12 weeks after pacemaker implantation in all patients from MRI group according to the study protocol. From that point to next 4 years follow up period only 2 (7.7%) patients required MRI (in first one MRI of abdomen due to colon cancer, and in second one MRI of lumbar spine due to herniated disc). In both, there were no MRI-related complications during and after the scans.
Conclusion: In this relatively small but typical anti-bradycardia pacemaker population sample, we have observed the sharp difference between literature and our real-world data in need for MRI in unselected patients.

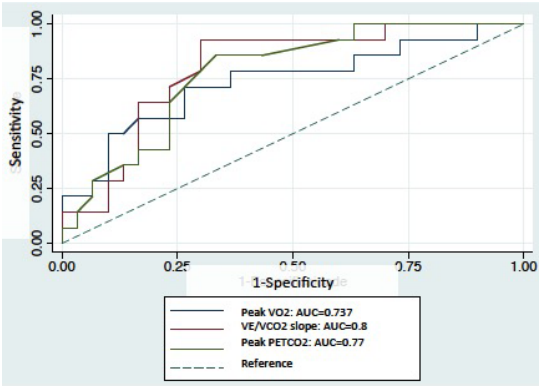
P1033

Diagnostic role of cardiopulmonary exercise testing for detecting pulmonary hypertension in patients with heart failure due to Chagas disease

P Pedro Schwartzmann[1]; HT Moreira[1]; D Mayumi[1]; JC Crescencio[1]; LFL Oliveira[1]; EEV Carvalho[2]; R Arena[3]; A Schmidt[1]; L Gallo-Junior[1]; MV Simoes[1]
[1]Medical School of Ribeirao Preto, University of Sao Paulo, Internal Medicine, Ribeirao Preto, Brazil; [2]Uberaba's University, Uberaba, Brazil; [3]University of Illinois at Chicago, Physical Therapy, Chicago, United States of America

Introduction: Pulmonary hypertension (PH) is an ominous manifestation in patients with heart failure (HF). Previous research has demonstrated that cardiopulmonary exercise testing (CPX), particularly variables reflecting ventilatory efficiency, is able to accurately diagnose secondary PH in patients with HF secondary to ischemic as well as in non-ischemic etiologies. However, assessment of the diagnostic ability of CPX for detecting PH in patients with Chagas heart disease is lacking.
Purpose: We sought to evaluate the ability of CPX-derived parameters to detect elevated pulmonary pressures in Chagas HF cohort.
Methods: This retrospective study included 44 patients with HF due to Chagas disease that underwent both symptom-limited CPX and echocardiography. PH was defined as echocardiographic-derived pulmonary systolic arterial pressure (PSAP) > 40 mmHg. CPX parameters studied were minute ventilation/carbon dioxide production (VE/VCO2) slope, partial pressure of end-tidal carbon dioxide (PETCO2), and peak oxygen consumption (VO2). Correlation between CPX-derived variables and PSAP was evaluated by Pearson's correlation coefficient (r), while diagnostic value for identifying patients with PH was assessed by ROC curves. P < 0.05 was considered significant.
Results: Mean age was 57 ± 13 years, 27 (61%) were men, with mean left ventricular ejection fraction of 38 ± 19%. NYHA functional class I, II, III and IV were found in 27%, 30%, 39%, and 5% of the participants, respectively. Mean PSAP was 37 ± 13 mmHg, while PH was identified in 13 (30%) patients. Mean VE/VCO2 slope, VO2 and

peak PETCO2 were 36.6 ± 11.8, 15.5 ± 6.3mlO2.kg-1.min-1 and 35.7 ± 8.8 mmHg, respectively. Significant moderate correlations between CPX-derived variables and PSAP were found: VE/VCO2 slope (r = 0.46, p = 0.006), PETCO2peak (r=-0.44, p = 0.002) and VO2 (r=-0.41, p = 0.003). VE/VCO2 slope showed the greatest area under the curve (AUC) = 0.800, confidence interval of 95% (95%CI = 0.664-0.936], followed by PETCO2peak (AUC = 0.777, 95% 95%CI = 0.638-0.916), and VO2 (AUC = 0.737, 95%CI = 0.565-0.909). There was no statistical difference between the AUCs.
Conclusion: In patients with HF due to Chagas disease, CPX-derived variables related to ventilatory efficiency were correlated to PSAP. Our results suggest that, similar to patients with HF of other etiologies, CPX may play a diagnostic role in identifying PH in patients with HF caused by Chagas cardiomyopathy.



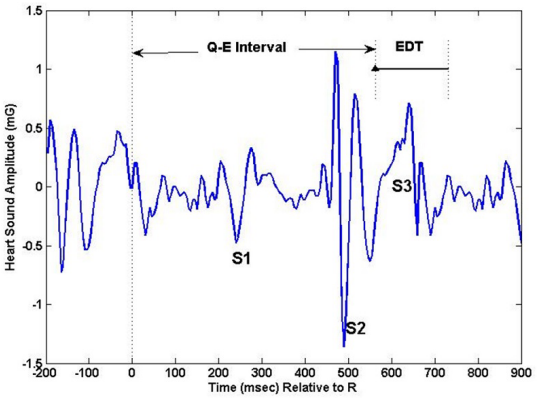
P1034

Third heart sound during atrial fibrillation? Confirming the existence of cardiac vibrations during deceleration phase of early diastolic filling while in atrial fibrillation

J Boehmer[1]; P Thakur[2]; Q An[2]; V Averina[2]; G Mark[3]
[1]Penn State Hershey Medical Center, Hershey, United States of America; *[2]Boston Scientific, St. Paul, United States of America*; *[3]Cooper University Hospital, Camden, United States of America*

Funding Acknowledgements: Boston Scientific

Introduction: The third heart sound (S3), caused by rapid deceleration of the blood against a stiff ventricle during early diastolic filling, is an early and specific sign of heart failure and elevated filling pressure. Studies have shown S3 to be coincident with deceleration phase of E-wave and associated with a steeper E-wave. Atrial fibrillation (AF) is a common comorbidity in HF, however questions have arisen regarding the ability to reliably detect S3 during AF as typically it is difficult to auscultate an S3 during AF. Here we present a case of simultaneous implanted device measured heart sound and echo data while the patient was in AF.
Methods: MultiSENSE enrolled patients implanted with COGNIS CRT-D devices and followed for up to a year. At enrollment CRT-Ds were converted to enable collection of heart sound data using device based accelerometer. Heart sound data was periodically collected as ensemble averaged (EA) waveforms of multiple neighboring beats that closely matched in RR interval. An optional echo was conducted if the patient was hospitalized for worsening HF. An independent core laboratory measured parameters from the echo images, including E-wave timing within the cardiac cycle (Q-E interval and E-wave deceleration time or EDT). EA waveforms over multiple days around the day of echo that matched the average heart rate (HR) around the echo exam to within 10 beats per min were identified and compared against E-wave timing.
Results: The patient, enrolled in November 2011 and reported to have a history of AF, was hospitalized for worsening HF on day 38 post enrollment. Device interrogation revealed ongoing AF burden of 24 hours since enrollment which transiently terminated on day 41 for several days before reverting to 24 hour AF burden. Patient underwent an echocardiogram starting at 9:22AM on day 39, which showed a Q-E interval of 562msec and EDT of 169msec. Figure shows one heart sound EA recorded at 10:49AM and clearly shows cardiac vibrations during the deceleration phase of the E-wave as deduced from Q-E interval and EDT (horizontal line). This observation is consistent across all EAs collected over 5 days around the day of the echo with matched HR.
Conclusion: Consistent with its known physiologic genesis, S3 measured using an implanted device occurred during the deceleration phase of early diastolic filling even when the patient was in AF. A device based objective measure may provide more consistent assessment of S3 than auscultation in the midst of an arrhythmic rumble of AF.



P1035

Impact of ethnic groups on device based diagnostic sensor measurements in ambulatory heart failure patients

J Boehmer[1]; G Mark[2]; G Wen[3]; P Thakur[3]; GZ Duray[4]
[1]Penn State Hershey Medical Center, Hershey, United States of America; *[2]Cooper University Hospital, Camden, United States of America*; *[3]Boston Scientific, St. Paul, United States of America*; *[4]Military Hospital, Budapest, Hungary*

Funding Acknowledgements: Boston Scientific

Background: An implantable device based multi-sensor algorithm was recently shown to detect impending worsening Heart Failure (HF) events with high sensitivity. The objective of this analysis was to characterize the relationship between sensor measurements and ethnicity of HF patients.
Methods: In the MultiSENSE trial, 792 patients implanted with a COGNIS CRT-D were enrolled in the United States, and followed up to 1 year. Device software was modified to permit collection of chronic diagnostic sensor data including heart sounds, respiration, thoracic impedance, heart rate and activity. Sensor data were combined into a multi-sensor alert algorithm (HeartLogic). Patients (N = 791) were classified into four ethnic groups: Caucasian (N = 602), Black or African American (N = 127), Hispanic or Latino (N = 50) and Others (N = 12). Average sensor data from patients in different ethnic groups were compared using a one-way ANOVA.
Results: At enrollment, Black/African group had significantly lower LVEF (25.89 ± 10.63) as compared to Caucasian (30.65 ± 6.62) or Hispanic group (29.85 ± 7.36), whereas Hispanic group had a greater prevalence of NYHA Class III/IV (53%) as compared to Caucasian (26%) or Black/African group (32%). On average, patients in the Black/African group had higher Day-time Rapid Shallow Breathing Index (RSBI) (Table), whereas, Caucasian group had lower activity. No statistical differences were detected in the other five sensor trends, and the resulting HeartLogic Index. With Bonferroni correction for multiple comparisons, none of the sensor trends were statistically different across the ethnic groups.
Conclusion: There are differences in physiologic parameters associated with heart failure between groups based on ethnicity including differences in day-time RSBI and activity despite no difference in the overall predictive score of the HeartLogic Index.

HF Sensor Measurements Across Ethnicity

Daily Trend	Caucasian	Black/African	Hispanic/Latino	p value
S1 (mG)	2.57±0.94	2.60±0.97	2.39±0.93	0.388
S3 (mG)	0.97±0.33	0.96±0.31	1.00±0.39	0.688
Thoracic Impedance (Ohm)	49.69±8.73	48.56±8.30	48.00±11.21	0.217
Daytime RSBI (br/min/Ohm)	8.35±2.55	9.08±2.85	8.53±2.52	0.017
Night Heart Rate (bpm)	71.16±7.88	72.48±8.14	72.06±8.01	0.199
Respiratory Rate (median, br/min)	17.74±2.41	17.68±2.39	18.17±2.70	0.45
Activity (hours)	2.02±1.90	2.36±1.83	2.56±2.20	0.045
HeartLogic Index	6.80±5.29	5.96±4.83	7.95±5.67	0.064

S1, S3 = 1st, 3rd heart sound,RSBI = Rapid Shallow Breathing Index,Day = 6am to 12am,Night = 12am to 6am

P1036

Association neurohumoral indicators with parameters remodeling left ventricular in patients with chronic heart failure in the relationship with dysfunction of kidney

ZD Rasulova[1]; UK Kamilova[1]
[1]*Republican Specialized Scientific-Practical Medical Center Therapy and Medical Rehabilitation, Cardiology, Tashkent, Uzbekistan*

Purpose: Examine the relationship levels of brain natriuretic peptide (BNP), aldosterone (Al) and norepinephrine (NE) in the serum with parameters remodeling the left ventricle (LV) and functional status of kidneys in patients with II and III functional class (FC) chronic heart failure (CHF).
Material and methods. Were examined 46 patients with coronary heart disease (CHD) with CHF with II ((24) and III (22) FC, according to the classification of the New York Association of cardiologists. All patients were carried out echocardiography, was determined creatinine of serum, calculated method determined the rate of glomerular filtration (cGFR) according to the formula MDRD, the level of Al, BNP and NE was determined by immunosorbent assay.
Results: In CHF there was a significant increase the level of BNP, NE and Al in the blood plasma, correlative with a degree of disease progression, at the same time in patients with II FC is dominated by medium-high levels neurohormones, and in patients with III FC higher levels of these indicators. In patients with CHF II FC there was an increase in the content of BNP, NE and Al to 187%, 30% and 36% ($p < 0,001$) and in patients III FC to 330%, 56% and 66.3% ($p < 0,001$), respectively, in comparison with the control group.
Installed the dependence of the degree of dysfunction kidney and processes remodeling of the level of neurohumoral factors (BNP, Al, and NE) in patients with CHF. Revealed association of the level of neurohormones BNP, Al and NE with the indicators remodeling heart: high inverse correlation with ejection fraction (EF) of LV ($r = 0.76$, $r = 0.70$ and $r = 0.72$, respectively), the average contact with cGFR with the coefficient of correlation $r = 0.45$, $r = 0.35$ and $r = 0.38$, respectively, and direct correlation with the final diastolic volume of LV ($r = 0.75$, $r = 0.78$ and $r = 0.70$, respectively).
Conclusion: Thus, in patients with CHF significant increase in neurohumoral factors (NE, BNP and Al) associated with FC CHF, the degree of systolic dysfunction LV and dysfunction kidney. In patients with II FC CHF prevailed medium-high values neurohormones, with III FC CHF - high level of improving neurohormones NE, BNP and Al.

Chronic Heart Failure - Treatment

P1037

Real-world patterns of loop diuretics dose adjustment and association with outcomes in outpatients with chronic heart failure: observations from the ESC Heart Failure Long-Term Registry

C Chris Kapelios[1]; C Laroche[2]; MG Crespo-Leiro[3]; M Metra[4]; M Piepoli[5]; S Anker[6]; G Filippatos[7]; A Maggioni[8]; P Seferovic[9]; G Rosano[10]; A Mebazaa[11]; T Mcdonagh[12]; M Lainscak[13]; F Ruschitzka[14]; LH Lund[15]
[1]*Laiko University General Hospital, Athens, Greece*; [2]*European Society of Cardiology, Sophia-Antipolis, France*; [3]*University Hospital Complex A Coruña, A Coruña, Spain*; [4]*University of Brescia, Brescia, Italy*; [5]*Guglielmo da Saliceto Hospital, Piacenza, Italy*; [6]*Charite University Hospital, Berlin, Germany*; [7]*Attikon University Hospital, Athens, Greece*; [8]*ANMCO Foundation For Your Heart, Florence, Italy*; [9]*University of Belgrade, Belgrade, Serbia*; [10]*San Raffaele Hospital of Milan (IRCCS), Milan, Italy*; [11]*University Paris Diderot , Paris, France*; [12]*King's College Hospital, London, United Kingdom*; [13]*General Hopsital Celje, Celje, Slovenia*; [14]*University Heart Center, Zurich, Switzerland*; [15]*Karolinska University Hospital, Stockholm, Sweden*

Introduction: Loop diuretics are the mainstay of treatment in heart failure(HF) patients with congestion. However, there are concerns over deleterious neurohormonal effects and associations with reduced survival. Guidelines recommend that diuretics should be used in the lowest effective dose. We investigated a) loop diuretics dose adjustment at outpatient visits, b) associations between dose adjustment and outcomes and c) factors associated with appropriate dose decrease, in the ESC HF Long-Term Registry.
Methods: Of 9,749 outpatients we included the 8,130 (83.4%) CHF patients who received diuretics both prior to and at end of outpatient index visit. Loop diuretics were converted to furosemide equivalents based on: 1 mg bumetanide = 20 mg torsemide = 40mg furosemide. Patients were considered as clinically stable if they were in NYHA class I-II, had no history of HF hospitalization during the past 6 months and had no signs of congestion or hypoperfusion. Appropriate dose decrease was defined as a decrease in diuretics dose during index visit and no death, HF hospitalization or increase in NYHA class or diuretics dose during the 12-month period after the dose decrease.
Results: Mean age was 66 ± 13 years, 71% men. Mean left ventricular ejection fraction was 37 ± 14% (62% HFrEF, 19% HFmrEF, 19% HFpEF). Median [IQR] daily dose of diuretics was 40 [25,80] mg. During index visit, diuretic dose was increased in 1,279 patients (15.7%), decreased in 671 (8.3%) and unchanged in 6,180 (76.0%). Among 3,168 patients (39.8%) who were stable at index visit, 270 patients (8.5%) had diuretic dose increased, 284 (9.0%) had diuretic dose decreased, and 2,614 (82.5%) had diuretic dose unchanged.
During 12-month follow-up and with censoring at non-CV death, 385 cardiovascular (CV) deaths occurred (4.7%). Diuretics dose increase (vs. decrease) during index visit was associated with the risk of CV death (adj. HR: 2.01;95%CI: 1.19-3.39, $P = 0.009$), while maintenance of stable diuretic dose (vs. decrease) was also associated with a trend towards higher 1-year CV mortality (adj. HR: 1.61;95% CI: 1.00-2.61, $P = 0.052$).
Baseline variables independently associated with appropriate diuretic dose decrease was systolic blood pressure (adj. HR: 1.01 per mm Hg;95% CI: 1.00-1.02, $P = 0.032$), and with unsuccessful dose decrease the presence of sleep apnea (adj. HR: 0.24;95% CI: 0.09-0.69, $P = 0.008$), peripheral congestion (adj. HR: 0.48;95% CI: 0.29-0.80, $P = 0.005$) and moderate-severe mitral valve regurgitation (adj. HR: 0.57;95% CI: 0.37-0.87, $P = 0.008$).
Conclusion: Diuretic dose was unchanged in 76% of outpatients with CHF overall and in 82% even among stable patients. No dose reduction was associated with increased risk for 1-year CV death, independently of HF severity and other variables. Higher baseline systolic blood pressure and absence of sleep apnea, peripheral congestion and moderate-severe mitral valve regurgitation were independently associated with appropriate diuretic dose decrease.

P1038

Acute kidney failure and hyperkalaemia in patients with chronic hearth failure treated with aldosterone antagonists- a risk-benefit network meta-analysis

M Seiz[1]; H Froehlich[1]; T Taeger[1]; L Frankenstein[1]
[1]*University Hospital of Heidelberg, Heidelberg, Germany*

Background: Aldosterone antagonists (AAs) improve mortality in patients with chronic heart failure (CHF). However, they may also cause acute renal failure and hyperkalaemia. The relative risk-benefit ratio of the available AAs spironolactone, eplerenone and canrenone with respect to acute renal failure and hyperkalaemia is unclear.
Methods: We conducted a systematic review and network meta-analysis following PRISMA-P and PRISMA-NMA guidelines. 7 individual databases, 6 individual clinical trial registries, and 3 individual grey literature databases were searched up to January 2017 for randomized controlled trials with an active treatment of either spironolactone, eplerenone, or canrenone/potassium-canreonate in adults with symptomatic CHF due to systolic dysfunction (left ventricular ejection fraction < 40%) reporting on acute renal failure or hyperkalaemia. The pooled effect estimates were ranked by the surface under the cumulative ranking curve (SUCRA).
Results: We identified 5 trials including 4,923 CHF patients informing on acute kidney failure and hyperkaliaemia as safety endpoints. The relevant network plot is shown in figure 1. The analyzed results were under the influence of Beta-blocker treatment. They appear to favour spironolactone over eplerenone (OR: 3.47 [1.44-8.37]; spironolactone as reference) for acute kidney failure but did not reach significance for hyperkalaemia (OR: 18.51 [0.98-350.44]).
Conclusion: The risk-benefit ratio of spironolactone with respect to acute renal failure and hyperkalaemia appears favourable as compared to eplerenone. These results, presenting in this study could be a further evidence in the treatment of patient with CHF.

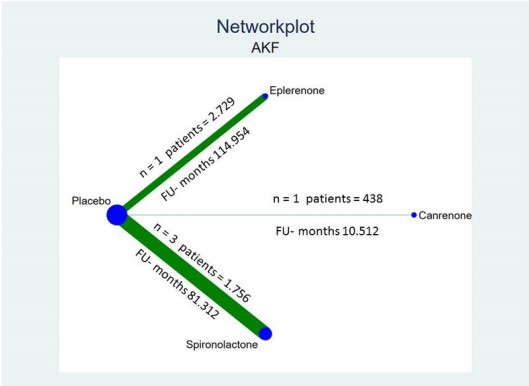


figure 1

P1039

Intermittent administration of levosimendan ambulatory in patients with advanced chronic heart failure: experience in our center.

P Arenas Martin[1]; IJ Sanchez Lazaro[1]; R Lopez Vilella[1]; I Husillos Tamarit[1]; C Borras Almenar[1]; M Ezzitouny[1]; V Donoso Trenado[1]; J Sanz Sanchez[1]; L Martinez Dolz[1]; L Almenar Bonet[1]
[1]Hospital Universitario y Politécnico La Fe, Valencia, Spain

Introduction: Chronic heart failure has a high morbidity and mortality, so new therapeutic strategies should be considered. In recent years there has been a growing interest in levosimendan for this type of patients. Levosimendan is an arterial and venous vasodilator drug with a positive ionotropic effect, since it increases the sensitivity to calcium of troponin c, increasing cardiac contractility.
Purpose: Our purpose was to assess the effectiveness of ambulatory levosimendan in advanced heart failure.
Methods: We have used the Lion Heart protocol (NCT01536132) of six cycles of levosimendan (0.2 µg/Kg/min) in 6 hours every 14 days. The number of admissions caused by heart failure decompensation in the year prior to entering into the program and in the year after the end of the program, PRO-BNP and renal function were computed, as well if the patients reached heart transplantation. 30 patients were included.
Results: Of the 30 patients, 93.3% were male, with a mean of 60 years. The etiology of heart failure was 50% ischemic, 26.7% corresponded to idiopathic dilated cardiomyopathies, 3.3% were valvular, and 13.3% were congenital heart diseases.
Of the 30 patients included in the program, 9 did not complete the 6 treatment cycles. The reasons for not completing the cycles were heart transplantation (5 patients), poor tolerance (3 patients) or due to the appearance of intercurrent processes such as myocardial infarction (1 patient).
The mean admissions in the year previous to treatment with levosimendan was 2 (SD 1,6), reducing to 0.14 (SD 0.44) after the same (p: 0.001).
The average levels of PRO-BNP before starting the program were 7132 pg / ml (SD 6525) and at the end of the month it was reduced to 5447 pg / ml (SD 5335) (p: 0.25).
The mean of the GFR before the start of the cycles was 47,16 ml / min (SD 17,7), and at the end of the cycle it remained stable (mean of 50,33 ml / min, SD 16,64) (p: 0.5).
Of the 8 patients included in the transplant list before starting treatment, 6 arrived at the transplant. The 2 patients who did not receive a transplant were due to a bad baseline situation and hematologic disease.
Conclusions: The intermittent use of levosimendan ambulatory significantly reduces the number of admissions, decreases PRO-BNP and does not affect renal function. In addition, it allows patients waiting for a transplant to reach it without decompensation.

P1040

Sildenafil for chronic heart failure : a meta-analysis

C Ariano[1]; R De Vecchis[2]
[1]Division of Geriatrics, " Casa Sollievo della Sofferenza" Hospital, S. Giovanni Rotondo, Italy; *[2]Preventive Cardiology and Rehabilitation Unit, DSB 29 "S. Gennaro dei Poveri Hospital", Napoli, Italy*

Introduction: According to 2015 ESC/ERS guidelines for the diagnosis and treatment of pulmonary hypertension(PH), no specific drug is currently indicated for PH related to left heart disease(PH-LHD), i.e., the one secondary to left chronic heart failure (CHF), which coincides with the group 2 of the PH classification endorsed by the above-mentioned guidelines. In fact, adoption of therapies that specifically apply for so-called pulmonary arterial hypertension (group 1 of the PH classification) has been regarded as substantially contraindicated in patients with PH-LHD. Nevertheless, based on some previous studies, sildenafil would seem to exert a beneficial effect in CHF patients , although the comparison between these studies shows quite inconsistent or heterogeneous findings. Thus, in order to better evaluate the effects of sildenafil therapy in CHF patients, we performed a meta-analysis of randomized controlled trials (RCTs).
Methods: We searched PubMed and EMBASE electronic archives for RCTs that compared sildenafil with placebo in CHF with reduced (HFREF) or preserved (HFpEF) left ventricular ejection fraction. The endpoints of interest were: a composite of all-cause death or hospitalization, adverse events, peak VO2, 6-minute walk test(6MWT), left ventricular ejection fraction (LVEF), E/e' ratio, mean pulmonary arterial pressure (mPAP), pulmonary arterial systolic pressure (PASP) and pulmonary vascular resistance (PVR).
Results: 14 studies, enrolling a total of 928 patients, were comprised in the meta-analysis. Among these, 13 were RCTs and one was a subgroup analysis. Among patients with HFREF(no.555), a significant benefit was conferred by sildenafil against the risk of the composite endpoint of death and hospitalization (OR= 0.28; 95% CI: 0.10 to 0.74; p = 0.03) . Furthermore, among HFREF patients, therapy with sildenafil ameliorated peak VO2 (difference in means [MD] = 3.76 ml/min/kg; 95% CI: 3.27 to 4.25) as well as 6MWT (MD= 22.7 meters ; 95% CI: 8.19 to 37.21). For patients with HFREF, sildenafil therapy yielded a nonsignificant decrease in mPAP, while PASP was significantly reduced (MD: -11.52 mmHg; 95% CI: -15.56 to -7.49 mmHg; p <0.001). By contrast, in the RCTs of patients with HFpEF(no.373), no benefit ensued from sildenafil use regarding all of the investigated clinical, ergospirometric or hemodynamic endpoints.
Conclusions: Therapy with sildenafil caused a statistically significant improvement of clinical outcomes, exercise capacity and pulmonary hemodynamics in patients with HFREF, but not in HFpEF. However, in view of the relatively small sample size of the HFpEF population recruited so far in the RCTs that investigated the effects of sildenafil treatment, further research in this field is required to clarify whether sildenafil is really beneficial even in this subset.

P1041

The dilemma of recurrent hyperkalaemia and use of renin-angiotensin-aldosterone system inhibitors in heart failure with reduced ejection fraction: a European multi-national targeted chart review

P Rossignol[1]; M Pignot[2]; G Georgiana Cornea[3]; L Zakin[3]; T Schulmann[3]
[1]Institut lorrain du coeur et des vaisseaux Louis Mathieu, Centre d'Investigations Cliniques-Plurithématique Pierre Drouin - INSERM - CHRU de Nancy, Nancy, France; *[2]Kantar Health GmbH, Real World Research & Value, Munich, Germany*; *[3]Vifor Pharma Group, Glattbrugg, Switzerland*

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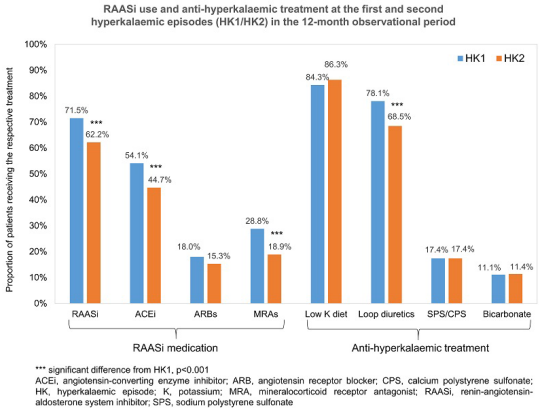
Background/Introduction: ESC and ACCF/AHA guidelines recommend the use of renin-angiotensin-aldosterone system inhibitors (RAASi) at the highest tolerated targeted doses to reduce the risk of morbidity and mortality in patients with heart failure with reduced ejection fraction (HFrEF). RAASi increase the risk of hyperkalaemia (HK), especially with advancement of chronic kidney disease (CKD), and therefore are often underused, reduced or discontinued in patients with HFrEF.
Purpose: To describe the contemporary multidimensional management of recurrent HK (defined as = 2 episodes per year) and count hospitalisations in patients with HFrEF in routine clinical practice across Europe.
Methods: A targeted retrospective chart review was conducted in France, Germany, Italy, Spain and the UK. Patients with HFrEF not on dialysis with recurrent HK (serum K+ = 5.5 mEq/L) within a 12-month observational period starting with the first HK episode (HK1) were included. Demographic and clinical characteristics were documented at HK1. HK treatment and RAASi medications were recorded at each visit. If the regimen changed during a visit, the new prescription was recorded. HK treatment and RAASi use were compared between the first and second HK episode (HK1, HK2) and among countries. Hospitalisations were documented.
Results: Data collected between June and September 2016 included 333 patients with HFrEF [left ventricular ejection fraction (LVEF) = 40%]. Their mean (SD) age was 68.5 (11.11) years and 67.0% were men. At HK1, 77.8% had an LVEF of 30-40%, the mean estimated glomerular filtration rate was 43.4 (23.5) mL/min/1.73 m^2, and 70.8% had CKD. Of these patients, 82.6% had 2 documented HK and 17.4% had 3 or more episodes.
During the observational period, 116 hospitalisations were documented for 108 patients (1.2 [0.6] hospitalisations per patient). This included 41 hospitalisations (36 patients) related to HK and 54 hospitalisations (53 patients) for cardiovascular reasons.

The proportion of patients receiving RAASi was significantly lower in HK2 than in HK1, especially for angiotensin-converting enzyme inhibitors (ACEi) and mineralocorticoid receptor antagonists (MRA) (Figure 1). In HK2, the proportion of patients receiving the full target dose for the most used ACEi Ramipril was significantly lower than in HK1 (35.1% vs 50.9% of those receiving Ramipril; p < 0.001). HK treatment options used similarly in HK1 and HK2 encompassed a low potassium diet, sodium/calcium polystyrene sulfonate (SPS/CPS) and bicarbonate. Loop diuretic use was lower in HK2 than in HK1 (Figure 1).
Conclusion(s): In this population with HFrEF, ACEi and MRA discontinuation was observed between the two HK episodes. One-third of the hospitalisations were due to HK. Thus, more effective HK mitigation strategies are needed.



P1042

Gender differences in heart failure treatment in the Netherlands: a subgroup analysis of the CHECK-HF registry

J F Jesse Feiko Veenis[1]; HP Brunner-La Rocca[2]; AW Hoes[3]; GCM Linssen[4]; JJ Brugts[1]
[1]Erasmus Medical Center, Cardiology, Rotterdam, Netherlands; *[2]Maastricht University Medical Centre (MUMC), Cardiology, Maastricht, Netherlands*; *[3]University Medical Center Utrecht, Utrecht, Netherlands*; *[4]Hospital Group Twente, Cardiology, Twente, Netherlands*

On behalf of: CHECK-HF investigators
Funding Acknowledgements: Servier, the Netherlands, funded data inclusion and software programme. Analysis was conducted, interpreted, and reported independently of the sponsor

Background/introduction: The poor prognosis of chronic heart failure (HF) can be optimized by adherence of medical therapy according to the guidelines. The rate of drug prescription and dosage are often used as benchmark of quality of care. Data on gender differences in HF treatment are scarce.
Purpose: Evaluation of gender differences in HF treatment in the Netherlands.
Methods: The current analysis is part of a cross-sectional registry of 10,910 chronic HF patients at 34 Dutch outpatient clinics in the period of 2013 until 2016 (CHECK-HF). Demographic parameters, laboratory and echocardiographic values as well as medication use (type, dosage and frequency and total daily dose) were recorded.
Results: We studied 8,360 patients with HF with reduced ejection fraction (HFrEF; 78.7%), of which 63.9% were male and 36,1% were female. Females were slightly older (71.6 vs. 73.4 years, male vs. female resp., p < 0.01), had more often a non-ischemic cause of HF (58.5% vs. 39.6%, p < 0.01) and hypertension (37.9% vs. 43.2%, p < 0.01), and eGFR was lower (61.4 vs. 56.6 ml/min/1.73 m2, p < 0.01). Diabetes rates were equal between men and women (25.3% vs. 25.7%, p = 0.72). Current HF medication use is presented in Table 1. Females received less RAS-inhibitors and more beta-blocker, ivabradine and diuretics, independently of other factors. We observed a lower percentage of ICD and CRT-D in females. Lifestyle interventions were more often observed in females as compared to males.
Conclusion: In this large registry, we observed a lower prescription of RAS-inhibitors, and implantation of ICD and CRT-D, but a higher prescription of beta-blocker, ivabradine and lifestyle therapy in females with HFrEF, as compared to males.

P1043

Age differences in heart failure treatment in the Netherlands: a subgroup analysis of the CHECK-HF registry

J F Jesse Feiko Veenis[1]; HP Brunner-La Rocca[2]; AW Hoes[3]; GCM Linssen[4]; JJ Brugts[1]
[1]Erasmus Medical Center, Cardiology, Rotterdam, Netherlands; *[2]Maastricht University Medical Centre (MUMC), Cardiology, Maastricht, Netherlands*; *[3]University Medical Center Utrecht, Utrecht, Netherlands*; *[4]Hospital Group Twente, Cardiology, Twente, Netherlands*

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Background/introduction: The poor prognosis of chronic heart failure (HF) can be optimized by adherence of medical therapy according to the guidelines. The rate of drug prescription and dosage are often used as benchmark of quality of care. Data on age differences in HF treatment are scarce.
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Methods: The current analysis is part of a cross-sectional registry of 10,910 chronic HF patients at 34 Dutch outpatient clinics in the period of 2013 until 2016 (CHECK-HF). Demographic parameters, laboratory and echocardiographic values as well as medication use (type, dosage and frequency and total daily dose) were recorded.
Results: We studied 8,360 patients with HF with reduced ejection fraction (HFrEF; 78.7%), with a mean age of 72.3 years (y). In elderly, we observed more hypertension (< 60y 29.1%, 60-69y 38.0%, 70-79y 42.4%, >80y 43.0%, p < 0.01) and diabetes (20.0%, 24.9%, 28.9%, 24.6%, p < 0.01) as well as lower eGFR (79.3, 67.3, 58.1,

P1042 Table 1. Gender and HF therapy in HFrEF

	Unadjusted analysis	Age adjusted analysis (OR [95% CI])	Multivariate analysis (OR [95% CI])*			
Pharmacotherapy	Males	Females	p-value			
	Beta-blocker,% (n = 8181)	79.1	82.0	<0.01	1.24 [1.11-1.39]	1.26 [1.11-1.43]
	RAS-inhibitors, % (n = 8181)	82.6	78.9	<0.01	0.85 [0.76-0.96]	0.84 [0.74-0.95]
	MRA, % (n = 8181)	52.8	53.3	0.65	1.04 [0.95-1.14]	1.03 [0.93-1.13]
	Ivabradine, % (n = 8323)	4.2	5.2	0.04	1.32 [1.07-1.62]	1.37 [1.08-1.74]
	Diuretics, % (n = 8181)	81.6	84.9	<0.01	1.22 [1.08-1.38]	1.22 [1.06-1.39]
Device therapy						
	ICD / CRT-D (n = 6635)	35.5 / 18.4	22.2 / 14.5	<0.01 / <0.01	0.53 [0.47-0.60] / 0,77 [0.67-0.88]	0.59 [0.52-0.68] / 0.72 [0.62-0.83]
	Pacemaker (n = 6635)	8.0	9.3	0.07	0.95 [0.79-1.15]	0.86 [0.71-1.06]
Lifestyle therapy						
	Fluid / sodium restriction (n = 6724)	72.6 / 74.6	76.0 / 77.9	0.02 / 0.02	1.16 [1.03-1.30] / 1.16 [1.03-1.31]	1.23 [1.08-1.39] / 1.20 [1.05-1.36]

* Adjusted for ischemic cause of HF, age, hypertension and eGFR

P1043 Table 1. Age and HF therapy in HFrEF

	<60 years (11.4%)	60-69 years (21.9%)	70-79 years (32.7%)	>80 years (31.0%)	p-value	
Pharmacotherapy						
	Beta-blocker, % (n = 8218)	84.2	81.7	80.1	77.0	<0.01
	RAS-inhibitors, % (n = 8218)	89.7	86.4	83.2	71.7	<0.01
	MRA, % (n = 8218)	59.5	53.6	51.2	51.3	<0.01
	Ivabradine, % (n = 8360)	9.3	5.1	4.1	2.5	<0.01
	Diuretics, % (n = 8218)	72.5	78.7	82.7	90.3	<0.01
Device therapy						
	ICD (n = 6666)	44.1	41.4	36.4	11.3	<0.01
	CRT-D (n = 6666)	16.7	19.5	21.2	11.0	<0.01
	Pacemaker (n = 6666)	1.4	3.1	6.8	17.1	<0.01
Lifestyle therapy						
	Fluid restriction (n = 6758)	64.2	72.8	73.8	79.4	<0.01
	Sodium restriction (n = 6762)	66.6	74.5	76.0	81.1	<0.01

48.2 ml/min/1.73 m2, p < 0.01) between groups. Current HF medication use is described in Table 1. Elderly patients received less beta-blocker, RAS-inhibitors, MRA and ivabradine, but more diuretics (all p < 0.01). Furthermore, we observed less ICD and CRT, but more pacemaker therapy in elderly (p < 0.01). Elderly were more often treated with lifestyle treatment (p < 0.01).

Conclusion: In this large registry of HFrEF patients, we observed significant differences in medical, device and lifestyle therapy between age-groups.

P1044

Comparative efficacy of long-term digoxin and ivabradine therapy on prognosis, left and right heart functional parameters in patients with chronic heart failure and mid-ranged ejection fraction

LR Liana Tumasyan[1]; KG Adamyan[1]
[1]*Institute of Cardiology, Yerevan, Armenia*

The aim of study was to assess the comparative efficacy of digoxin (D, 0.25 mg) and ivabradine (I, 15 mg) therapy on prognosis, left (LV) and right ventricular (RV), left (LA) and right (RA) atrial parameters, NT-pro-BNP and hsCRP levels in III-IV NYHA functional class chronic heart failure with mid-ranged ejection fraction (HFmEF).

Methods: 135 pts (age 60.1) with symptomatic HFmEF in sinus rhythm with HR>70 bpm were randomly assigned to groups A (n = 44, receiving D), B (n = 46, receiving I) and C (n = 45, non-receiving both drugs) in addition to ACEI, beta-blockers and diuretics. Tricuspid annulus plane systolic excursion (TAPSE), tissue Doppler-derived tricuspid lateral annular systolic velocity (s'), LV mean e' septal and lateral wall, pulmonary artery (PA) ejection time (ET), RA and LA functional index (RAFI and (LAFI), pulmonary vein (PV) systolic contribution (SC), difference between duration of reversal atrial flow (Ar) and late (A) transtmitral filling, NT-pro-BNP and hsCRP levels were assessed at baseline, 12, 24 and 36 months.

Results: 1-, 2- and 3-year mortality were (%) 29.5, 38.6 and 45.5; 28.3, 37.0 and 41.5; 40, 53.3 and 62.2 in groups A, B and C, respectively. 1-, 2- and 3-year hospitalization rates were (%) 43.2, 52.2 and 60.9; 43.5, 50 and 60, 75.6 and 84.4 in groups A, B and C, respectively. Event-free analysis showed lower probability [relative risk (RR) reduction, (%) p < 0.05] of 1-year at 26.3 and 29.3, 2-year at 27.6 and 30.6 and 3-year mortality at 26.8 and 30.1 and 1-year at 32.5 and 32.9; 2-year at 31 and 33.9; and 3-year hospitalization at 27.8 and 28.9, respectively, in groups A and B compared to group C. 1-year I treatment significantly (%, p < 0.05 for all) improved only HR at 21.2, levels of NT-pro-BNP at 40.2. and RV functional parameters (TAPSE at 51.2, s' at 35.2, PA ET at 18.8) . 1-year D treatment significantly (%, p < 0.05 for all) decreased HR at 20.2, levels of NT-pro-BNP at 38.9, hsCRP at 44.6, e' at 39.2, Ar-A at 72.1, increased PV SC at 57.1, RAFI at 50.9 and LAFI at 43.9 Reduction of e' = 50%, NT-pro-BNP, hsCRP = 40%, HR = 25%, Ar-A = 70% , increase of RAFI and LAFI, PV SC, s" = 50%, PAET at = 25% was associated with significant improvement of prognosis compared to decrease of e' < 30%, NT-pro-BNP, hsCRP < 25%, HR < 15%, Ar-A < 50% , increase of RAFI and LAFI, PV SC, s' < 30%, PAET < 15% (RR 0.35, 0.33, 0.34,0.32, 0.37, 0.36, 0.35, 0.34, 0.32 and 0.33, p < 0.05, respectively).

Conclusions: 1) Changes of Ar-A = 50%, RAFI and LAFI, s', e' = 50%, NT-pro-BNP, hsCRP = 40%; PAET and HR = 25% identified pts with cardiovascular risk reduction. 2) I and D use associated with almost similar significant reduction of morbidity and mortality. 3) Prognostic Improvement, associated with I use, was due to significant decrease of HR and NT-pro-BNP level, and RV functional parameters improvement, while D treatment resulted to HR reduction, improvement of LA and RA functional, LV diastolic parameters, neurohormonal and inflammation status.

P1045

The reverse remodeling response to sacubitril/valsartan therapy in heart failure with reduced ejection fraction.

P Pieter Martens[1]; H Belien[1]; M Dupont[1]; W Mullens[1]
[1]*Hospital Oost-Limburg (ZOL), Cardiology, Genk, Belgium*

Background: Major classes of medical therapy for heart failure with reduced ejection fraction (HFrEF) induce left ventricular reverse remodeling. The revere remodeling response to sacubitril/valsartan remains unstudied.

Methods: We performed a single center, prospective assessor-blinded study to assess the reverse remodeling response of sacubitril/valsartan-therapy in HFrEF-patients with a class I-indication (New York heart Association [NYHA]-class II-IV, Left ventricular ejection fraction [LVEF] <35%, optimal dose with Renin-Angiotensin-System Blocker [RAS-blocker]). Doses of sacubitril/valsartan were optimized to individual tolerance. Images were assessed offline by an investigator blinded to clinical data and timing of echocardiograms.

Results: Sixty HFrEF-patients (68 ± 11years) were prospectively included between October 2016 and May 2017. Over a median(IQR) follow-up of 104 (77-150) days, LVEF improved (26 ± 6 vs. 30 ± 6; p <0.001) and Left ventricular systolic volume (LVESV) dropped (165 ± 55ml vs. 149 ± 55ml; p = 0.003), paralleled by an improvement in stroke volume (58 ± 23 ml vs. 71 ± 30ml; p = 0.002) and cardiac output (3.94 ± 1.6 L/min vs. 4.53 ± 2.0; p = 0.032). Volumetric remodeling associated with a reduction in the amount of mitral regurgitation (1.59 ± 1.0 vs. 1.11 ± 0.8; p <0.001; graded on a 0-4 scale). Metrics of diastolic function improved; including a drop in the E/A-wave ratio (1.9 ± 1.3 vs. 1.4 ± 0.9; p = 0.008) and diastolic-filling time prolonged (expressed as % of cycle-length, 47 ± 9% vs. 53 ± 1%; p = 0.002). The percent of patients with a restrictive mitral filling pattern, defined as an E/A-ratio>2 or E/A-ratio>1 with deceleration time of the E-wave <140 msec, dropped from 51% to 29% (p = 0.010). A dose-dependent effect was noted for reverse remodeling changes in LVEF (p <0.001) and LVESV (p = 0.026), with higher doses of sacubitril/valsartan leading to more reverse remodeling. Furthermore, both metrics of improved systolic (?LVEF, ?LVESV) and diastolic function (?E and ?A-wave velocity) correlated with functional improvement (reduction in NYHA-class, p-value all <0.05). The amount of RAS-blocker before (56 ± 32% of target dose) and after (58 ± 32% of target dose) switch to sacubitril/valsartan was similar (p = 0.820), indicating individual optimal dosing of sacubitril/valsartan. Furthermore, indicating that the incremental reverse remodeling was a resultant of the additive neprilysin inhibition.

Conclusion: Switching therapy in eligible HFrEF-patients from a RAS-blocker to sacubitril/valsartan induces dose-dependent beneficial reverse remodeling of both metrics of systolic and diastolic function.

P1046

Assessment of safe prescribing of common cardiac medications in final year undergraduate medical students.

SELINA Jarvis[1]; SHEBA Jarvis[2]
[1]*St Thomas' Hospital, Acute Medicine , London, United Kingdom*; [2]*Imperial College London, London, United Kingdom*

Background: Medication errors are a major concern with ˜50,000 medication related incidents reported by the National patient safety agency annually.1 The General

Medical Council has highlighted the urgent need for testing prescribing skills during medical school training.2 In hospital, poor prescribing will have not only safety implications but can affect time spent with patients since 19% of nursing time is already spent on medication tasks with increasing frequency of repeated interruptions such as clarification of prescriptions.3 Recently, it has been shown that medication errors pertaining to cardiac and diabetes medications are the most common.4

Purpose: To assess safe prescribing behaviours in final year medical students using clinical case examples after a pharmacist-led teaching session focused on cardiac and diabetes medications.

Methods: A senior pharmacist delivered a 1-hr teaching session with notes provided to final year medical students (1 month from sitting final medical examinations) with specific emphasis on cardiac medications followed by a safe prescribing test 24hrs later where students had full access to the British National Formulary.

Results: 188 students attended the course and sat the safe prescribing test utilising real hospital drug charts. The majority of students correctly documented allergy status with type of reaction and 80% prescribed drugs were transcribed into the correct sections. Common prescribing errors pertained to antocoagulation with low molecular weight heparin written incorrectly by 35.3% (e.g. wrong route, incorrect preparation or dose) as well as difficulties with prescribing warfarin. 48% of students inappropriately prescribed ACE inhibitors in patient scenarios involving renal dysfunction, dehydration or hypotension. Prescription of calcium channel blockers and diuretics were correct in 90% and 75% of students respectively. Finally, although there were no major issues with the prescription of oral antidiabetic agents, insulin errors were more common with incorrect spelling of insulin (6.8%), route of administration (8.7%) or timing i.e. with meals/bedtime (18.6%) were observed.

Conclusions: Despite a structured teaching session, senior medical students still struggle with commonly prescribing medications used in patients with common cardiac conditions such as heart failure with often coexist with diabetes. Safe prescribing at undergraduate level requires urgent attention. Intensive integration of safe prescribing at the earliest stage of medical training is essential and national standardised drug charts may help reduce error

P1047

Retroespective analysis of sildenafil/bosentan in type ii pulmonary hypertension (ph)

JM Jose Maria Vietez Florez[1]; S Del Prado[1]; G Alonso[1]; M Abellas-Sequeiros[1]; A Lorente[1]; S Hernandez[1]; M Castillo[1]; E Gonzalez[1]; JL Zamorano[1]
[1]*University Hospital Ramon y Cajal de Madrid, Cardiology, Madrid, Spain*

Background: Pulmonary hypertension (PH) is a common complication of left heart disease (LHD), however there are no evidence to support the use of specific treatment due in part to the lack of studies. Up to the present, controversy exists over the benefit of pulmonary artery vasodilators, but recently, SIOVAC trial showed negative

Purpose: To analyse the clinical benefit of pulmonary artery vasodilators in PH-LHD a consecutive series of patients diagnosed of severe PH by echocardiogram in a tertiary hospital was evaluated.

Results: 50 PH-LHD patients were retrospectively compared: 20 patients were treated with arterial vasodilators, 17 were on sildenafil and 3 on bosentan treatment; 30 patients were treated with standard treatment. The follow up was 39 months ($\pm$21,57). 64% were women, median age was 73.9 $\pm$ 7.37 .

Only two etiologies of PH-LHD were included: it was valve disease in 65% in treatment group vs 60% in control group, without significant differences (p = 0. 8). Heart failure with depressed ejection fraction was other etiology.

The systolic pulmonary artery pressure was similar in two groups (69.01 $\pm$ 14.2 vs 62.7 $\pm$ 13.3, p = 0.133). There were no differences in E/e' index, EF nor auricular volume. Pulmonary artery vasodilators group had worst renal function (42,6 $\pm$ 15,6 vs 61,9 $\pm$ 21,2, p = 0,001).

Eleven patients died (55%) in the group of sildenafil/bosentan compared with three (10%) in the control group (p= 0,001). Cardiovascular mortality was significantly higher in the treatment group compared with control group (35% 6.7%, p= 0.011). Median hospitalization days due to worsening of heart failure was 4 (range 0-10) and 0,5 (0-7) for the groups of treatment and control respectively (p= 0,004).

Conclusions: Treatment with pulmonary vasodilator (sildenafilo/bosentan) in PH-LHD was associated with all mortality causes, including cardiovascular mortality, and hospitalizations.

These results are consistent with recently presented SIOVAC trial who shows the increasing mortality PH-LHD treated with pulmonary artery vasodilators. More studies in order to define appropriate treatment are needed.

P1048

Sacubitril-Valsartan: real-world single-centre experience.

HMC Herminio Morillas Climent[1]; AVL Alvaro Vicedo Lopez[1]; JSM Julia Seller Moya[1]; EAT Edgard Alania Torres[1]; EGJ Emilio Galcera Jornet[1]; ALR Ainhoa Larumbe Rodriguez[1]; CNP Carlos Nunez Piles[2]; AVM Alfonso Valle Munoz[1]
[1]*Denia Marina Salud Hospital, Alicante, Spain*; [2]*University Hospital Doctor Peset, Valencia, Spain*

Background: Sacubitril-Valsartan clinical trials results are remarkable. However, real world data are scarce, mainly due to a short postcommercialization observation period.

Purpose: The aim of our study is to describe clinical use of Sacubitril-Valsartan in real world practice, taking into account its efficacy, tolerance, dose used and impact on different imaging and laboratory markers.

Methods: We performed a retrospective evaluation of Sacubitril-Valsartan prescriptions from the first drug prescription until the 10th January 2018. Inclusion criteria was any sustained prescription of the drug by Cardiology and/or General Practitioners. Patients were excluded if no data were available, prescription had an inadequate indication or if the drug was stopped before 2 months of follow-up without a clear reason.

We collected baseline characteristics of the patients, major adverse cardiovascular events, data of tolerance and information regarding imaging parameters and laboratory markers.

Statistical analysis was performed using SPSS Software for MAC, 20.0 version. Cualitative and cuantitative values were described as percentage and median +/- standard deviation. Changes in cuantitative values over time were analyzed using T-Test for paired samples.

Results: From the 19th October 2016 to the 8th January 2018, 114 patients were included. 18 patients were excluded from final analysis (3 no data available, 2 inadequate indication for prescription, 13 premature interruption).

96 patients remained. 60% of them were men. Mean age was 69 years. 25% were diabetic, 41% hypertensive and 52% received lipid lowering drugs. Ischaemic heart disease was the main cause of heart failure (59%). 60% of the patients reported NYHA functional class II symptoms, 33% NYHA III and 7% NYHA I. Baseline treatment was optimal.

During a medium follow-up of 203 +/- 101 days, 8 patients (8,4%) were admitted to the hospital due to heart failure and 4 patients died (all cardiovascular deaths). Sacubitril-Valsartan was withdrawn in 8 patients (8,4%) because of symptomatic hypotension. 3 patients complained about headache (2 possibly related to hypotension). Only 1 case of hyperkaliemia and no acute renal failure was reported. 3 patients referred economic issues and stopped medication. At the end of the follow-up, 87,5% of the patients continued taking the treatment, the majority of them at low doses (24/26 mg, 58%).

Pretreatment LVEF was 30,37%. During follow-up, LVEF increased to 34,47% (p 0,001). NTproBNP decreased from 3557 to 3019 pg/ml, with a trend towards significant reduction in idiopathic dilated cardiomyopathy subgroup (3787 vs 2099 pg/ml, p = 0,08). Ca125 levels decreased non-significantly over time (42,96 vs 29,17 pg/ml, p = 0,098).

Conclusion: Sacubitril-Valsartan prescription for heart failure with reduced ejection fraction is increasing in real world practice. Although tolerance is good, it is difficult to reach high dose prescriptions, mainly due to low blood pressure.

P1049

Association of body surface area with target dose guideline-directed therapy in an international cohort of patients with heart failure

T-H K Tiew-Hwa Katherine Teng[1]; W T Tay[2]; N Luo[3]; L B Cooper[4]; J Tromp[5]; W Kraus[3]; D Whellan[3]; C Chandramouli[2]; I Pina[6]; J J L Yap[7]; C M O'connor[4]; I Anand[8]; R Mentz[3]; C S P Lam[9]
[1]*National Heart Centre Singapore; School of Population Health, University of Western Australia, Singapore, Singapore*; [2]*National Heart Centre Singapore, National Heart Research Institute Singapore, Singapore, Singapore*; [3]*Duke Clinical Research Institute, Durham, United States of America*; [4]*Inova Heart & Vascular Institute, Heart Failure/Transplant, Falls Church, Virginia, United States of America*; [5]*University Medical Center Groningen, Groningen, Netherlands*; [6]*Montefiore Medical Center, Dept. of Medicine (Cardiology), Bronx, NY, United States of America*; [7]*National Heart Centre Singapore, Singapore, Singapore*; [8]*University of Minnesota, Veterans Affairs Medical Center, Minneapolis, United States of America*; [9]*University Medical Center Groningen; Duke-NUS Medical School; National Heart Centre Singapore, Singapore, Singapore*

On behalf of: ASIAN-HF and HF-ACTION

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Background: For patients with heart failure and reduced ejection fraction (HFrEF), practice guidelines advocate for evidence-based HF medications at optimal

doses(GDD). In clinical practice, many physicians may believe that Asian patients need reduced dosages of medications studied in clinical trials due to their smaller body size and possible heightened sensitivity to cardiovascular drugs.
Aims: (1) To describe the usage patterns of ACE-inhibitor (ACEi) or angiotensin-receptor blockers (ARB) and ß-blockers in Asia vs. U.S./Canada/France; (2) to evaluate the association of body surface area (BSA) with prescribed doses of ACEi and ß-blockers; (3) to examine if the association is mediated by country of origin or ethnicity.
Methods: We compared patients with chronic HFrEF (EF = 35%) from the ASIAN-HF and HF-ACTION multinational studies for differences in dosing patterns of ACEi and ß-blockers. Drug doses at baseline were standardized by using lisinopril equivalents for ACEi and carvedilol equivalents for ß-blockers. Regression models were used to examine the association of BSA with maximum prescribed doses (as a continuous variable) and attainment of GDD (Yes/No) for ACEi (defined as = 20mg lisinopril equivalents) and ß-blockers (= 50mg carvedilol equivalents), adjusting for differences in baseline characteristics.
Results: Among a combined cohort of 6,683 patients with HFrEF (mean age 59 ± 13 years, 23% women), two-thirds (4,543) were Asian and one-third (2,140) were non-Asian from North America/Europe. Asian (vs. non-Asian) patients had a lower BSA (1.74 ± 0.22 vs. 2.11 ± 0.29 m2). Usage patterns of HF medications varied considerably across geographical regions. Compared to North America/Europe, patients in Asia were less likely to be prescribed ACEi/ARBs (76% vs 94%) and ß-blockers (78% vs 95%). Median lisinopril and carvedilol equivalents in Asians were half of those in non-Asians: 10 (IQR 5-20) mg vs. 20 (10-40) mg and 12.5 (6.25-25) mg vs. 25 (13-50) mg, respectively.
BSA was associated with crude beta-coefficients of 14.43 (SE 0.89) for maximum prescribed doses for ACEi and 21.51 (SE 0.90) for ß-blockers ($p < 0.001$), respectively. Adjusted for age, sex and NYHA class, BSA (per unit increment) was associated with OR 5.12 (95% CI 4.09-6.41) and OR 9.92 (95% CI 7.90-12.47) for attainment of GDD for ACEi and ß-blockers. The association of BSA with attainment of GDD for ACEi and ß-blockers persisted on additional multivariable adjustment ($p = 0.016$). Notably, geographic region modified the association of BSA ($p_{interaction} = 0.006$) with attainment of GDD for ACEi (but not ß-blockers), such that patients in US, Canada, South Asia had higher odds of attaining GDD (2.3-3.8) but not France, East Asia and Southeast Asia.
Conclusions: Our multinational data suggest that both geographic region and body size are related to dosing patterns of ACEi and ß-blockers in HFrEF. Larger body size is associated with higher doses of ACEi in some regions, but not all.

P1050

What are the predictors of positive response to trimetazidine in patients with severe chronic heart failure with reduced left ventricular ejection fraction?

M Michal Bohdan[1]; I Stopczynska[1]; P Wisniewski[2]; A Kowalczys[1]; J Morys[1]; A Frankiewicz[1]; P Niedoszytko[3]; W Sobiczewski[1]; M Rafalowska[1]; M Gruchala[1]
[1]Medical University of Gdansk, 1st Dept of Cardiology, Gdansk, Poland; *[2]Medical University of Gdansk, Department of Endocrinology and Internal Diseases, Gdansk, Poland*; *[3]Medical University of Gdansk, Department of Rehabilitation Medicine, Gdansk, Poland*

Background: Trimetazidine (TMZ) is an anti-anginal agent that modulates cardiac metabolism but its use in heart failure still remains controversial. The data concerning the effects of TMZ in heart failure with reduced ejection fraction (HFrEF) were derived mainly from retrospective studies. The aim of the study was to evaluate the effects of TMZ on exercise capacity, left ventricular ejection fraction (LVEF), NYHA class, mortality and quality of life in stable patients with severe HFrEF.
Methods: Forty-five patients aged 58.2 ± 10.6 years with stable severe HFrEF treated with optimal medical therapy were randomised in a prospective, single-centre, open-label, cross-over study to trimetazidine (35 mg b.i.d.) on top of standard medical therapy or standard pharmacotherapy for two periods of 30 days and one period of 6 months. Patients were randomised to two groups: Group I - standard pharmacotherapy and additionally TMZ 35mg b.i.d. for 1 month, then standard pharmacotherapy without TMZ for the following 1 month and once again TMZ 35mg b.i.d. for 6 months; Group II - standard pharmacotherapy without TMZ for 1 month, then standard pharmacotherapy and additionally TMZ 35mg b.i.d. for the following 1 month and once again standard pharmacotherapy without TMZ for 6 months. Initially and at the end of each period all patients underwent: cardiopulmonary stress testing, six-minute walk test (6MWT), 2D-echocardiography, symptom severity in NYHA class and quality of life assessment.
Results: Etiology of HFrEF was ischaemic in 66.6% of patients. There were 20% of responders to TMZ treatment (n = 9) in terms of LVEF improvement of = 5%. We found that patients who had a rise in LVEF = 5% during TMZ treatment had significantly lower initial BNP (262.3 ± 282.7 pg/ml vs. 714.1 ± 653.9 pg/ml, $p < 0.05$), lower 1-year and 2-year risk of death (3.6 ± 4.5% vs. 6.9 ± 5.3%; $p < 0.05$ and 6.9 ± 7.9% vs. 13.2 ± 9.7%, $p < 0.05$, respectively) and higher predicted life expectancy assessed in Seattle Heart Failure Model (15.5 ± 7.3 years vs. 10.7 ± 6.0 years, $p < 0.05$) in comparison to the patients without significant rise in LVEF during TMZ treatment (n = 36). Both after 1 month and 6 month of TMZ treatment, however, no significant changes were observed in both groups with regards to peak VO2 uptake, 6MWT, left ventricular ejection fraction or quality of life. In addition, TMZ had no effect on mortality or cardiovascular events (odds ratio: 0.5, 95% CI 0.2-1.2, NS).
Conclusions: Patients with less advanced HFrEF may have a better response to TMZ treatment with regards to left ventricular systolic function.

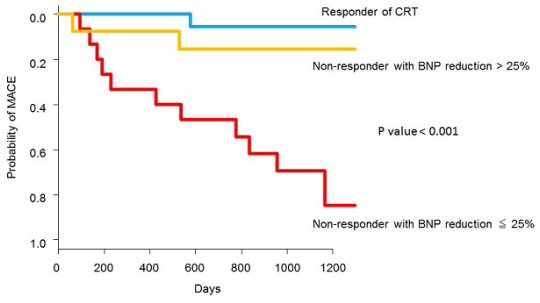
P1051

Lack of brain natriuretic peptide reduction at 30-day significantly predicts worse clinical outcomes in non-responders of cardiac resynchronization therapy

S Matsumoto[1]; YI Ikari[1]
[1]Tokai University School of Medicine, Cardiology department, Kanagawa, Japan

Backgrounds: Cardiac resynchronization therapy (CRT) is beneficial for heart failure with reduced ejection fraction accompanied by severe dyssynchrony, and responders of CRT obtain improved clinical outcomes. However, approximately 60% of patients who undergo CRT do not obtain left ventricular reverse remodeling, i.e. non-responder of CRT, and further decision criteria for additional interventions are needed. Brain natriuretic peptide (BNP) is a useful marker for management of heart failure, while associations between BNP transition and clinical outcomes after CRT were not well-known.
Purpose: We investigated long-term clinical outcomes of CRT and evaluated whether short-term BNP transition was available for the management of non-responders.
Methods: Between 2011 and 2015, we enrolled consecutive 80 patients who underwent CRT and evaluated transition of BNP levels from baseline to 30-day after implantation. In the present study, responder was defined as a reduction of left ventricular systolic volume > 10% after 6-month, and major adverse cardiac events (MACE) was all-cause death, hospitalization of heart failure, and ventricular tachycardia or fibrillation.
Results: Of consecutive 80 CRT implantations, non-responders were 35 (43.8%). During mean 3.1-year follow up, although the incidence of MACE in responders was only 2.2%, the incidence in non-responders achieved 54.3%. When focusing on the 35 non-responders, lack of BNP reduction above 25% from baseline to 30-day was significantly associated with frequent occurrence of MACE (Figure), whereas baseline BNP levels were not significantly associated with clinical outcomes after CRT. Lack of BNP reduction at 30-day was significantly associated with the presence of moderate-severe mitral regurgitation after CRT (P value = 0.02).
Conclusions: Lack of BNP reduction at 30-day significantly predicts worse clinical outcomes in non-responders of CRT and significantly associated with remaining mitral regurgitation. Early next treatment step should be considered in these patients.

Figure. Logrank test about MACE



Clinical outcomes after CRT

P1053

PR-prolongation and long-term mortality in patients with congestive heart failure treated with cardiac resynchronization therapy

AM Soldatova[1]; VA Kuznetsov[1]; VA Kuznetsov[1]; TN Enina[1]; TN Enina[1]; SM Dyachkov[1]; SM Dyachkov[1]
[1]Tyumen Cardiology Research center, Tyumen, Russian Federation

Background: Female gender, left bundle branch block (LBBB), QRS width were good predictors of cardiac resynchronization therapy (CRT) response and outcome.

Recent data indicate that PR prolongation was associated with increased risk for mortality in general population.
Aim: To analyze the relationship between clinical, functional parameters, PR-prolongation and long-term mortality in patients with congestive heart failure (CHF) treated with CRT.
Methods: 85 CRT patients (mean age 55.1 ± 9.9 years, 81.2% men) with CHF (53% ischemic and 47% non-ischemic etiology) II-IV NYHA functional class were enrolled. At baseline, 1month, 3 months and each 6 months after implantation we evaluated clinical and echocardiographic parameters. Median of follow-up period was 21.0[5.5;44.0] months. Patients were stratified according to PR width: I group - normal PR (<200 ms; n = 52) and II group - prolonged PR (= 200 ms; n = 33).
Results: At baseline groups didn't differ in main clinical and functional characteristics. In the II group history of myocardial infarction (MI) was observed more frequently (p = 0.005), left ventricular ejection fraction (LVEF) was lower (p = 0.032). Also in the II group there was a tendency to higher percentage of male gender patients (p = 0.058) and higher left ventricular end-systolic volume (LVESV) (p = 0.076). Presence of LBBB and width of QRS complex didn't differ between groups. The survival rates were 76.1% in the I group and 26.9% in the II group (Log-rank test p <0.001). Cox regression showed that LVESV (HR 1.012; 95% CI 1.006-1.018; p <0.001), PR interval (HR 1.012; 95% CI 1.005-1.020; p = 0.001) and presence of MI (HR 1.116; 95% CI 3.190-6.520; p = 0.001) were associated with long-term mortality. In ROC-analysis PR interval >197.5 ms with sensivity 63.2% and specificity 80.9% predicted long-term mortality, for LVESV - >168.4 ml with 73.7% and 74.5% respectively.
Conclusion: In patients with CHF treated with CRT LVESV, PR interval and history of MI can be used as independent predictors of long-term mortality but not LBBB and QRS width.

P1054
Increasing exercise capacity in the first year after implantation of a cf- left ventricular assist device

SEA Felix[1]; MIF Oerlemans[1]; LW Van Laake[1]; FZ Ramjankhan[2]; MP Buijsrogge[2]; JH Kirkels[1]; FW Asselbergs[1]; N De Jonge[1]
[1]University Medical Center Utrecht, Cardiology, Utrecht, Netherlands; [2]University Medical Center Utrecht, Cardiothoracic surgery, Utrecht, Netherlands

Background: Mechanical circulatory support (MCS) by a continuous flow left ventricular assist device (cf-LVAD) has shown to improve survival and quality of life in selected patients with end-stage heart failure, as a bridge to transplantation or as destination therapy. Furthermore, in previously performed studies in small numbers of patients, exercise tolerance of patients on cf-LVAD support was increased after cf-LVAD implantation, as compared to the pre-operative situation, though did not increase after the first few months after the implantation. Because of shortage of donor hearts, the number of patients on a cf-LVAD as destination therapy is increasing, thereby having MCS for a longer term. Especially in this category of patients, where functional capacity and reintegration into the society is of importance, insight into the exercise tolerance is essential.
Purpose: To give insight in the sequential exercise tolerance of patients in the first year after cf-LVAD implantation in a large cohort of patients.
Methods: 99 cf-LVAD-patients (69% male, mean age 49.5 ± 5,0 years) underwent a cardiopulmonary exercise test (CPET) at 3-6 and 12 months after implantation. In all patients a respiratory exchange ratio (RER) > 1,05 was seen, indicating satisfactory effort during the test.
The results of both moments of CPET were analyzed in SPSS ® with two-tailed paired test or non-parametric test if not normally distributed. Percentage of predicted values was calculated according to Jones.
Results: Power increased from 105 ± 36 W to 115 ± 41 W (p = 0.000), peak VO2 significantly improved both uncorrected and corrected for weight from 1.27 ± 0.43 L/min (53 ± 12% predicted) to 1.36 ± 0.47 L/min (57 ± 13% predicted) (p = 0.000) and 16.5 ± 5.0 ml/kg/min (52 ± 12% predicted) to 17.3 ± 5.6 ml/kg/min (55 ± 13% predicted) (p = 0.004) respectively, where respiratory quotient, heart rate and EqCO2 did not differ.
Conclusion: In this large cohort of patients, a further improvement in peak-VO2 levels at 12 months was seen compared to 3-6 months after cf-LVAD implantation. This is important information for the growing group of patients on long term cf-LVAD support.

P1055
Comparison of Echocardiographic Parameters influenced by

B Bernd Schulze[1]; B Fujita[1]; KT Puhlmann[1]; U Schulz[1]; J Gummert[1]; L Paluszkiewicz[1]
[1]Heart and Diabetes Center NRW, Clinic for Thoracic and Cardiovascular Surgery, Bad Oeynhausen, Germany

Background: Detection of Acute cellular rejection (ACR) still remains a challenge for clinical echocardiography. Our objective was to evaluate and compare various echocardio-graphic parameters identifying patients with biopsy-proven ACR after heart transplantation.
Methods: 204 consecutive transplant recipients were prospectively examined shortly after endomyocardial biopsy (EMB) blinded to the Results. Various conventional and deformation derived parameters of the left and right ventricle were analysed.
Results: ACR-Grade 0R was found in 135 (67%), grade 1R in 52 (26%) and grade 2R in 15 (7%) patients. Comparing group G0R with G1/2 significant differencies were increase of septal (GOR 12 (11-13) vs. G1/2R 13 (11-14), p < 0,01) and posterior wall thickness ((11 (11-12) vs. 12 (12-13), p < 0,001) , tricuspid regurgitation equal or greater than mild (25,5% vs. 41,8%, p = 0,02), presence of pericardial effusion (54% vs. 68,7%, p = 0,046), higher E/e' at the lateral mitral annulus (8 (6-10) vs. 9 (7-12), p = 0,03) , decrease of the TDI systolic velocities at the lateral mitral (10 (8,8-11,2) vs. 9,7 (8,1-10,7), p = 0,049) and tricuspid annuli (10,5 (9,3-11,8) vs. 10 (8,3-11,2), p = 0,02), increase of RV-Tei index (0,23 (0,15-0,31) vs. 0,28 (0,12-0,44), p = 0,047) and decrease of GLS-LV (-20,8 (17,6-24) vs. -19,5 (15,9-23,2), p = 0,01 and LS-RV (-22,9 (20-26,8) vs. -21,3 (16-26,6), p = 0,03. Combined cut-off analysis of the GLS-LV, LS-RV, twist, apical rotation and rotation rate resulted in a negative predictive value (NPV) of 83.3% and positive predictive value (PPV) of 79.3%. Combined analysis of GLS-LV and LS-RV resulted in a high NPV of 97%, but a low PPV of 11.7% for detection of G2 rejection.
Conclusion: Speckle-tracking of LV/RV had the highest NPV/PPV of all significant parameters for ACR enabling clinical decision making to reduce routinely performed EMB.

P1056
Heart failure patients with sleep-disordered breathing: dynamics of this highly common comorbidty before and after heart transplantation

H Fox[1]; T Bitter[1]; D Horstkotte[1]; O Oldenburg[1]
[1]Herz- und Diabeteszentrum NRW, Ruhr-Universität Bochum, Clinic for Cardiology, Bad Oeynhausen, Germany

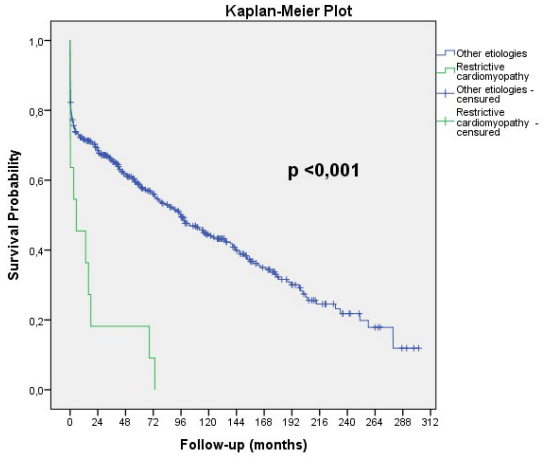
Background: The comorbidity of sleep-disordered breathing (SDB) is known to be highly common in heart failure (HF) patents and SDB is associated with deterioration of quality of life as well as with increased morbidity and mortality in HF. Details on SDB interactions with HF and vice versa are widely unknown, because SDB and HF share many symptoms and measureable parameters. Therefore the rationale of our study was to investigate the interplay of SDB and HF in patients listed for heart transplantation (HTx) to analyze SDB characteristics in the same subject initially presenting with end-stage HF and subsequently with normal cardiac function after HTx.
Methods and Results: We included 80 HF patients listed for HTx for this study (left ventricular systolic ejection fraction 20 ± 19.5 %, 83 % male, BNP 420 ± 755 pg/ml), who were examined with cardiorespiratory polygraphy, revealing a SDB prevalence of 94.6 % (AHI > 5/h). In addition, 83.3 % of the patients had moderate to severe SDB (AHI = 15/h), mean apnea hypopnea index (AHI) before HTx was 29.6 ± 18.8 /h which decreased to 12.7 ± 13.1 /h after HTx (p < 0.05).
Conclusion: The model of HTx demonstrates the close and tight interplay of HF and SDB, with SDB representing a very common comorbidity in end-stage HF patients listed for HTx. Further studies are needed to elucidate the interdependent interaction of HF and SDB to allow successful therapy approaches for the future.

P1057
Heart transplantation in patients with restrictive cardiomyopathy: a single center experience.

A Antonio Grande-Trillo[1]; L Perez-Gomez[1]; D Rangel-Sousa[1]; JM Sobrino-Marquez[1]; E Lage-Galle[1]
[1]University Hospital of Virgen del Rocio, Seville, Spain

Introduction: Restrictive Cardiomyopathy (RCM), formed by a group of heterogeneous pathologies, is poorly represented in heart transplantation (HT) series and has been related to worse prognosis.
Methods: Retrospective study that includes patients with RCM who underwent to HT in our center (1992-2017). We analyzed RCM etiology and prognosis in comparison with the rest of our series.
Results: 11 patients (42 ± 16 years old; 82% women) with RCM were evaluated (2.5 % of our HT series). The RCM etiology was classified as follows: light chain amyloidosis (AL) (28%, 3 patients), transthyretin related amyloidosis (ATTR) (9%, 1 patient), polyglucosan storage disease (9%, 1 patient) and idiopathic RCM (64%, 7 patients). There were no significant differences in pre-transplant hemodynamic study (right heart catheterism) or liver test parameters (bilirubin, AST and ALT) between RCM group and the rest of the HT series. Primary graft failure was more frequent in RCM group without statistical signification (36% vs 16% respectively; p = 0.09). 5 RCM patients (45%) died during post-HT hospitalization: 4 due to primary graft

failure and 1 due to sepsis. The rest of the sample (n = 6) also died during the follow up: 4 deaths were related to progression of the underlying disease (AL or ATTR) at 5, 16, 18 and 72 months after HT; one patient voluntary interrupted immunosuppressive treatment, dying 14 months after HT. Last patient died due to graft vascular disease at 60 months after HT. The comparative survival curve is shown in the graph.
Conclusions: RCM has worse prognosis in our study. These results, which are comparable to others series, are mainly related to a high in-hospital mortality. In addition, those cases due to amyloidosis have unfavorable evolution because of the underlying disease itself. These data highlight that a careful selection of patients is mandatory for HT evaluation in patients with RCM.



Comparative survival

P1058

Frailty prevalence in patients listed for heart transplantation

A Ayesta Lopez[1]; MJ Valero Masa[1]; MT Vidan Astiz[1]; I Martin De Miguel[1]; I Sousa Casasnovas[1]; E Zatarain Nicolas[1]; P Navas Tejedor[1]; C Ortiz Bautista[1]; J Yanez[1]; A Villa Arranz[1]; F Fernandez- Aviles[1]; M Martinez- Selles[1]
[1]University Hospital Gregorio Maranon, Madrid, Spain

Background and Aim: Frailty (F) reflects a state of decreased physiological reserve. Its prevalence among patients with heart failure (HF) is 20-50%. Frailty assesment is recommended before listing for heart transplantatio (HT). Our aim was to analyze the prevalence of F, depression (D), and cognitive impairment (CI) in a consecutive cohort of younger patients with advanced HF listed for HT.
Methods: The FELICITAR registry is a prospective observational study that includes adults listed for HT in Madrid since January 2017. In the present analysis we include patients from our center. Data were collected when listed. F was assessed using the Fried Frailty Phenotype (FFP) (frail = 3/5); to assess D we used the PHQ9 scale (= 5); and Montreal Cognitive Assessment (MoCA) test was used to assess CI (CI < 26).
Results: A total of 22 patients were listed for HT in our center during 2017, 15 (68.2 %) were included in the FELICITAR. 1 patient (6.67 %) was included in emergency list 1, and the rest in elective list.
Most of the patients were men (60%), were 50 ± 17 years old and had a low rate of comorbidities (Charlson score 2.2 ± 0.6). Most of them were in NYHA class III (60.7%) with a LVEF of 31 ± 15 and generally well treated (Beta blockers 60%, ACEI/ARA2/ARNI 66.7%, Ivabradine 13.7%, ICD 66.7%, CRT 26.7%). There were several causes for HF (ischemic 6.7%, valvular 20%, dilated 20%, congenital 13.3% and other 40%). 4 patients (26.7%) were frail (FPP score of 1.5 ± 1.5) , 6 (40%) had any degree of D (PHQ-9 score 7 ± 6.9) and 3 (20%) had CI (MoCA 26.9 ± 2.5).
Conclusions: The prevalence of F in patients listed for HT is relatively high. The study of its influence before and after HT could contribute to a better understanding of the characteristics of the optimal candidate for HT.

P1059

Neurohormonal blockage score - the higher the better?

D David Cabrita Roque[1]; M Santos[1]; J Augusto[1]; J Baltazar Ferreira[1]; D Candeias Faria[1]; J Simoes[1]; A Oliveira Soares[1]; C Morais[1]
[1]Hospital Prof Fernando da Fonseca EPE, Cardiology, Amadora, Portugal

Background: Current treatment of HF is based on the blockage of the named neuro-hormonal response, and guidelines recommend up-titration of this drugs to its maximum dose whenever possible according to patient tolerance: angiotensin-converting-enzyme inhibitors/angiotensin II receptor blockers (ACEi/ARB), beta-blockers (BB), mineralocorticoid receptor antagonist (MRA).
Purpose: We aim to evaluate, in patients admitted for acute heart failure, the relation between a neuro-hormonal blockage score (NHB) with in-hospital outcomes and the same neuro-hormonal blockage score at discharge with outcomes at 1 year follow-up.
Methods: Retrospective study of 258 consecutive patients admitted in the emergency department for ADHF, defined by the presence of = 2 signs or symptons of heart Failure. The HF profile was assessed as according to the ESC guidelines. We evaluate the drug therapy patients had before admission, during hospitalization and at discharge, and developed a NHB (ACEIs/ARB, BB and MRA) score, based on the percentage of their maximum dose; the higher the value, in theory, the greater the blockage power in the patient.
Results: We evaluated 258 patients with ADHF (45.7% male, mean age of 74.6 ± 16.6 years). Mean NHB score at admission according to the drugs and their doses was 61.1 ± 3.2%. Patients who died in-hospital had significantly lower NHB scores at admission (mean 38.7 vs 63.1%, p = 0.019) and during hospitalization (mean 45.3 vs 76.3%, p = 0.003). NHB scores at admission and during hospitalization were not significantly associated with length of stay (p = 0.802 and p = 0.884, respectively), hyperkaliemia (p = 0.780 and p = 0.390, respectively), peak heart rate during hospitalization (p = 0.204 and p = 0.731, respectively), peak systolic blood pressure (p = 0.141 and p = 0.487, respectively) and nadir systolic blood pressure during hospitalization (p = 0.113 and p = 0.277, respectively). NHB at admission was not significantly associated with nadir eGFR during hospitalization (p = 0.944), but higher NHB during hospitalization correlated with higher eGFR (r = 0.370, p = 0.001).
At discharge, mean NHB score was 66.6 ± 3.2%. Discharge NHB score was not significantly associated with readmissions at 6-month (p = 0.969), 9-month (p = 0.574) or 12-month follow-up (p = 0.117) or all-cause mortality at 12 months after discharge (p = 0.222).
Conclusion: Calculate the NHB score at hospital admission and during hospitalization can be a useful tool to predict intra-hospital mortality in patients admitted for acute decompensated heart failure, and is a wake up call for the importance of progressing, whenever possible, in the dose of heart failure drugs until the maximum dose tolerated by the patient.

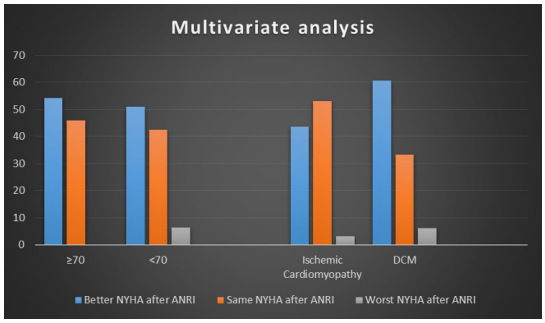
P1060

Sacubitril/valsartan treatment and its impact over functional class: does the age and the heart failure aetiology matter?

M Singh[1]; M Fernandez-De-Sanmamed-Giron[1]; M Galvan Ruiz[1]; R Montiel Quintero[1]; M Groba-Marco[1]; E Perez-Nogales[2]; JM Medina Gil[2]; E Caballero Dorta[1]; V Quevedo Nelson[1]; M Lopez Perez[1]; A Antonio Garcia Quintana[1]
[1]University Hospital De Gran Canaria "Dr. Negrin", Las Palmas de Gran Canaria, Spain; [2]University Hospital Insular of Gran Canaria, Las Palmas De Gran Canaria, Spain

Background: Despite the advances in optimal medical treatment, Heart Failure with reduced Ejection Fraction (HFrEF) is an important cause of cardiovascular death. Sacubitril/ Valsartan (SV), as an Angiotensin Neprilysin Receptor Inhibitor (ANRI), has been a milestone in HFrEF management, and has shown improved cardiovascular outcomes (PARADIGM-HF), but further real-life data is necessary in order to evaluate its role in daily clinical practice.
Purpose: To analyse the evolution of the HFrEF symptoms, according to the New York Heart Association (NYHA) classification, and its relation with the age and HFrEF aetiology, in patients with HFrEF after ANRI treatment in a real-life study.
Methods: Ambispective registry of consecutive 106 patients with HFrEF, from two hospitals, under treatment with ANRI initiated during a period of 14 months, from October 2016 to December 2017, was performed. After initiating the ANRI at dose of 24/26mg or 49/51mg, the patients were followed-up with clinical and analytical assessment with an interval of 1-3 months. Titration to the maximum dose, 97/103mg, was performed if it was feasible. The symptoms were evaluated using NYHA classification by the treating physician. Multivariate statistical analysis was later performed.
Results: Our population (n = 106) had a mean age of 63.5 ± 11.68 years, 69% were men and 31% were women. Baseline NYHA functional class was 49.1% NYHA II, 44.3% NYHA III and 6% without NYHA evaluation. HFrEF aetiology was classified in 4 groups: 49,1% had Ischemic Cardiomyopathy (ICM), 39,65% had idiopathic Dilated Myocardiopathy (DCM), 3,8% had Chemotherapy related HFrEF, 7.45% miscellaneous (genetics, valvular). 23.07% of the cohort was on 24/26mg dose, 34.6% on 49/51mg dose, 27.88% had the maximum dose and the rest had intermediate doses. After ANRI treatment the clinical assessment showed a symptomatic evolution to 22% of NYHA I, 66% of NYHA II, 12% NYHA III. In patients with < 70 years after ANRI 27% had NYHA I functional class, in front of only 12% of = 70 years aged. In patients with = 70 years, 54.17% improve their NYHA class, 45.83% maintain the same NYHA, and none of them worsened. Whereas in patients

with < 70 years 51.06% improve the NYHA, 42.55% maintain the same one and 6.38% worsened their NYHA. Related to the HFrEF aetiology, 43.75% patients with ICM had a better NYHA after treatment, 53.13% maintain the same one and 3.13% worsen their NYHA, while in patients with DCM up to 60.61% of the patients improve their NYHA class, only 33.33% maintain the same and 6.06% had a worse NYHA.
Conclusions: Sacubitril/Valsartan has shown a significant improvement in the functional class of our patients. Aged patients seem to have better symptomatic evolution when compared to the younger ones, same as patients with DCM when compared to ICM as the cause of HFrEF. Younger patients achieve NYHA class I more frequently than older patients.



Change of NYHA for age and aetiology

P1061
Evaluation of high sensitivity C-reactive protein in vericiguat-treated patients with heart failure with reduced ejection fraction

F Kramer[1]; S Voss[2]; B-W Igl[3]; J Butler[4]; CSP Lam[5]; AP Maggioni[6]; L Roessig[7]; SJ Shah[8]; JA Spertus[9]; B Pieske[10]
[1]Bayer AG, Experimental Medicine CV/HEM, Wuppertal, Germany; *[2]Chrestos Concept GmbH & Co. KG, Essen, Germany*; *[3]Bayer AG, Research & Clinical Sciences Statistics, Berlin, Germany*; *[4]Stony Brook University, Division of Cardiology, Stony Brook, New York, United States of America*; *[5]Duke-NUS and National Heart Centre, 169857, Singapore*; *[6]Italian Association of Hospital Cardiologists (ANMCO) Research Center, Florence, Italy*; *[7]Bayer AG, Clinical Development, Wuppertal, Germany*; *[8]Northwestern University Feinberg School of Medicine, Division of Cardiology, Department of Medicine, Chicago, Illinois, United States of America*; *[9]St. Luke's Mid America Heart Institute, Kansas City, United States of America*; *[10]Charité - Universitätsmedizin Berlin, Department of Internal Medicine and Cardiology, Berlin, Germany*

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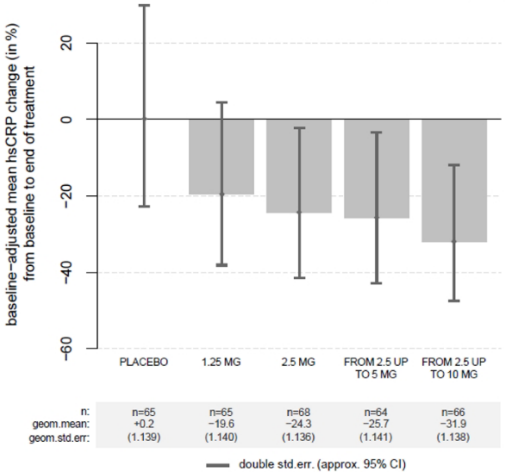
Background: Endothelial inflammation plays a key role in the development and progression of heart failure (HF) regardless of ejection fraction (EF), in part by suppressing downstream cyclic guanosine monophosphate (cGMP) signalling. Stimulation of guanylate cyclase (GC) may restore cGMP signalling, even in the presence of inflammation. We examined the effect of vericiguat, a soluble GC stimulator in development for HF, on high-sensitivity C-reactive protein (hsCRP), an established marker of inflammation, and prognosis in cardiovascular disease.
Methods: Circulating hsCRP was measured in the SOCRATES-REDUCED trial (NCT01951625), a 12-week, randomised, placebo-controlled, double-blind, dose-finding phase 2 study of vericiguat 1.25, 2.5, 5 and 10 mg once daily in patients with HF with reduced EF (HFrEF). Changes from baseline within each treatment arm were used to generate a linear mixed model and were adjusted for baseline hsCRP.
Results: In total, 328 of 456 randomised patients with available hsCRP values at baseline and week 12 were included (placebo [n = 65], vericiguat 1.25 mg [n = 65], 2.5 mg [n = 68], 2.5-5 mg [n = 64], and 2.5-10 mg [n = 66]). Exclusions were mainly due to protocol deviations. Overall median hsCRP was 3.68 mg/L (interquartile range: 1.41-8.41 mg/L) at baseline. Observed mean %-changes (geometric SD) from baseline were −0.5 (3.8), −26.7 (3.3), −23.2 (3.8), −26.7 (3.0) and −28.0 (3.1) for placebo, vericiguat 1.25, 2.5, 2.5-5 and 2.5-10 mg, respectively. After adjusting for baseline hsCRP, a dose-dependent treatment effect was revealed with a mean %-change in hsCRP of 0.2 for placebo, and −19.6, −24.3, −25.7, and −31.9 for increasing vericiguat doses [Figure]. This model indicated a significantly greater reduction in hsCRP in the highest vericiguat dose group of 2.5-10 mg relative to placebo (−31.9% vs 0.2%, respectively; p = 0.016). The model also demonstrated that vericiguat-treated patients in the 2.5-10 mg group were on average about 13 percentage points more likely to achieve a clinically meaningful hsCRP cut-off value of < 3.0 mg/L (e.g. 55% vs 40.6% in placebo for a baseline hsCRP of 4 mg/L and 33.4% vs 21.3% in placebo for a baseline hsCRP of 10 mg/L).
Conclusion: Vericiguat was associated with greater reductions in hsCRP levels at higher doses of the drug in patients with HFrEF.

Figure. Baseline adjusted mean hsCRP changes (%) from baseline to end of treatment across the vericiguat dose groups.



P1062
Single or combined cardiac transplantation for Cardiac Amyloidosis. A report from the French National Referral Center for Cardiac Amyloidosis

S Guendouz[1]; D Bodez[1]; A Galat[1]; M Kharoubi[1]; F Lebras[1]; K Belhadj[1]; JP Couetil[1]; JL Dubois Rande[1]; G D'honneur[1]; D Azoulay[1]; C Duvoux[1]; V Audard[1]; C Feray[1]; V Plante Bordeneuve[1]; T Damy[1]
[1]University Hospital Henri Mondor, cardiologie, Creteil, France

Cardiac Amyloidosis (CA) is caused by the extracellular accumulation of insoluble fibrillar proteins. Depending on the type of protein, disease history, localization to other organs, prognosis and treatment vary. The most common types of CA are AL amyloidosis (immunoglobulins), transthyretin amyloidosis: hereditary (hTTR) or senile (wTTR). In the absence of treatment and adequate care management, the prognosis for CA is poor. Heart transplantation is remains the final cardiac therapeutic option. Few centers offer this therapy, especially for AL CA. We report our experience of the French National Referral Center for CA.
Materials & Methods: This is a retrospective study that included all patients who had a heart transplant for CA from 2005 to 2017 (n = 15). We report the baseline and post-transplant data follow-up. Post-transplant immunosuppressive therapy included for all corticosteroids, tacrolimus, and MMF and for few anti-lymphocyte serum or basiliximab.
Results: Fifteen patients had a heart transplant, 11 (73%) had AL amyloidosis and 4 had hTTR (27%). None of them were wTTR. The average age was 56 years (43 to 66), the majority of patients were men (60%). Three patients had combined heart and liver transplant and all of them were hTTR. Three patients had combined heart and kidney transplant and all of them were AL. All AL patients received at least one cycle of chemotherapy before the surgery and 7 (82%) were in partial remission. Six patients (40%) were urgently transplanted (national priority list) of whom 5 were in cardiogenic shock treated by intravenous inotrope (n = 3) and/or extracorporeal life support-assisted patients (n = 2) and 1 had incessant ventricular arrhythmias. Prior to transplantation, 4 patients (27%) had severe ventricular arrhythmias or cardiorespiratory arrest (electromechanical dissociation). The 30-day survival is 100%, the one-year survival was 74% (n = 4). Three died from infection and 1 from severe hemorrhage due to scarpa rupture (vascular amyloidosis and vascular mycotic infection). The deaths occurred only in AL. 3 with single heart transplant and one with heart and kidney. No deaths at 1 year were associated with a recurrence of amyloidosis or graft rejection. In most AL with partial remission before the surgery, a slight decrease of light chains under immunosuppressive treatments was observed, allowing avoiding immediate postoperative chemotherapy for several months.
Discussion & Conclusions: Heart transplant is a therapeutic option for selected CA in AL and hTTR and can be combined with kidney or liver transplant. In severe AL CA cardiac transplant need to perform before expecting the complete remission as immunosuppressive therapy may stabilize or decrease the light chain after the

transplant. The survival of heart failure patients with CA treated by heart transplant is comparable to those without CA and patients with combined transplant might have a better survival than those with only heart transplant.

P1063

Prescribing patterns of evidence-based heart failure pharmacotherapy and outcomes: Insights from ASIAN-HF

T-H K Tiew-Hwa Katherine Teng[1]; J Tromp[2]; WT Tay[3]; I Anand[4]; W Ouwerkerk[5]; VK Chopra[6]; GS Wander[7]; J J L Yap[3]; M R Macdonald[8]; YMF Chia[9]; W Shimizu[10]; A M Richards[11]; A A Voors[2]; C S P Lam[12]
[1]National Heart Centre Singapore; School of Population Health, University of Western Australia, Singapore, Singapore; *[2]University Medical Center Groningen, Department of Cardiology, Groningen, Netherlands*; *[3]National Heart Centre Singapore, National Heart Research Institute, Singapore, Singapore*; *[4]University of Minnesota, Veteran Affairs Medical Center, Minneapolis, United States of America*; *[5]University of Amsterdam, Dept of Clinical Epidemiology, Biostatistics & Bioinformatics, Amsterdam, Netherlands*; *[6]Medanta Heart Institute, Gurgaon, India*; *[7]Dayanand Medical College & Hospital, Ludhiana, India*; *[8]Changi General Hospital, Singapore, Singapore*; *[9]Singapore General Hospital, Singapore, Singapore*; *[10]Nippon Medical School, Dept of Cardiovascular Medicine, Tokyo, Japan*; *[11]National University Health System, Cardiovascular Research Institute, Singapore, Singapore*; *[12]Duke-NUS Graduate Medical School Singapore, University Medical Center Groningen, National Heart Centre Singapore, Singapore, Singapore*

On behalf of: ASIAN-HF investigators
Funding Acknowledgements: National Medical Research Council (Singapore), A*STAR Biomedical Research Council, Boston Scientific and Bayer.

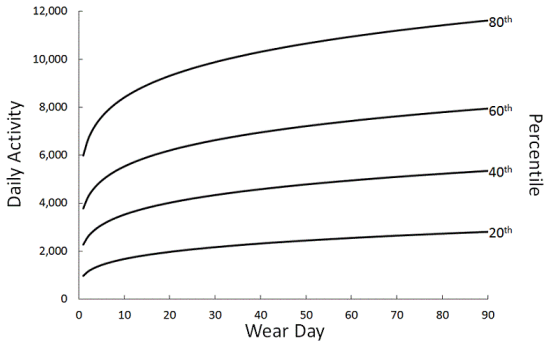
Background: It is a common perception that Asian patients with heart failure and reduced ejection fraction (HFrEF) are treated with lower doses of guideline-directed medical therapies (GDMT) such as angiotensin-converting enzyme inhibitors or angiotensin receptor blockers (ACEi/ARBs), ß-blockers and mineralocorticoid receptor antagonists (MRAs). However prospective multinational data from Asia on prescribing patterns of GDMT and its impact on outcomes have thus far been lacking.
Methods: In the prospective multinational ASIAN-HF registry, we examined GDMT uptake, achieved doses as proportions of guideline-recommended doses (GRD), and its association with 1-year composite outcome of all-cause death or HF hospitalization.
Results: Among 5,276 patients with HFrEF [mean age: 59.6 (SD13.2) y, 77.3% men, body mass index: 24.9 (5.1) kg/m2, 33.4% NYHA class III/IV], ACEi/ARBs were prescribed in 76%, ß-blockers in 78% and MRAs in 57%, with significant regional variation. GRD was achieved in only 17% of cases for ACEi/ARB, 12.5% for ß-blockers and 29.2% for MRAs. Factors associated with attainment of GRD included country (all 3 drug classes), increasing body mass index (ACEi/ARBs, MRAs), and in-patient recruitment (ACEi/ARBs, ß-blockers) (all p <0.05). Adjusted for indication bias, higher doses [including low doses (1- <25% GRD)] were associated with lower hazards of a 1-year composite outcome for ACEi/ARBs and ß-blockers compared to non-users. The lowest adjusted hazards were observed in the group that attained the GRD (HR 0.54 [95% CI 0.50-0.58] for ACEi/ARBs, HR = 0.47 [0.46-0.50] for ß-blockers, and HR = 0.77 [0.72-0.81] for MRAs). Low dosages (<50% GRD) of MRAs were associated with no better, or worse, outcomes vs non-users.
Conclusions: These first prospective multinational data from Asia demonstrate under-utilization of GDMT at recommended doses in patients with HFrEF, and suggest that effort to improve uptake and up-titration of GDMT is warranted for better patient outcomes.

P1064

Activity trends in patients recovering from acute myocardial infarction: recordings from a wearable cardioverter defibrillator

C Connor Tripp[1]; A Burch[1]; A Hain[2]; JW Erath[3]; S Sears[1]
[1]East Carolina Heart Institute, Psychology , Greenville, United States of America; *[2]Kerckhoff Heart and Thorax Center, Department of Cardiology, Bad Nauheim, Germany*; *[3]JW Goethe University, Department of Cardiology, Frankfurt am Main, Germany*

Background: Normative data for patient activity levels post-myocardial infarction (MI) does not exist. Wearable Cardioverter Defibrillators (WCDs) are equipped with accelerometers to provide information about patient activity levels. Patient management could benefit by establishing norms for objective physical activity assessment in post MI patients.
Purpose: To describe the activity level and trends in activity change after the diagnosis of acute MI.
Methods. Retrospective analysis of 480 WCD patients, 40 per month from the year 2016. Included were adult patients diagnosed with acute MI and LVEF = 35% who wore the WCD for 90 days with >100 hours of use during days 1-7 and 84-90. Age, daily wear time, and daily activity (measured by device accelerometer as steps divided by time worn) were examined. Descriptive analyses and relationship between activity levels and days of wear were examined to provide normative data during post MI recovery.
Results: Patients were mostly male (342, 71%) with a median age and 25th to 75th percentile range of 64 [56, 71]. Step count increased during the first weeks of post-MI recovery, nearly doubling before plateauing after 30 days. Median and percentile range of steps was 3100 [1300, 5700], 5600 [2700, 9100] and 6100 [3500, 9900] on days 1, 30 and 90, respectively. Patients who recorded a high number of steps at day 1, those above the 75th percentile of 5700 steps, maintained a high level of steps throughout the entire 90 day observation period: 8900 [6900, 11400], 10000 [6800, 13900] and 9200 [5500, 12000] on days 1, 30 and 90, respectively. Analysis of patients by age cohort < 65 (241, 50%), = 65 to < 75 (163, 34%) and = 75 (76, 16%) was performed. Although each age cohort increased steps during the first 30 days, age inversely correlated with median steps with age < 65 having the most and >75 the fewest: 6800 [3800, 10400] versus 3700 [1700, 5100], respectively. The figure summarizes daily activity for all post MI patients during the first 90 days of recovery.
Conclusions. Benefits associated with WCD wear include objective assessment of physical activity, thus enabling feedback and coaching in post MI patients at risk for ventricular arrhythmias.



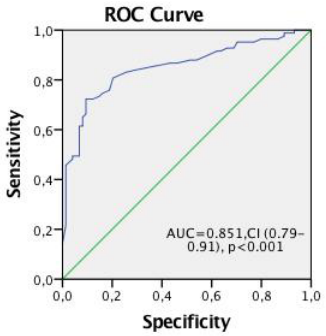
P1065

How to predict diuretic resistance in acutely decompensated heart failure patients

F Francisco Gama[1]; A Felix Oliveira[1]; P Freitas[1]; A Tralhao[1]; J Ferreira[1]; I Araujo[2]; F Marques[2]; C Fonseca[2]
[1]Hospital de Santa Cruz, Lisbon, Portugal; *[2]Hospital de Sao Francisco Xavier, Lisbon, Portugal*

Background and aim: diuretic resistance is common in heart failure (HF) patients and is associated with poorer functional capacity, recurrent hospital admissions and increased mortality. However, the clinical and pathophysiologic characteristics associated with this phenomenon remain incompletely understood. We aimed to identify predictors of diuretic resistance (DR) in HF patients across the ejection fraction range.
Methods: single-center retrospective cohort study of consecutive patients admitted to a dedicated heart failure inpatient unit between January 2013 and December 2014 with a diagnosis of decompensated HF showing clinical signs of congestion requiring intravenous furosemide. DR was defined as urine output below 20 milliliters per milligram of furosemide in the first 24 hours after loop diuretic initiation. A multivariate regression logistic model was used to determine independent predictors of diuretic resistance. A ROC curve was used to determine model's discriminative power.
Results: in a population of 159 patients, mean age was 79 years (IQR 14), 46% (n = 79) were male and 42% had resting symptoms. 39% (n = 62) had reduced ejection fraction (defined has lower than 40%) and 46% (n = 73) had ischemic etiology. Median pre-admission clearance and serum B-type NT-terminal natriuretic peptide level were 56 (Q25-75: 39.15-78.64) mL/min/1.73 m2 and 8260 (P25-75: 3160-9800) pg/ml, respectively. 53% (n = 84) of patients had diuretic resistance according to study definition. DR was significantly associated with cardiovascular death at 30 months median follow-up (HR 3.066 (1.21-7.79; p-value = 0.019). After multivariate analysis, higher serum chloride (OR 1.18 [1.02- 1.20], p = 0.015), previously on oral different diuretic classes (OR 2.74 [1.04-7.27], p = 0.03) and NYHA IV (OR 20.78

[8.04-53.71], p <0.001) emerged as independent predictors of DR. This 3-variable model had good discriminative power (c-statistic = 0.85, [0.79-0.91], p <0.001) as shown in graphic.
Conclusions: in a population of patients requiring hospital admission for decompensated HF, diuretic resistance was common. NYHA IV, previous oral diuretic association and hyperchloremia were independent predictors of DR. A simple model including two clinical variables and a single laboratory value presented a good predictive accuracy of diuretic resistance and may anticipate appropriate therapies.



Graphic 1: discriminative power of the 3-variable model on predicting diuretic resistance

Graphic

P1066
Predictors of efficiency of long aerobic training for reverse myocardial remodeling in heart failure patients

T Tatiana Lelyavina[1]; VL Galenko[1]; PS Kozlov[1]; MA Bortzova[1]; MYU Sitnikova[1]
[1]*Almazov Federal Center of Heart Blood & Endocrinology, Saint Petersburg, Russian Federation*

To evaluate the effects of long-term aerobic training, designed with individualized method based on lactate threshold definition, on myocardial remodeling in heart failure patients and to detect its predictors.
Methods: We evaluated 197 HF patients, mean age 52+/-3.3, 116 men, with NYHA class III, LVEF 37,6+/-2,1%. CPET performed on a treadmill ("Oxycon Pro") at baseline, in every 8 weeks and after 9 months. All patients were randomized into following groups: 137 patients of study group (SG), who underwent physical rehabilitation program (PRP), calculated due to lactate threshold; and 60 HF patients control group (CG), who underwent physical training, calculated based on VO2 percentage.
Results: At baseline CPET results in both groups did not significantly differ. V?2 at lactate threshold and V?2peak were 8.8+/-0,5; 13,5+/-0,9 ml/min/kg and 9.0+/-0.9; 13,6+/-1,2 ml/min/kg in study group and control group, respectively (p1 = 0,08, p2 = 0,07, respectively). After 9 months of training V?2LT and V?2peak were better in the study group than in control group: the increase was 16% and 24% in the main group, and 4% and 7% in the control group, respectively (p1 < 0,01, p2 < 0,01). 54 pts from study group have trained every day more than 1,5 hour on their own. After 9 months of aerobic training it was significant improvement of myocardial contractile function in this 54 patients: LA, at baseline and after training were 5,5 ± 0,1 and 5,1 ± 0,6 sm; , LVEDD 6,4 ± 0,4 and 5,9 ± 0,2sm; LVESD 5,9 ± 0,3 and 5,3 ± 0,3 sm, LVEF 33 ± 3,7 and 46 ± 5,5%, p < 0,001. In control group patients and other 83 pts SG the improvement of myocardial contractile function was not observed: LA, at baseline and after training were 5,4 ± 0,3 and 5,4 ± 0,3 sm; , LVEDD 6,3 ± 0,5 and 6,3 ± 0,2 sm; LVESD 5,9 ± 0,5 and 5,8 ± 0,3sm, LVEF 36 ± 5,3 and 40,2 ± 4,7%, p>0,05. We found correlation between LVEDD changes and duration of training (r = 0,9, p < 0,05), LVEDD changes and BMI (r= 0,7, p < 0,05), LVEDD changes and b-blockers dose (r = 0,4, p,0,05), LVSED changes and blood creatinine (r=-0,4, p < 0,05). Conclusions. Aerobic exercise, designed with individualized method based on lactate threshold definition, increase exercise tolerance, improves myocardial contractile function more than aerobic training, calculated based on VO2peak percentage. There are correlation between LVEDD changes and duration of training (r = 0,9, p < 0,05), LVEDD changes and BMI (r= 7, p < 0,05), LVEDD changes and b-blockers dose (r = 4, p,0,05), LVSED changes and blood creatinine (r = 4, p < 0,05).

P1067
An economic analysis of an outpatient intravenous diuretic service for the delivery of therapy to ambulant patients with advanced heart failure

A Abdallah Al-Mohammad[1]; J Gosai[2]; A Birchall[1]; M Warriner[1]; K Morton[1]; NT Lewis[1]; D Rogers[1]
[1]*Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, United Kingdom*; [2]*Bradford Royal Infirmary, Cardiology, Bradford, United Kingdom*

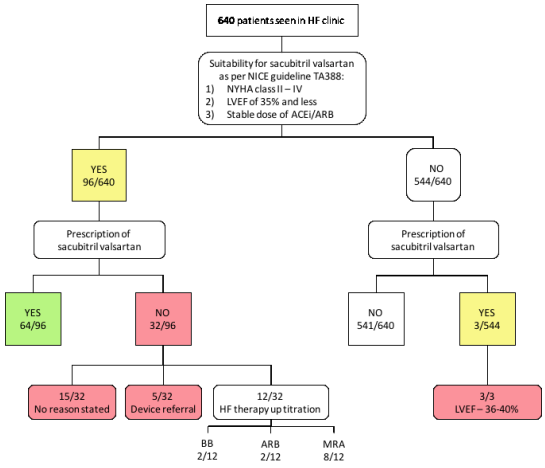
Introduction and Purpose: Services established for the administration of high dose intravenous diuretic therapy to ambulant patients with heart failure have been reported and demonstrated clinically effective, acceptable to patients, safe and feasible. They are associated with a reduction in unplanned hospital admissions. We report on the cost analysis of setting up one such service in a single cardiothoracic unit in Sheffield, United Kingdom, serving a population of approximately 500,000.
Methods: The service was set up as a multi-disciplinary service to run within an existing day case unit. Patients selected were ambulant, haemodynamically stable, and fit to transfer daily by taxi to the hospital from home. Initially, the selected patients were existing inpatients to shorten the length of stay, and later this was extended to outpatients as an admission avoidance strategy. Both those with reduced and preserved left ventricular ejection fraction were included. Dedicated support from heart failure cardiologists, heart failure specialist nurses, ward nurses, domestic and administrative staff was included in the cost calculations. Patients attended daily Monday to Friday for intravenous therapy and were given equivalent doses of oral therapy to maintain weight over the weekend. Renal function was monitored closely during therapy. Patients were discharged from the service when clinically euvolaemic or at target weight. Data from the electronic records of all patients using the service between January 2015 and September 2017 were used to calculate the costs and duration of therapy for patients. Hospital administrative and national tariff data were used to calculate potential cost and admission savings.
Results: In 32 months, 133 patients were treated for a total of 1613 sessions across 186 spells of treatment. The mean number of treatments per spell was 8.67 (minimum 2, maximum 52). 100 patients had one spell of treatment during the period studied, 33 had more than one spell of treatment. 27 patients were readmitted to hospital within 30 days of their last intravenous therapy. The cost of running the service was £302.28 per day with a capacity for six patients. This suggested an estimated cost saving of between £264,989 and £392,416, and up to 3878 bed days which would have been incurred had this cohort of patients been admitted to hospital instead.
Conclusions: Setting up and running a service to deliver intravenous diuretic therapy to ambulant patients within a cardiothoracic centre in the UK is feasible. The service was well-used and associated with considerable potential cost savings. 24% of patients required more than one spell of therapy, and 20% were readmitted to hospital within 30 days of finishing therapy. The service was not associated with a reduction in heart failure admission numbers to our hospital, and many patients who require intravenous diuretic are not fit to attend a daily outpatient service.

P1068
Does prior MRA use limit eligibility for sacubitril valsartan in a heart failure clinic? Insights from real world experience and implications for ESC and NICE guidelines

L Myslivecek[1]; E Sammut[2]; Y Ismail[2]; H Lightfoot[2]; H Donaldson[2]; B Pearson[2]; M Williams[2]; R Baker[2]; A K Angus K Nightingale[2]
[1]*University of Bristol, Bristol Medical School, Bristol, United Kingdom*; [2]*Bristol Heart Institute, Department of Cardiology, Bristol, United Kingdom*

Background: The 2016 ESC Guidelines on the pharmacological treatment of heart failure with reduced ejection fraction (HFrEF) recommend consideration of angiotensin receptor neprolysin inhibitors (ARNI) if a patient remains symptomatic with an ejection fraction (EF) of = 35% after maximal treatment, including a mineralocorticoid receptor antagonist (MRA). In contrast, the NICE 2016 updated guidelines for management of chronic heart failure in England suggest that ARNI is second line treatment after ACEi/ARB and B-blocker (BB) and could be initiated either before or after MRA therapy.
Purpose: Sacubitril valsartan (ARNI) was approved by NICE in April 2016 (TA388). We wanted to investigate the proportion of patients suitable for ARNI therapy in an general HF clinic. In addition, we speculated that a high rate of MRA use, as recommended by the ESC, might reduce the number of ARNI eligible patients, due to either low BP or severe chronic kidney disease (CKD).
Method: Retrospective audit of stable outpatients seen in a secondary care heart failure clinic in England between May 2016 and April 2017. Data was collected on inclusion criteria for ARNI (EF = 35%, NYHA class 2-4 and stable dose of ACEi/ARB), and exclusion criteria (systolic BP < 100mmHg, pregnancy/breast feeding, hepatic impairment and severe renal impairment) as well as use of devices and MRA prescription rates.
Results: 640 patients were seen in the clinic in the 12-month period after sacubitril valsartan was licensed. 96 (15%) met the ARNI inclusion criteria and 64 (69%) of

these were prescribed sacubitril valsartan. 3 patients did not meet the inclusion criteria but were prescribed sacubitril valsartan; all of these had EF 36-40%. 32/96 were suitable for ARNI but NOT prescribed; 5 were waiting for device implantation and in 15 no reason was given. 8 patients were initiating MRA and 4 were up-titrating ACEi/ARB or BB prior to re-evaluation of suitability for ARNI.
There was a high rate of MRA prescription (72%, 69/96) and device use (54%, 52/96) in those eligible for ARNI treatment, suggesting this clinic population was well treated according to ESC and NICE guidelines.
Only 2/96 patients otherwise suitable for ARNI had BP = 100mmHg. 6/96 had eGFR < 30 mL/min/1.73m2 (needing the lowest starting dose of sacubitril valsartan). All patients had potassium in the normal range.
Conclusion
In a large general heart failure clinic, 15% of patients were suitable for prescription of ARNI therapy.
Of these two thirds were actually on this therapy in the first year after it was approved by NICE in England.
Despite a high rate of MRA use in the group who were suitable for ARNI, there was a very low rate of exclusion due to low BP or CKD.
Optimising heart failure treatment according to the ESC guidelines, including MRA first, does not reduce eligibility for ARNI therapy in a real world heart failure clinic environment.



Patient flow chart

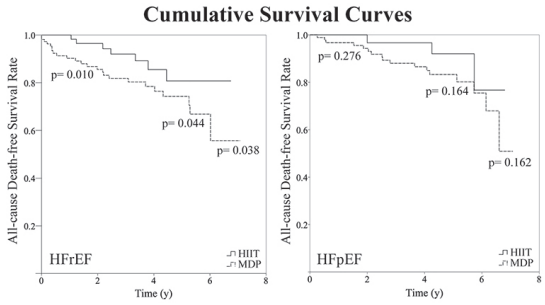
P1069

Effects of high-intensity interval exercise training on survival of heart failure patients

C-C Hsu[1]; T-C Fu[1]; J-S Wang[2]; C-H Wang[3]
[1]Keelung Chang Gung Memorial Hospital, Physical Medicine and Rehabilitation, Keelung, Taiwan ROC; *[2]Chang Gung University, Institute of Rehabilitation Science, Taoyuan, Taiwan ROC*; *[3]Keelung Chang Gung Memorial Hospital, Cardiology, Keelung, Taiwan ROC*

On behalf of: Heart Failure Research Center, Keelung Chang Gung Memorial Hospital
Funding Acknowledgements: Keelung Chang Gung Medical Research Program and the Taiwan Ministry of Science and Technology

Background: High-intensity interval training (HIIT) increases peak oxygen consumption (VO2peak) and alters cardiac geometry. However, no studies have reported effects of HIIT on survival of HF patients.



Survival curves of heart failure patient

Purpose: The cohort study aimed to determine effects of HIIT on long-term survival of heart failure (HF) patients.
Methods: HF patients, enrolled between 2009 and 2016, received multidisciplinary disease management program (MDP) and serial assessments of VO2peak, echocardiography, b-type natriuretic peptide, and quality of life questionnaire. 181 participants with left ventricular ejection fraction (LVEF)= 40% and 133 with LVEF> 40% were classified as having HF with reduced EF (HFrEF) and preserved EF (HFpEF), respectively. 72 HFrEF and 38 HFpEF patients who underwent= 36 times of HIIT were classified as the HIIT group. The remaining HF patients were classified as the MDP group. Generalized estimating equation (GEE) and survival analysis were used to assess clinical presentations during follow-up.
Results: In HFrEF patients, GEE model estimated that VO2peak increased significantly by 0.519 MET/year associated with decreases of LV end-diastolic diameter by -2.6 mm/year, LV end-systolic diameter by -5.2 mm/year, and BNP by -377 pg/mL/year during HIIT as compared with MDP subjects. In HIIT subjects with HFrEF, the 1-year (100% vs 90.9%), 5-year (80.8% vs 74.3%), and 7-year (80.8% vs 55.7%) survivals were significantly greater than the MDP subject(Figure 1). The survival was similar between the two groups in HFpEF patients.
Conclusions: HIIT increases VO2peak, reverses cardiac remodeling, and finally improves long-term survival of HFrEF patients. HIIT cannot provide cardiac protection and improve survival for HFpEF patients.

P1070

Effect of vitamin D on endothelial function in patients with chronic heart failure

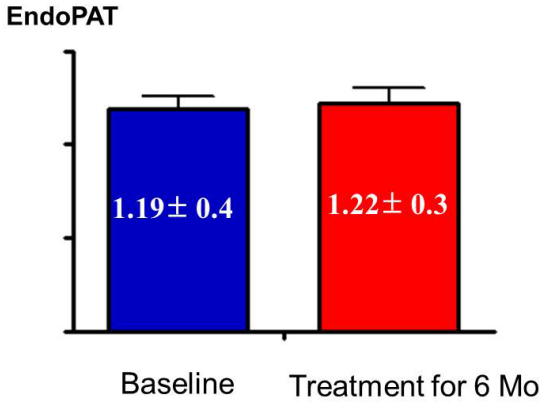
S J Ha[1]; DG Shin[1]; YM Woo[1]; YJ Song[2]; WD Bang[1]; SY Yoo[1]; SS Cheong[1]
[1]GangNeung Asan Hospital, Cardiology, GangNeung, Korea Republic of; *[2]Haeundae Paik Hospital, Cardiology, Busan, Korea Republic of*

Background: In patients with heart failure (HF), low levels of 25-hydroxyvitamin D (25OHD) are common and are associated with increased mortality risk.
Objectives: The VIVID-HF (Ventricular and Vascular function of Vitamin D in Patient with Heart Failure) study was an investigator-initiated, multicenter, prospective, randomized, placebo-controlled trial to establish safety and efficacy of oral vitamin D3 (cholecalciferol) supplementation in stable HF patients.

P1070 Mean weight and BMI of LVAD recipients

	Baseline	6 months	12 months	18 months	24 months	36 months	48 months
Weight (kg)	75.0 (±14.2)	80.8 (±14.8)	85.0 (±15.1)	85.8 (±15.3)	87.1 (±19.1)	103.4 (±9.9)	112.0 (±4.1)
BMI	25.1 (±4.4)	27.0 (±4.4)	28.5 (±4.4)	28.6 (±4.9)	29.4 (±6.8)	34.1 (±7.6)	40.3 (±8.8)

Mean weight and BMI (±standard deviation) of LVAD recipients during follow up (p<.001 for all mean values compared to baseline value)



Endo PAT

Methods: Seventy three HF patients with 25OHD level <75 nmol/L (30 ng/mL) were randomized to receive 4000 IU vitamin D daily or matching placebo for 6 months. The primary endpoint was the change of endothelial function assessed by EndoPAT between baseline and 6 months. Secondary endpoints included the change in echocardiographic parameters and differences of quality of life (6 minute walk test and New York Heart Association functional status: NYHA status) at 6 month.

Results : During study periods, there was no adverse event in both groups. Vitamin D supplementation did not improve endothelial dysfunction (Figure, EndoPAT: baseline, 1.19 ± 0.4 vs 6 month later, 1.22 ± 0.3, p = 0.65). In addition, 6-minute walking distance (baseline, 292.9 ± 120.35 vs 6 month later, 283.7 ± 116.84 m, p= 0.125), and NYHA status also did not improve. In this period, there was no significant change in echocardiographic parameters.

Conclusions: : A daily vitamin D dose of 4000 IU would be safe but did not improve endothelial function, echocardiographic parameters, 6-minute walking distance, and NYHA status.

P1071

A retrospective study of metabolic dysfunction in left ventricular assist device recipients indicating these patients are at excessive risk of cardiac transplant ineligibility

W Wasim Javed[1]; P Chaggar[1]; T Entwistle[1]; R Venkateswaran[1]; S Shaw[1]
[1]*University Hospital of South Manchester NHS Foundation Trust, Manchester, United Kingdom*

Background: LVADs are increasingly utilised in advanced heart failure. Whilst improved nutritional status has been observed following implantation, excess weight gain has also. This may impact on cardiac transplantation eligibility.

Purpose: To confirm observational claims of excess weight gain with prolonged LVAD use and define any impact on transplant eligibility.

Methods: Case records of consecutive bridge-to-transplant (BTT) patients implanted with LVAD over 6 years were reviewed retrospectively. Baseline data collection included demographics, aetiology, co-morbidity and LVAD type. Height, weight and metabolic parameters were examined 6-monthly during LVAD support for up to 2-years. Statistical analyses were performed using paired t-test.

Results: 53 patients received an LVAD as BTT. The mean age was 48.5 years and ischaemic cardiomyopathy was the commonest heart failure aetiology (67.9%). The majority were white British ethnicity (92.5%) and male (73.6%). Pre-LVAD diabetes incidence was low (7.6%).

Weight gain was observed in 86.8% of LVAD recipients. LVAD recipients who received cardiac transplantation gained significantly less weight over 12 months (mean 5.2kg) than those who did not (10.4kg). 21.7% of those with pre-LVAD body mass index (BMI (kg/m2)) under 30 experienced a rise in BMI to 30 or above during LVAD support. Table 1 displays mean weight and BMI of LVAD recipients during follow up.

Cholesterol increased significantly from a median baseline value of 3.0 to 4.5mmol/L (p= .004) at final follow up.

Conclusion: Excess weight gain was frequently observed in LVAD recipients in a time-dependent manner. Other indices of obesity-related metabolic dysfunction were observed including increased cholesterol. These patients are more likely to become ineligible for cardiac transplantation due to raised BMI or complications of metabolic syndrome. In our study, over 20% exceeded a BMI over 30, classifying them as obese. As expected, patients receiving cardiac transplant experienced less weight gain.

Active weight management is required for LVAD recipients due to an increased risk of obesity. This is vital for BTT patients to avoid cardiac transplantation ineligibility. This may be achieved with a MDT approach including a dietitian or metabolic physician. Clearly, LVADs should not be utilised for weight loss in patients already transplant ineligible due to obesity.

P1072

Clinical experience of using cardiac contractility modulation devices in patients with heart failure:the true or wrong way to success?

M Trukshina[1]; E Lyasnikova[1]; V Galenko[1]; T Lelyavina[1]; M Sitnikova[1]; I Kim[1]; Z Abakarov[1]; M Abramov[1]; E Mikhaylov[1]; E Zubarev[1]; M Vander[1]; K Simonova[1]; D Lebedev[1]; O Stovpyuk[1]; E Shlyakhto[1]
[1]*Almazov National Medical Research Centre, Heart Failure, St.Petersburg, Russian Federation*

Funding Acknowledgements: Clinical approbation programme "Cardiomodulation" Russian Federation Ministry of Healthcare

Introduction: Cardiac Contractility Modulation (CCM) is an original approach in new device therapy to improve contractility in patients with heart failure with reduced ejection fraction (HFrEF), on OMT, with sinus rhythm (SR) and narrow QRS complex.

Purpose: To assess the dynamics of the CHF, adverse events rate, structural and functional parameters of the heart in patients with implanted CCM devices during follow-up period.

Methods: From 20 Oct 2016 till 12 Sep 2017 CCM devices n = 55 (50 - Optimizer IVs, 5 - Optimizer Smart) were implanted to the patients with CHF I-IV fc NYHA, > 18 y.o. (55,0 ± 10,6), SR, QRS < 120 ms. 46 male,9 female, 36 - CAD, DCM - 19, fc NYHA I/II/III/IV- 1/37/12/5; 10 patients were with ICD. Patients were followed-up by CHF cardiologists every 3 months in outpatient HF clinic with physical examination, device programming, assessment of the life quality, cardiopulmonary exercise test, ECG, Holter Monitoring (HM), Echocardiography(Echo) and NT-proBNP level.

Results: Patients had good compliance and tolerance of CCM stimulation. No hospitalizations due to CHF or outpatient decompensation occurred among 43 patients who passed 6 month follow-up control visit. 11 of them felt clinical improvement, 4 - worsening, 28 –without any changes; fc NYHA I/ II/ III/IV- 3/33/7/0. The positive trend in Echo and NT-proBNP data was observed: LVEF increased 26.0 ± 5.4 (15-38%) vs 30.5.0 ± 7.95% (17-41), p = 0,08; LVEDV and LVESV decreased accordingly: 244.0 ± 59.8 ml (145-360) vs 233.5 ± 59.6 ml (116-380), 185.0 ± 50.9 ml (85-273) vs 163.0 ± 51.0 ml (70-290). NT-proBNP level - 1049.5pg/ml (241-20 198) vs 771pg/ml (42-3 962). ECG and HM data did not reveal any PQ, QRS, QT interval prolongation and significant rhythm and conduction disorders. Within 6 months, the following adverse events occured: 2 patients were hospitalized with unstable angina (conservative treatment), 2 died suddenly. In 12 patients stimulation of the CCM pocket was due to dislocation of the ventricular leads, in 14 patients 1 lead was disconnected because of technical problems, replacement of 2 leads was planned for 3 patients, in 1 patient CCM was deimplanted in early postoperative period time due to the device pocket infection.

Conclusions: First clinical experience in 6-month follow-up of patients with CCM devices showed the stability of clinical status, decrease in CHF fc, good patients tolerance of stimulation, absense of arrhythmogenic effects, in some patients, mostly with DCM, tendency to improve cardiac remodeling. Ventricular lead insulation failure complications and pocket device stimulation which required switching off one of the ventricle leads present the most common negative aspects of a new method and may diminish the potential treatment effect. Long-term follow-up will help to identify the subgroup of patients to get the true way and maximum benefit.

P1073

Specialised heart failure clinics are more needed in rural regions

A Klabnik[1]; J Murin[2]
[1]*Outpatient cardiology clinic, Namestovo, Slovak Republic*; [2]*1st Department of Internal Medicine , University Hospital Bratislava, Slovak Republic*

Purpose: Only 3 heart failure (HF) clinics are active in metropolitan areas of Slovakia. No organised HF disease management programme exists in rural region.

Methods: We compared clinical characteristics, evidence-based medications and outcomes in 134 patients (pts) from one regional center with others centres in Slovakia (n = 354) participated in the Heart Failure Long-Term registry. We statistically analysed the reasons for differences in benchmark report, separately for outpatients and hospitalized pts.

Results: In regional centre were as outpatients recruited significantly ($p < 0.05$) more older pts than 65 years (73.9 % vs 33.9 %, odds ratio, OR > 5), with non-ischemic etiology (68.1 % vs 41.7 %, OR 2.99, predominantly valvular etiology), more advanced HF (in NYHA class III-IV: 62.3 % vs 31 %, OR 3.69) and fewer males (62.3 % vs 70.2 %, OR 0.57). Common comorbidities were in outpatients significantly ($p < 0.05$) more often present in regional center: diabetes (44.9 % vs

25.6 %, OR 2.37), chronic renal dysfunction (31.9 % vs 11.9 %, OR 3.46), current malignant cancer (17.4 % vs 1.2 %, OR > 5), permanent atrial fibrillation (44.9 % vs 10.7 %, OR > 5).
At a glance it seemed that in regional center are in outpatients resp. hospitalized pts significantly ($p < 0.05$) underused ACE-inhibitors/sartans (72.5 % vs 90.5 %, OR 0.28, resp. 50.8 % vs 81.7 %, OR 0.23), beta-blockers (78.3 % vs 90.5 %, OR 0.38, resp. 66.2 % vs 86.6 %, OR 0.30) and mineralocorticoid receptor antagonists (31.9 % vs 63.1 %, OR 0.27, resp. 27.7 % vs 66.1 %, OR 0.20). But after accounting objective reasons for non-using these medications in regional center these differences were disappeared.
In regional center significantly ($p < 0.05$) more outpatients, respectively hospitalized pts have a history of previous hospitalisation (69.6 % vs 30.1 %, OR > 5, resp. 70.8 % vs 33.3 %, OR 4.84). During 12 month follow-up significantly ($p < 0.05$) more outpatients, resp. hospitalized pts in regional center died (20.3 % vs 9.3 %, OR 2.5, resp. 39.7 % vs 20.9 %, OR 2.48) and were more often re-hospitalisated: 1st re-hospitalisation (66.1 % vs 20.5 %, OR > 5, resp. 77.6 % vs 45.1 %, OR 4.21), 2nd re-hospitalisation (48.7 % vs 25 %, OR 2.85, resp. 48.9 % vs 38.3 %, OR 1.54, not significant). The hazard of death and re-hospitalisation increased with higher age, multiple comorbidities.
Conclusion: In Slovakia are HF clinics urgently needed in regional settings to achieve better quality of HF care and optimized outcomes.

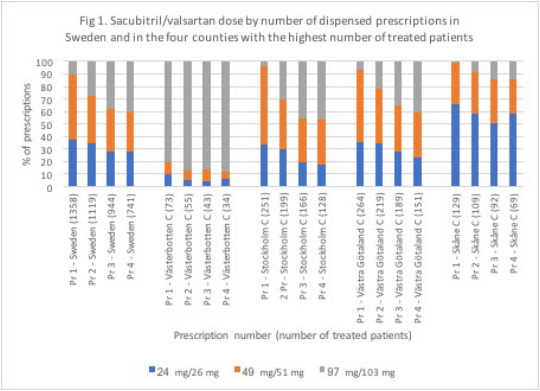
P1074

Early real-world implementation of sacubitril/valsartan in Sweden

O Ola Vedin[1]; P Vasko[2]; E Bachus[3]; U Dahlstrom[4]; M Fu[5]; K Lindmark[6]; B Svennblad[7]; D Johansson[8]; F Calado[9]; LH Lund[10]
[1]Uppsala University Hospital, Department of Medical Sciences, Cardiology, Uppsala, Sweden; *[2]Central Hospital, Vaxjo, Sweden*; *[3]Lund University, Malmo, Sweden*; *[4]Linkoping University Hospital, Linkoping, Sweden*; *[5]Sahlgrenska Academy, Gothenburg, Sweden*; *[6]Umea University, Umea, Sweden*; *[7]Uppsala Clinical Research Center, Uppsala, Sweden*; *[8]Novartis Sweden AB, Stockholm, Sweden*; *[9]Novartis Pharma AG, Basel, Switzerland*; *[10]Karolinska Institute, Stockholm, Sweden*

Funding Acknowledgements: Novartis

Introduction: Sacubitril/valsartan (s/v) improves outcomes in heart failure (HF) with reduced ejection fraction, is recommended in international guidelines, and reimbursed in Sweden since April 2016. However, information on its real-world use is scarce.
Purpose: To assess temporal trends in s/v use, dose titration strategies, background medications and demographic factors in the Swedish population who were prescribed s/v.
Methods: The Swedish Prescribed Drug Register covers all drug dispensations in Sweden. In patients with = 1 dispensation of s/v, we collected data on demographics, prior HF medications, and dose trends for consecutive dispensations on a national level and for the four (out of 21 in total) geographic regions with the highest dispensation numbers.
Results: Between January 2016 and August 2017, there were 1358 patients with = 1; 1119 patients with = 2; 944 patients with = 3; and 741 patients with = 4 s/v dispensations. Mean age of all patients was 68.0 years, 30.3% were = 75 years, 3.3% were = 85 years, and 19.1% were female. Prior to the first s/v prescription 92.9% had a RAAS inhibitor (ACE inhibitor/ARB), 93.9% a beta-blocker and 75.4% a mineralocorticoid receptor antagonist. The majority of the first dispensations were 24/26 and 49/51 mg doses but also a large proportion of subsequent dispensations were at low doses. Some regions started s/v and continued it at lower doses whereas others generally initiated treatment at the highest dose (Figure 1).
Conclusions: In this nationwide study with complete coverage of actual dispensations, a majority of patients were treated with guideline recommended HF medications prior to the first s/v dispensation. The following trends were observed: (1) lower use of HF medication in women and elderly; (2) insufficient s/v dose uptitration; and (3) highly variable s/v dosing between regions.



Figure

P1075

Iron in heart failure: time to practise what is preached

S Ng[1]; J Pan[1]
[1]St Thomas' Hospital, London, United Kingdom

Background: Iron-deficiency, present in 30-50% of patients with chronic heart failure is associated with increased morbidity and mortality. Intravenous iron supplementation has been shown to improve functional capacity, quality of life and reduce hospitalisation in patients with heart failure with reduced ejection fraction (HFrEF) who have iron deficiency (irrespective of the presence of anaemia).
Purpose: Despite guidelines recommending routine testing for iron deficiency (ID), this practice is inconsistent. This study investigates the practice of screening for ID in HFrEF patients seen in general cardiology and heart failure clinics at a teaching hospital in the United Kingdom.
Methods: A cross-section analysis was performed on patients seen in the heart failure clinic throughout October 2017. Outcomes measured were the presence of iron studies within 6 months of the clinic appointment, aetiology of HFrEF, presence of ID or anaemia and oral iron supplementation. Patients with symptomatic HFrEF defined as ejection fraction (EF) < 45% with a New York Heart Association (NYHA) functional classification = 2 were included.
Results: A total of 106 patients met inclusion criteria. Of these, 75% were male, age ranged from 33 to 90 years (median age 68). A majority of 71% of patients were classified as NYHA class II. The mean EF was 31.5% and the major aetiology of HF is ischaemic cardiomyopathy (59.4%). A biventricular pacing device was present in 25% of patients. Iron studies were completed in 28% of the cohort and only 60% of these iron studies included both ferritin and transferrin saturation. Iron deficiency was present in 50% of patients who had iron studies. Anaemia was present in 37% of the cohort. Less than 4% of the cohort was on oral iron replacement therapy.
Discussion and Conclusion: In the present study centre, iron deficiency remains underdiagnosed and undertreated in HFrEF patients, while pharmacological and device therapy are optimised. A significant proportion of iron studies in HFrEF patients were performed by other specialities (e.g. renal and haematology). When performed, essential components of iron studies were neglected, complicating the diagnosis of iron-deficiency in the context of heart failure.
To encourage screening for iron deficiency in HFrEF, a multi-discplinary and systematic approach is required. Crucial to this is also the setup of an outpatient or ambulatory system for administration of intravenous iron to treat patients identified with iron-deficiency. Further effort is required to raise awareness of accurate diagnosis of ID in HFrEF patients and optimising systems to translate trial data to clinical practice.

P1076

Acceleration training improves sarcopenia and frail factors in elderly outpatients with chronic heart failure

K Keisuke Kida[1]; S Doi[1]; C Ito[1]; N Suzuki[1]; Y Sato[1]; K Ashikaga[1]; S Kou[1]; T Harada[1]; YJ Akashi[1]
[1]*St.Marianna University School of Medicine, Department of Internal Medicine, Division of Cardiology, Kawasaki, Japan*

Background: The prevention strategies for sarcopenia and frail in cardiac rehabilitation are a future challenge. Nowadays, newly developed muscle training, such as Kaatsu training and electrical nerve stimulation, has become a focus of attention. Our previous studies have reported the safety and effectiveness of acceleration training using Power Plate®, although, no studies focusing on sarcopenia and frail have not been published in outpatients with chronic heart failure (HF).
Aims: This study aimed to assess the effect of acceleration training on sarcopenia and frail in outpatients with chronic HF.
Methods: This study conducted on 27 elderly outpatients with chronic HF undergoing acceleration training once in a week for 24 weeks. Grip strength, 10-meter walking speed, muscle volume, knee extension muscle strength and the Kihon checklist scores were assessed.
Results: After the 12-week training, grip strength (21.5 ± 4.4 to 22.7 ± 4.9kg, p = 0.0005), walking speed (1.37 ± 0.24 to 1.72 ± 0.32sec/m, p < 0.0001), knee extension muscle strength (20.9 ± 5.3 to 24.1 ± 6.2kgf, p = 0.0006) and the Kihon checklist scores (7.2 ± 4.8 to 5.1 ± 3.7, p = 0.0039) were significantly improved, whereas no significant improvement in muscle volume was found.
Conclusions: The result of this study demonstrated the usefulness of acceleration training for improving sarcopenia outcome measure, including grip strength and walking speed, in elderly outpatients with chronic HF. Although no increases in muscle volume were found, the patients could walk faster after 24-week training, suggesting that lower-limb muscle strength should be improved. Since the scores in the Kihon checklist were also improved, acceleration training might probably prevent sarcopenia and frail in elderly outpatients with chronic HF.

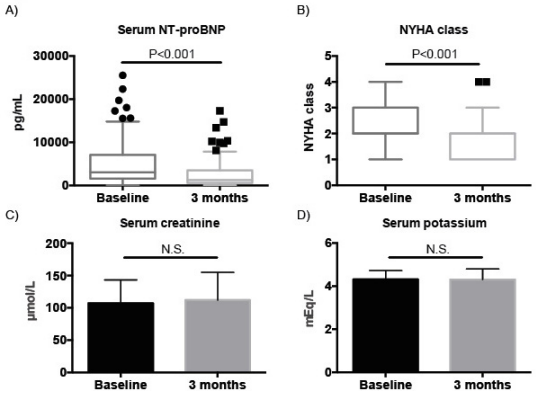
P1077

ARNI use leads to improved NYHA class and NT-proBNP levels in a Singaporean cohort

VJL Vera Goh[1]; N Koh[1]; CK Teoh[2]; JS Hon[1]; LLY Teo[1]; CP Lim[1]; DKL Sim[1]
[1]*National Heart Centre Singapore, Singapore, Singapore*; [2]*National Heart Institute, Kuala Lumpur, Malaysia*

Background/Introduction: LCZ696, the first-in-class Angiotensin Receptor-Neprilysin Inhibitor (ARNI), has been shown to improve outcomes in symptomatic HF with reduced ejection fraction (HFrEF). The effects of ARNI use in our local multi-ethnic Singaporean HFrEF population remain to be studied.
Purpose: We aimed to evaluate the short-term effects of ARNI use on New York Heart Association (NYHA) class and N-terminal pro B-type Natriuretic Peptide (NT-proBNP) levels in a multi-ethnic Singaporean HFrEF population.
Methods: 274 patients who initiated ARNI use between November 2015 and December 2016 were retrospectively followed up until they reached one of the following end points of death or LVAD implantation. An intention to treat analysis was performed on the data collected.
Results: Our cohort had a mean age of 61 ± 1 years and were 77% male. 92% of the cohort were either on an angiotensin converting enzyme inhibitor or an angiotensin receptor blocker prior to starting an ARNI. Over a median follow-up period of 4.2 [2.6, 6.0] months, the mortality rate due to cardiovascular causes was 2.2% and the rate of heart failure hospitalisations was 17.2%. The rate of discontinuation of ARNI due to adverse events was 15%. There was a significant decrease in NT-proBNP observed at three months compared to baseline (3041 [1570, 7095] vs 1284 [574, 3506] pg/mL, P < 0.001) (Figure 1A). Furthermore, there was also a significant decrease in NYHA class three months after starting ARNI (2.3 ± 0.6 vs 1.8 ± 0.6, P < 0.001) (Figure 1B). Conversely, there was no significant difference in serum creatinine (107 ± 36 vs 112 ± 43 μmol/L, P = 0.2) (Figure 1C) or serum potassium (4.3 ± 0.4 vs 4.3 ± 0.5 mEq/L, P = 0.7) (Figure 1D) at baseline and at three months respectively.
Conclusions: ARNI use in our multi-ethnic Singaporean HFrEF population was associated with decreased NT-proBNP levels and improvement in NYHA class, but no difference in serum creatinine or potassium at three months compared to at baseline.

Figure 1

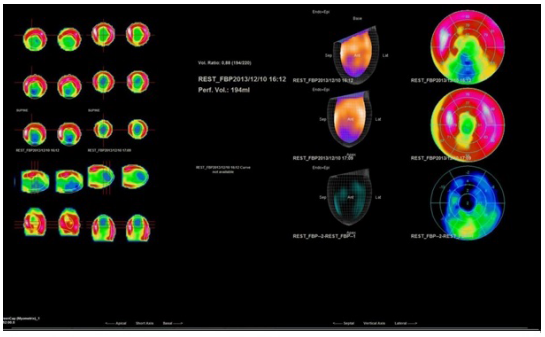


P1078

Iodine-123 Metiodobenzylguanidine (MIBG) imaging for selection heart failure patients eligible to an implantable automatic defibrillator (ICD) in primary prevention

C Chahinez Ketfi[1]
[1]*Hospital Bichat-Claude Bernard, Paris, France*

Objectives: to assess the prognostic value of cardiac iodine-123 metaiodobenzylguanidine (123)I- MIBG) scintigraphy to predict ventricular arrhythmias in patients with heart failure (HF) listed for implantable cardioverter-defibrillator (ICD) devices as primary prevention.
Methods: a prospective cohort study in 51 patients with HF referred for ICD (123) I-MIBG scintigraphy was performed with calculation of early and late heart to mediastinum (H/M) ratios washout rate and a summed score calculated innervation-perfusion mismatch was evaluated by comparing SPECT scores



results 10 patients (19.6%) experienced a significant arrhythmic event(AE) Compared with patients who suffered no event the early H / M ratio was 1.5 +/- 0.1 and the late H / M was 1.40 + / 0.2 with no significant difference between the two groups there was no significant difference for wash out (49.3 +/- 12.1 vs 55.5 +/- 17.37) there was no significant difference for the 123-I MIBG SPECT defect score (31.3 +/- 9.5 versus 37.3 +/-11.8) the rest perfusion defect score was also (16.6 +/-8.2 vs 22.1 +/-10.9) with 123-I MIBG / infusion mismatch higher score (8.2 + _4.2 vs 6.4 + - 3.7) twenty-five patients (50%) had cardiac events with a significant difference in the late H / M ratio of 1.3 ± 0.1 versus 1.4 ± 0.1 (p < 0.05).
Conclusion: the 123I-MIBG scintigraphy may be a useful examination to evaluate HF patients eligible for primary ICD imaging to predict the risk of arrhythmic events occurrence

P1079

Adherence to the pharmacotherapy in patients with cardiac resynchronisation therapy

M Brozova[1]; V Vorisek[2]; P Parizek[1]; J Ceral[1]; R Praus[1]; M Solar[1]
[1]University Hospital Hradec Kralove, 1st Department of Internal Medicine - Cardioangiology , Hradec Kralove, Czech Republic; *[2]University Hospital Hradec Kralove, Institute of Clinical Biochemistry and Diagnostics,, Hradec Kralove, Czech Republic*

Funding Acknowledgements: Supported by research project PRVOUK P037/03

Background: The cardiac resynchronisation therapy (CRT) is very effective in selected heart failure (HF) patients. However, the pharmacotherapy still remains a cornerstone of HF treatment.
Aim of the study: The aims of the study were: 1) to assess the occurrence of medication non-adherence in patients referred for the CRT and those already treated by the CRT; 2) to estimate the cost effectiveness of the medication adherence testing in routine clinical practice.
Subjects and Methods: Enrolled to the study were both the patients who were referred for the implantation of biventricular pacemaker and those who were chronically treated by the CRT.
The adherence to the medication therapy was evaluated by the estimation of the serum drug levels (SDL). Serum drug concentrations were measured by using high pressure liquid chromatography combined with mass spectrometry (beta blockers, ACE-inhibitors, angiotensin receptor blockers, diuretics and calcium antagonists) and immunoanalysis (amiodarone, digoxin). The non-adherence was diagnosed when the given drug was not detected in the serum.
Results: The study enrolled 55 patients. Twenty patients (group A) were examined before the initiation and 35 (group B) were tested during the chronic CRT.
The estimation of SDL confirmed full medication adherence in 15 (75 %) patients in group A and 25 (71.4 %) patients in group B. The partial non-adherence was diagnosed in 5 (25%) patients in group A and 10 (28.6 %) patients in group B, when some of the recommended medications were not found in the serum. No case of complete non-adherence was identified. The average cost of diagnosing one case of partial non-adherence was estimated to be 1000 €.
Conclusions: The medication non-adherence in CRT patients is not a rare problem. Although the costs of the SDL testing are not low, they are not un-proportional to the costs related to the CRT. Routine medication adherence testing can help to identify uncooperative patients who require focused counselling. The efficacy of CRT may be augmented by this approach.

P1080

Heart transplantation in Korea: 24 years of experience

M S Min Seok Oh[1]; J O Choi[1]; G Y Lee[1]; E S Jeon[1]
[1]Samsung Medical Center, Division of Cardiology, Department of Medicine, Seoul, Korea Republic of

Background: Heart transplantation has become the gold standard treatment option for end-stage heart failure. We report 24-years of experience in Korea.

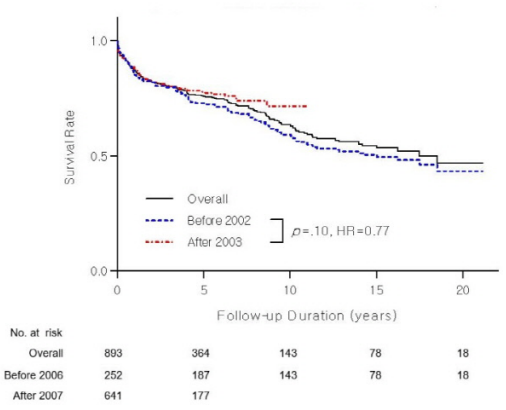


Figure 1

Methods: From January 1992 to December 2015, 1,163 patients were undergone orthotropic heart transplantation. We retrospectively reviewed the available medical records of 1,028 subjects. Patients with multi-organ transplantation (n = 33), and pediatric recipients (18 years old or younger, n = 96) were excluded for analysis of survival rate.
Results: Heart transplantation had been performed in 18 institutes. Mean age of recipients was 47.6 ± 13.6 years and 71.3% were men. Gender-matched transplantation was proceeded in 71.3%. Leading primary diagnosis for heart transplantation was dilated cardiomyopathy (59.3%). Perioperative mortality (within 1 month) was 3.3% (n = 30) and infection was the most common cause of death (43.3% of all-cause death, n = 13). After 1-, 5-, 10- years of follow-up, overall survival rates were 88.8%, 78.0%, and 67.0%, respectively (Figure 1). Malignancy-free survival rates were 98.8%, 95.1%, and 87.9%. Chronic allograft vasculopathy was occurred in 9 patients. After 2007, all-cause mortality rate (p = .060, hazard ratio = 0.78, 95% confidence interval; 0.56 -1.01) and malignancy-free survival rate (p = .31, hazard ratio = 1.42, 95% confidence interval; 0.72 - 2.79) was not statistically remarkable compared to before 2006.
Conclusion: In Korea, actuarial survival after heart transplantation were similar to those reported by the International Society of Heart and Lung Transplantation (ISHLT).

P1081

Transition from a cardiology hospitalization ward to heart failure units. Profile of the patient referred for the first time.

CN Carlos Nicolas Perez Garcia[1]; D Enriquez-Vazquez[1]; TS Luque-Diaz[1]; A Travieso-Gonzalez[1]; C Olmos-Blanco[1]; D Vivas-Balcones[1]; R Bover-Freire[1]; P Martinez- Santos[1]; M Perez-Serrano[1]; I Vilacosta[1]; C Macaya-Miguel[1]
[1]Hospital Clinic San Carlos, Instituto Cardiovascular Clínico San Carlos, Madrid, Spain

Background: ambulatory follow-up of patients with HF has been favored after the development of Heart Failure Units (HFU) that coordinate after discharge the role of nursing, primary and specialized care, achieving a multidisciplinary management.
Purpose: to describe the features of referred patients, comparing with those not referred, in order to better recognize the profile who benefits the most of this alternative.
Methods: all patients admitted to our Cardiology ward during 12 months diagnosed of HF were prospectively collected. We compared the subgroup referred to a HFU with those with the same diagnosis, not derived during the same period.

Table 1

N = 336	NON-REFERRED HFU (N = 246)	REFERRED HFU (N = 90)	P-VALUE
BETA-BLOCKERS	67,2%	81,1%	0,013
ACEI/ARB	59,8%	63,3%	NS
MRA	31,6%	61,1%	<0,001
DIURETIC	71,7%	86,7%	0,005
IVABRADINE	1,6%	7,8%	0,010
DIGOXIN	7%	15,6%	0,016
ICD/CRT	4,5% /5%	21,1%/15,6%	<0,001 /0,001

TABLE 1. Prescribed treatments at discharge of non-referred and referred patients to a HFU.

Results: from 336 patients, 90 (27%) were referred to a HFU. There were significant differences in sex (males 74% vs 44%, p <0.001) and age (72 vs 77 years, p 0.001), without differences in terms of dependency or frailty. Enolism was significantly more frequent in the first group (14% vs 6%, p 0.03) with no differences in other CVRF or comorbidities, as well as a greater proportion of patients with HF without known trigger (36 vs 9.3 %, p <0.001), more readmissions (31% vs 5%, p <0.001) and a longer average stay (5.1 vs 4.6 days, p <0.001). There was a greater referral of patients with reduced LVEF (71.6% vs 42.8%, p <0.001) and right ventricular dysfunction (47.1 vs 22.2, p <0.001). Regarding treatment at discharge, the prescription of beta-blockers, MRA, ivabradine, digoxin, diuretics and devices was higher in referred patients (table 1).
Conclusions: the referred patient to a HFU tends to be younger, more frequently male and with more risk factors. This, together with the greater proportion of left and right ventricular dysfunction and the frequent readmissions for HF, make necessary more aggressive therapeutic strategies for an optimal management.

P1082

Is acute renal failure associated to worse prognosis after a cardiac device implant?

LCSP Luiz Carlos Passos[1]; WN De Carvalho[2]; AGQ De Jesus[2]; VRS Souza[3]; AA Fagundes[2]; AMP De Lima[2]; YM Lira[4]; EL Garrido[3]; EOM Andrade[3]; NFC De Oliveira[4]; AMAF De Jesus[2]; TM Trindade[2]
[1]Federal University of Bahia, Internal Medicine, Salvador, Brazil; *[2]Ana Nery Hospital, Salvador, Brazil*; *[3]Federal University of Bahia, Faculty of Nursing, Salvador, Brazil*; *[4]Bahiana School of Medicine and Public Health, Salvador, Brazil*

On behalf of: EPICO
Funding Acknowledgements: EPICO

Background: Controversial results have been published concerning to the involvement of acute renal failure over the outcomes of heart failure patients underwent to electronic cardiac device implants (resynchronization therapy and implantable cardioverter defibrillator). Renal function has been told to be a factor for worse prognosis among these patients.
Purpose: The aim of this study was to describe the clinical differences concerning clinical profile, in-hospital and post-discharge outcomes of patients submitted to electronic cardiac device implant according to the presence of renal failure during in-hospital stay.
Methods: Cohort data from 212 patients admitted in a tertiary cardiac referral centre for cardiac electronic device implant (resynchronization therapy and implantable cardioverter defibrillator) between march 2015 and december 2017. All the data was collected from medical records. Heart failure was defined according to the European Society of Cardiology (ESC) guidelines. Renal failure was defined as a creatinine clearance level < 30mL/min.
Results: A sum of 212 patients was assessed and 17.5% (23) showed a creatinine clearance level <30mL/min during hospital stay. Renal failure patients were older (62.5 ± 10.1 vs 57.3 ± 12.9; $P = 0.02$) and had higher lethality during hospital phase (8.6% vs 1.1%; $P = 0.03$). The need of intensive unit care support was higher among renal failure patients (32.4% vs 9.1%; $P = 0.001$) and this group had also a greater lenght of hospital stay (medians of 12 vs 3.0; $P < 0.001$). Post-discharge mortality (1 to 6 months) was higher among renal failure patients (17.4% vs 3.8%; $p < 0.02$).
Conclusion: Patients who had renal failure at the time for electronic device implant were older and showed a higher amount of unfavorable clinical outcomes during hospital stay and after hospital discharge, as well. This finds suggest that the electronic cardiac device implant should be avoided or employed more judiciously among these patients.

P1083

Comparing physical,cognitive and psychological aspects of frailty before and after LVAD implantation-a retrospective study

EL E-Lynn Sng[1]; H Chen[1]; CP Lim[1]
[1]National Heart Centre Singapore, Singapore, Singapore

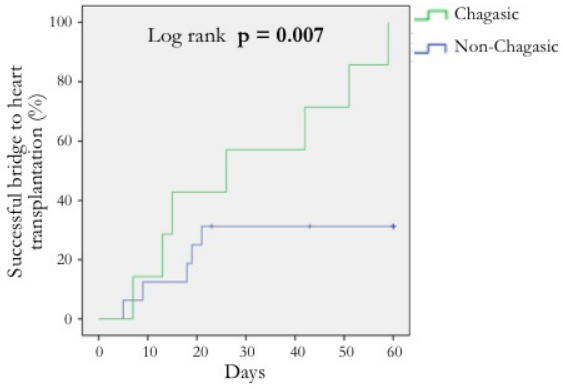
Background: Frailty is a biological syndrome characterized by weakness, fatigue and increased vulnerability to physiologic stressors. In patients with heart failure, the presence of frailty is associated with significantly worse outcomes due to the lack of physiologic reserve which may cause rapid functional deterioration and debility.
Purpose: To describe the prevalence of pre-operative physical frailty, cognitive impairment and depressive symptoms in patients referred for left ventricular assist device (LVAD) implantation and their impact on post-operative outcomes.
Methods: This is a retrospective review of patients referred for frailty assessment from January 2015 to August 2017. Frailty assessment was conducted at baseline and 3-months post-LVAD implantation. Physical frailty was assessed using the Fried Frailty Phenotype. Cognitive impairment was assessed using the Montreal Cognitive Assessment (MoCA) questionnaire. Screening for depression was done using the Center for Epidemiologic Studies Depression Scale-Revised (CESD-R). Post-LVAD implantation, all patients received multidisciplinary care, including inpatient physiotherapy rehabilitation.
Results: 22 patients (mean age of 56 years; 86% male and 14% female) had frailty assessment prior to their LVAD implantation. Of these patients, 50% were implanted as destination therapy and the other 50% as bridge to transplantation. 6 patients died before post-implantation assessment, 2 patients were lost to follow up, and 3 patients were awaiting frailty reassessment. 11 patients had both baseline and 3-months frailty reassessments performed. Prior to LVAD implantation, 6 out of 11 patient (54.5%) were considered extremely frail. 54.5% had cognitive impairment and 45.5% had possible depressive symptoms. At 3-months post-LVAD implantation, there were significant improvements in physical frailty, cognitive and psychological domains. None were considered extremely frail and 54.5% were non-frail. Only 9% still present with impaired cognition and 18.2% had possible depressive symptoms. Extremely frail patients were associated with a greater average length of stay (LOS = 34.8 days) as compared to intermediate frail patients (LOS = 26.0 days) and non-frail patients (LOS = 14.0 days). Extreme frailty was present in 54.5% of survivors versus 66.7% of patients who died within 3-months after LVAD implantation.
Conclusion: There was an improvement in the physical frailty, cognitive function and depression score after LVAD implantation. Extreme physical frailty was associated with prolonged hospitalization, but did not preclude a successful outcome after surgery.

P1084

Mechanical circulatory support as bridge to heart transplantation in Chagas cardiomyopathy: A single-centre 10-year experience.

JLV Vieira[1]; MGVS Sobral[1]; GGV Vasconcelos[1]; GPLA Almeida[1]; JRF Fernandes[1]; VLMPP Pessoa[1]; LCS Souza[1]; VRFC Cestari[1]; DLS Salles[1]; RSF Florencio[1]; DFMT Trompieri[1]; JDSN Souza Neto[1]; JACM Mejia[1]
[1]Hospital de Messejana Dr Carlos Alberto Studart Gomes, Division of Advanced Heart Failure and Transplant Cardiology, Fortaleza, Brazil

Background: Chagas cardiomyopathy (CC) is a major public health disease in Latin America and, due to migration, is becoming a worldwide health burden. Although heart transplantation (HT) was formerly contraindicated for CC, it is currently established as an important therapeutic option in patients with refractory heart failure (HF) due to CC. Considering the worse prognosis of CC patients listed as UNOS 1 as compared to non-chagasic patients (NCP) in the same condition, the use of inotropes, vasopressors and mechanical circulatory devices (MCS) should be valued in that etiology. However, the published data on MCS in patients with CC is scarce.
Purpose: We sought to determine the safety and feasibility of the implantation of MCS as a bridge to HT in patients with refractory HF due to CC.
Methods: We retrospectively assessed our experience with MCS in refractory HF over a 10-year period. We included any adult patients mechanically bridged to HT from January 2008 to December 2017. Information regarding the follow-up status was obtained from in-patient and outpatient clinical charts and telephone contact.
Results: Since 2008, we mechanically bridged 23 adults with refractory HF to HT. Seven of these patients had end-stage HF due to CC. Bridged CC patients were all male ($p = 0.21$ vs. NCP), with a mean age of 44.6 ± 13.8 years ($p = 0.31$ vs. NCP). We used the Abiomed AB500™ (n = 5) and the CentriMag™ (n = 2) (p = NS vs. NCP for both). Mean MCS support time was 26 days [range 7-58] ($p = 0.39$ vs. NCP). All CC patients were successfully bridged to HT in less than 60 days (log rank $p = 0.007$ vs. NCP, graphic).



Conclusion: Our experience shows that MCS in chagasic patients is associated with higher successful bridging when compared to non-chagasic patients. The favourable characteristics of chagasic patients, such as fewer comorbidities and lower pulmonary pressures, could be an advantage for a MCS indication in advanced HF. The major limitation to its applicability is its high cost.

P1085

Effect of sildenafil on hemodynamic parameters measured by right heart catheterisation in pts with end-stage chronic heart failure

K Krisztina Heltai[1]; L Vandor[1]; A Boros[1]; B Merkely[1]
[1]Semmelweis University Heart Center, Budapest, Hungary

Background: Sildenafil has been used in primary pulmonary hypertension (PH), however it is also has empirically administered to end-stage chronic heart failure

patients (CHF) with secondary PH being eligible for heart transplantation (HTX). Here, we aimed to test the effect of sildenafil on the hemodynamic parameters of right heart catheterisation (RHC) in this patient population.
Methods: In this single-centre, retrospective study a total of 34 CHF pts (7 woman, 27 men, age 53 ± 11 years) were admitted to the Heart and Vascular Center of Semmelweis University between 2013-2017 for eligibility check-up of HTX with increased pulmonary vascular resistance (PVR) (measured by right heart catheterisation: 5,9 ± 1,79 Wood unit). All patients underwent RHC at baseline and after 3 months sildenafil treatment (20 mg t.i.d., orally administered). 12 pts went through HTX or ventricular assist device implantation within 3 months, so there was no control measurement in them. Complete data was available in 22 cases.
Results: The cardiac output improved (3.2 ± 0.9 vs 3.7 ± 0.8 L/min, p = 0.06), the pulmonary capillary wedge pressure remained unaltered (25 ± 5 vs. 25 ± 7 mmHg, p = 0.71), both pulmonary artery pressure (43 ± 6 vs. 39 ± 10 mmHg, p = 0.05) and PVR decreased (5.6 ± 1.7 vs. 4.2 ± 1.4 Wood, p = 0.008). The clinical status of patients improved during the observational period and no adverse event occurred related to sildenafil.
Conclusions: We found that sildenafil treatment is safe and effective in CHF patients for reducing pulmonary vascular resistance and therefore it could be an optimal therapeutic choice in patients with secondary PH and helps to maintain the clinical status of pts waiting for HTX.

P1086
The influence of personalized program of physical trainings on tolerance to physical loading, aerobic physical capacity and character of myocardial vascularization in patients with terminal heart fail

V Volha Sujayeva[1]
[1]*Republican Scientific and Practical Centre of Cardiology, Minsk, Belarus*

Purpose: to develop personalized program of cardiac rehabilitation of patients with terminal heart failure before and after heart transplantation based on pathophysiological mechanisms of tolerance to physical loading decreasing and to estimate its efficiency.
Methods: 32 patients with terminal heart failure before heart transplantation (age 46.4 ± 12.1 y.o.) and 81 pts after heart transplantation (age 45.2 ± 12.1 y.o.). We defined both tolerance to physical loading (TPL) and aerobic physical capacity in condition of Spiro Bicycle Ergometry Test (spiroBET) before heart transplantation (I test), in 6 and 12 month after heart transplantation (II and III test, correspondingly). In the same times we also performed echocardiography (EcoCG) and endomyocardial biopsy (EMB) to study both myocardial rejection and character of myocardial vascularization.
Results: Before heart transplantation al pts had low TPL - 62.9 ± 4.4 Wt (33.9 ± 2.3% of age-appropriate level). Patients were randomized in to 2 Groups: Group 1 received individual controlled bicycle physical trainings, pts in Group 2 didn't have bicycle physical trainings. Type of the training load depended on individual character of blood circulatory system reaction on spiroBET. The main principle of the training loading selection - taking into the account individual level of power when anaerobic threshold was reached. In Group 1 we established more pronounced improvement of TPL than in Group 2. TPL in Group 1 increased from 62.9 ± 4.4 Et - at I test to 118.8 ± 23.9 Wt - at III test ($p < 0.05$), in Group 2 - to 87.5 ± 17.7Wt, $p < 0.05$. We estimated aerobic physical capacity according to maximal oxygen uptake (VO2max) level. It was 19.9 ± 4.0 ml/kg/min in Group 1 and only 15.4 ± 6.2 ml/kg/min - in Group 2 at III test ($p < 0.05$). In Group 1 we also revealed more pronounced than in Group 2 improvement of systolic and diastolic function of a left ventricle according to EcoCG within 12 months after heart transplantation ($p < 0.05$).
The average number of vessels on 10 fields of vision haven't changed significantly during all period of study: it was 69.5 ± 17.4 in Group 1 and 68.0 ± 13.3 - in Group 2 at the I test, 63,7 ± 12.4 and 70.8 ± 15.6 - at II, and 65.2 ± 3.3, 77.9 ± 7.0 - at III test, correspondingly (?>0,05). The sum of vessels on 10 fields of vision also haven't changed: it was 694.6 ± 173.8 and 679.7 ± 132.5 - in Group 1 and 2 at the I test, 637.4 ± 123.8 and 708.3 ± 155.9 - at the II test, 588,8 ± 117.2 and 779.0 - at III test, accordingly (?>0,05).
Thus, the cardiac rehabilitation improves TPL and aerobic physical capacity without significant influence on character of microvasculature in patients with heart failure after heart transplantation.

P1087
Treatment with ivabradine at the start of multidisciplinary care in an Advanced Heart Failure Unit

G L Alonso Salinas[1]; S Del Prado Diaz[2]; M Pascual Izco[2]; JM Vieitez Florez[2]; A Lorente[2]; M Abellas[2]; S Hernandez Jimenez[2]; M Plaza Martin[2]; E Gonzalez Ferrer[2]; JL Zamorano[1]
[1]*Health Institute Carlos III, CIBERCV, Madrid, Spain*; [2]*Hospital Universitario Ramón y Cajal, Cardiology, Madrid, Spain*

Background: Heart failure (HF) is the commonest reason for hospital admission in > 65 years patients, and is the first in-hospital cause of health expenditure in Spain. Maintaining heart rate (HR) below 70 bpm in these patients improves functional class and prognosis. Ivabradine is a negative chronotropic drug that, in patients in sinus rhythm treated with beta-blockers, has been shown to improve HR control and functional class. The aim of this study is to analyze the population that start a multidisciplinary care program in an Advanced Heart Failure Unit (AHFU) and receive ivabradine at the first visit.
Methods: All patients treated in the AHFU were analyzed. Only those in sinus rhythm were selected and data were collected from the physical examination, echocardiogram, treatment and blood samples. In addition, 6-minute walking test was performed to evaluate the functional class and hospital admissions during the follow-up were collected.
Results: From May'16 to March'17, 200 patients were evaluated, 87 (43.5%) of them were in sinus rhythm. Of these 87 patients, 17 (19.5%) were treated with ivabradine. Baseline characteristics of this sample is summarized in Table 1.
Patients on ivabradine had a lower LVEF than patients without ivabradine. In the first visit the patients were treated equally with ACEIs/ARBs and Beta-blockers. Patient treated with ivabradine tended to have a lower HR. There were no differences in functional class or admissions during the follow-up.
Conclusions:
Treatment with ivabradine at discharge can help to control the HR in patients with HF. Larger studies are needed to correlate it with prognosis or functional class during follow-up.

	Ivabradine (n = 17)	No ivabradine (n = 70)	p
Age (years)	69.7 ± 15.5	70.7 ± 16.4	0.83
Female sex	5 (29.4%)	21 (38.2%)	0.51
LVEF (%)	29.9 ± 7.9	36.5 ± 12.7	0.05
BNP (pg/ml)	700.9 ± 439.2	611.7 ± 644.4	0.68
Beta-blockers	14 (82.4%)	45 (81.8%)	0.96
ACEIs/ARBs	11 (64.7%)	37 (67.3%)	0.84
HR in visit 1 (bpm)	67.6 ± 9.4	73 ± 14.2	0.08
6-minutes walking test (m)	288.7 ± 53.4	257.4 ± 129.5	0.69
Admission rate	4 (23.5%)	10 (18.2%)	0.63

Table 1

P1088
Low-intensity dynamic and isometric exercises are safe and well tolerated in an early phase of ADHF

K Kinga Wegrzynowska-Teodorczyk[1]
[1]*University School of Physical Education of Wroclaw, Physiotherapy, Wroclaw, Poland*

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Physical training is recommended for stable HF patients, in accordance with class A recommendations of the ESC. Experts point out the need for early patient activation after the episode of AHF decompensation, which may prevent disability but there are no reports on the safety and effectiveness of the exercises in this phase.
The aim of the study was to assess the safety of early isometric and dynamic exercises in ADHF.
A study group comprised 18 patients admitted to our centre due to acute decompensated HF (100% male, median age 60 years, median NT-proBNP 5286 pg/mL, 15 with HFrEF - median LVEF 25%, 7 ischemic; 5 with HFpEF median LVEF 55%).
The haemodynamic parameters (CI, HR, BP, SVR) were monitored during 2 exercise tasks: isometric and dynamic. Isometric exercise included 45 repetitions of isometric contractions (1-2 seconds of contractions of the quadriceps thigh muscle with 50% MVC, followed by relaxation lasting two seconds). Dynamic exercise comprised 45 extensions of the lower limb in the knee joint (from the 45-degree bending position in the joint).
During dynamic and isometric exercises neither serious cardiac arrhythmias nor any signs of myocardial ischemia were observed (See: Table 1).
Supervised low intensity dynamic and isometric exercises performed in the early phase of AHF are safe and well tolerated by patients. The presented results may constitute to the basis for further research to develop cardiac rehabilitation specific for AHF.

P1088 Table 1

Variables	Median at Rest	Isometric Exercise (Median)	Dynamic Exercise (Median)	Rest vs. Isometric (p value)	Rest vs. Dynamic (p value)
HR (bpm)	84	81	90	0,72	0,58
SBP (mmHg)	120	125	116	0,89	0,34
DBP (mmHg)	78	78	77	0,62	0,71
CI [l/ min./ m2]	2,5	2,8	2,7	0,09	0,11
SVRI (dyn.s/cm5.m^2)	2698	2490	2628	0,08	0,61

HR - Heart Rate, SBP - Systolic Blood Pressure, DBP - Diastolic Blood Pressure, CI - Cardiac Index, SVRI - Systemic Vascular Resistance Index; p value was calculated using the Sign Test.

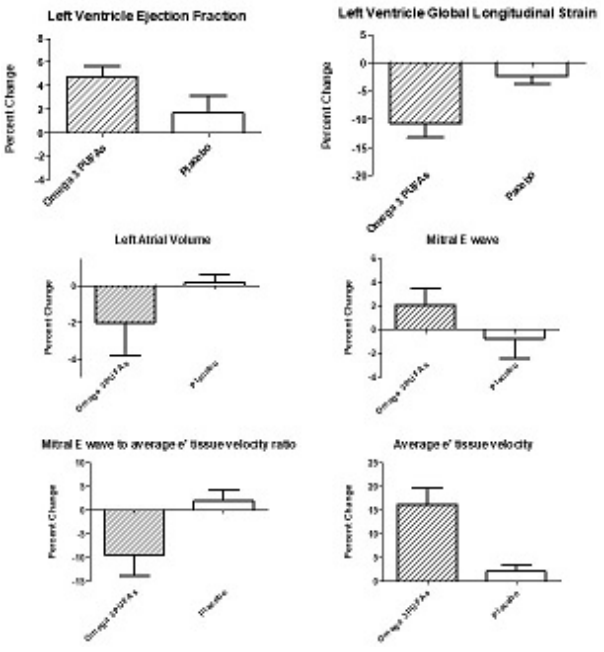
Comparison of the resting haemodynamic parameters with parameters obtained during dynamic and isometric exercises

P1089

Effects of Omega 3 polyunsaturated fatty acids on fibrosis, endothelial function and myocardial performance, in ischemic heart failure patients

E Evagelos Oikonomou[1]; G Vogiatzi[1]; D Karlis[1]; G Siasos[1]; C Chrysohoou[1]; T Zografos[1]; G Lazaros[1]; S Tsalamandris[1]; K Mourouzis[1]; G Georgiopoulos[1]; M Toutouza[1]; D Tousoulis[1]
[1]*Hippokration Hospital, University of Athens, 1st Department of Cardiology, Athens, Greece*

Background: Polyunsaturated fatty acids (PUFAs) may affect the cardiovascular system with a multiplicity of mechanisms. However, the exact mechanisms of action in patients with heart failure (HF) is unknown.
Purpose: To assessed the effects of Omega-3 PUFAs supplements on inflammation, fibrosis, left ventricle performance and endothelial function of ischemic HF patients.
Methods: In this double-blind, placebo controlled, cross-over trial we enrolled 31 patients with ischemic HF. Omega-3 PUFAs (2g daily, 8 weeks) were administered PO in the intervention arm. Left ventricle ejection fraction (EF), global longitudinal strain and the ratio E/e' (early ventricular filling to early mitral annulus velocities) were measured. Endothelial function was evaluated by flow mediated dilation and myocardial fibrosis by soluble ST2.



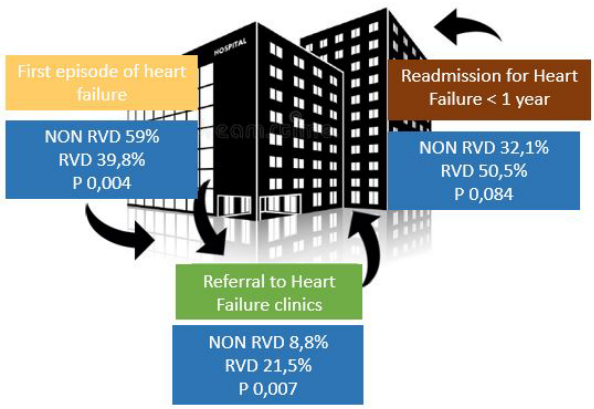
Results: At baseline there was no difference in the examined values (left ventricle EF, global longitudinal strain, and the ratio E/e') between the two treatment arms. Treatment with omega-3 PUFA, compared to placebo, improved: left ventricle EF (percent increased by 4.7% vs 1.7%, $p < 0.001$); global longitudinal strain (decreased by -10.6% vs -2.3%, $p < 0.001$); the E/e' ratio (decreased by -9.47% vs -2.1%, $p = 0.005$); ST2 levels (decreased by -4.53% vs -2.37%, 0.02); and flow mediated dilation (percent increased by 44% vs. 11%, $p = 0.003$). Interestingly, in the Omega-3 PUFAs treatment arm the improvement in FMD was associated with the improvement in the E/e' ratio ($r=-0.48$, $p = 0.005$)
Conclusion: Short term treatment with Omega-3 PUFAs in subjects with stable ischemic HF improved inflammatory and fibrotic status as well as endothelial function in parallel with systolic and diastolic performance of left ventricle. These findings emphasize the various beneficial mechanisms of Omega 3 PUFAs in patients with ischemic HF.

P1090

Patients with heart failure and right ventricular dysfunction: characterization and differential management

TS Tania Sonia Luque Diaz[1]; A Travieso Gozalez[1]; CN Perez Garcia[1]; D Enriquez Vazquez[1]; C Olmos Blanco[1]; J Higueras Nafria[1]; D Vivas Balcones[1]; I Vilacosta[1]
[1]*Hospital Clinic San Carlos, CARDIOLOGY, Madrid, Spain*

Introduction: Right ventricular dysfunction (RVD), traditionally little studied, is a prognostic marker and has important implications in different clinical conditions, such as heart failure (HF). The present study describes the clinical characteristics of patients with HF and RVD, defined with a TAPSE value of less than 17mm, as well as the main differences in the management of these with respect to patients with preserved right systolic function.
Methods: For one year, the clinical histories of patients admitted to the Cardiology service of a tertiary hospital with a diagnosis of HF have been evaluated prospectively, recording their baseline characteristics and their treatment during admission and discharge.



Results: The baseline characteristics of the patients are shown in table 1. Of the 321 patients included in total, 93 patients presented RVD. These patients were men in greater frequency and had a worse cardiovascular risk profile, although fewer patients had COPD among their antecedents. More cases were associated with depressed LVEF, especially if it was less than 40%. Analyzing the triggers of heart failure, in more cases in the RVD group it was not known and to a lesser extent it was the first episode. We also found difference in hospitalization time and NTproBNP at discharge.
Regarding treatment, patients with a lower TAPSE took more diuretic at admission (71% vs 48%, p = 0.001) as well as MRA (33% vs 18%, p = 0.014) and digoxin (18% vs 6%; p = 0.002). At discharge, more beta-blocker (77.4 vs 69.8), diuretic (82% vs 69.4), MRA (40.7 vs 24.5) and digoxin (16.1 vs 7.1) were used, although only the latter was statistically significant (p = 0.045). The use of ACEI or ARB was similar. Finally, more patients in the RVD group received an implantable automatic defibrillator (18.3% vs. 5.4%, p = 0.001), and they were referred to heart failure clinic visit at discharge (44.1% vs 19.8% ; p = 0.000)
Conclusion: The presence of RVD was not infrequent in patients admitted for HF, and was associated with a worse cardiovascular risk profile and lower LVEF. A shorter hospital stay and a higher value of NTproBNP at discharge were observed in these patients, and it was related to a greater use of diuretics, MRA and digoxin, more placement of an automatic defibrillator and greater referral to the HF clinical visit at discharge.

P1091

The effect of allopurinol on all-cause mortality and hospitalization in heart failure with reduced ejection fraction: a propensity-matched analysis

D Ural[1]; K Karauzum[2]; A Kandemir[3]; O Argan[4]; I Yilmaz Karauzum[2]; G Kozdag[2]; A Agir[2]
[1]Koc University, Istanbul, Turkey; *[2]Kocaeli University, Faculty of Medicine, Department of Cardiology, Kocaeli, Turkey*; *[3]Kocaeli University, Hereke Vocational School, Kocaeli, Turkey*; *[4]Kocaeli State Hospital, Department of Cardiology, Kocaeli, Turkey*

Background and Purpose: Hyperuricaemia is common in heart failure (HF) and may be caused or worsened by renal dysfunction and diuretic treatment. Although hyperuricaemia is associated with a poorer prognosis in HF with reduced ejection fraction (HFrEF), the effect of urate-lowering therapy with xanthine oxidase inhibitors is uncertain. This study aims to evaluate the association of allopurinol usage with all-cause mortality and hospitalization risk in HFrEF patients.
Methods and Results: This study was a retrospective propensity-matched analysis of HFrEF patients attending a HF clinic between years 2003 and 2016. Allopurinol prescription at discharge and its association with all-cause mortality and HF hospitalization was examined in median 55 ± 33 months follow-up. Of 629 patients (mean age 65 ± 12 years; 66% men), 112 (17.8%) were prescribed allopurinol due to hyperuricemia (uric acid level >8.5 mg/dl). Patients prescribed allopurinol had more frequent right-sided HF, lower haemoglobin, lower estimated glomerular filtration rate and albumin levels than the patients without allopurinol prescription. After propensity-matching, 108 couples were established according to presence and absence of baseline allopurinol usage. A total of 107 (49%) patients died during the follow-up period. In Cox regression analysis, allopurinol use was associated with a significantly increased mortality risk compared to not using allopurinol (HR = 1.38; 95% CI 1.18-1.53; p = 0.001), but this was not statistically confirmed by the propensity-matched analysis (HR = 1.06; 95% CI 0.65-1.35; p = 0.738). In both prematch and propensity matched analysis, allopurinol use was not associated with risk of hospitalization.
Conclusions: In this study, allopurinol therapy in HFrEF patients did not affect all-cause mortality and hospitalization risk during a long-term follow-up. These results suggest decision to use allopurinol in HFrEF should not be based on uric acid level alone, but also on the associated conditions like risk of developing gut and arthritis.

P1092

Like a bridge over troubled waters: VA-ECMO as a bridge to transplantation INTERMACS 1 to 3

V Vera Marinho[1]; S Costa[1]; F Franco[1]; R Baptista[1]; P Alves[1]; J Milner[1]; C Domingues[1]; J Ferreira[1]; D Prieto[1]; F Goncalves[1]; M Pego[1]; M Antunes[1]
[1]University Hospitals of Coimbra, Cardiology, Coimbra, Portugal

Introduction: Veno-Arterial Extracorporeal Membrane Oxygenation (VA ECMO) is an effective and increasingly used therapy in patients with advanced heart failure (HF) in severe INTERMACS strata as a bridge to high-urgency heart transplantation (BTT). We analyzed the use and outcomes of VA-ECMO for BTT in our cohort of advanced HF patients.
Methods: We conducted an observational, retrospective study including all patients admitted to our HF unit and described the clinical characteristics and outcomes of patients who received VA-ECMO as BTT. The primary endpoint was heart transplantation (HTx) and the secondary endpoint 30-day all-cause mortality.
Results: A total of 12 patients received VA-ECMO as a BTT. The median age was 50 [36-64] years and 50% were female. Familiar dilated cardiomyopathy (33%), coronary artery disease (25%) and post–inflammatory cardiomyopathy (25%) were the most common causes for HF. The mean LVEF was 22[20-25]% and the median cardiac index was 1.7[1.3-2.2] L min-1. Most patients had pulmonary hypertension (75%). Before insertion, 58% were under inotropic support with two drugs and 17% with 3 drugs; one patient was in electrical storm without inotropic support. In 36% of patients, acute kidney injury with need of continuous hemofiltration was present and 64% were mechanically ventilated. Accordingly, regarding the INTERMACS classification, 58% were in profile 1, 25% were in profile 2 and 1 patient in profile 3. The median time in VA-ECMO was 7(2-12) days. The major complications due to VA-ECMO included thrombocytopenia (64%), bleeding (55%) and nosocomial infection (45%). Pericardial tamponade and femoral artery dissection occurred each in 1 patient. Regarding the primary outcome (heart transplantation), all patients were successfully transplanted. VA-ECMO was used in period post-transplant in 3 patients. At follow up, the 30 days all-cause mortality was 18%; in long term follow up the global mortality was 64%. Of these, 6 patients died during the immediate post-transplant period. The main causes of death were septic shock in 3 patients, primary graft dysfunction in 2 patients and acute humoral rejection in 1 patient. One patient died during the long term follow-up.
Conclusions: All patients in cardiogenic shock that received VA-ECMO were successfully transplanted. The post-transplant all-cause mortality is higher than for patients transplanted electively but in line with the published results from other centers.

P1093

Risks of therapeutic interchange in HFrEF

G Marazzi[1]; G Caminiti[1]; F Pelliccia[2]; L Iaia[3]; L Cacciotti[4]; G Cice[5]; R Massaro[1]; B Sposato[1]; M Volterrani[1]; G M C Giuseppe M C Rosano[1]
[1]San Raffaele Pisana Hospital IRCCS, Rome, Italy; *[2]Umberto I Polyclinic of Rome, Cardiology, Rome, Italy*; *[3]Giovanni Calibita Fatebenefratelli Hospital, Rome, Italy*; *[4]Ospedale Vannini, Rome, Italy*; *[5]Second University of Naples, Naples, Italy*

Therapeutic interchange or substitution of an originator cardiovascular drug with a generic drugs or drugs that are similar, albeit not identical, has raised several safety. Generic drugs are believed to be therapeutically similar. However, the interchangeability between generic drugs and the bio-creep that reduces their therapeutic equivalence to the originator may pose efficacy and safety issues in patients where a narrow therapeutic interval should be sought.
We assessed the pharmacodynamics equivalence of branded and generic beta-blockers in 612 patients with heart failure and reduced ejection fraction (HFrEF). Patients were started and up-titrated on branded bisoprolol/carvedilol/nebivolol/metoprolol and referred to their general practitioner for continuation of their prescriptions. Heart rate and blood pressure were assessed at discharge and at 1 and 3 months. At discharge heart rate was 62+7 bpm and blood pressure was 118+12 mmHg.Patients who remained on branded beta-blockers at 3 months showed no significant change in either heart rate or blood pressure while patients switched to generic beta-blockers showed a significant variability in heart rate and blood pressure values at 3 months compared to end of up-titration (Table 1). Patients switched to generic beta-blockers showed a greater need of dose adjustment and augmentation of diuretic therapy. No difference between branded beta-blockers and branded generics was detected.
These findings suggest that in patients with HFrEF therapeutic interchange should be practiced with caution. Originator and branded generics have similar pharmacodynamics while non-branded generics do not guarantee adequate safety and efficacy, thereby suggesting that drugs to be used in HFrEF should be classified as drugs with narrow therapeutic interval.

Table 1

	Branded beta-blockers (pooled)	Generic beta-blockers (pooled)
Mean age Male Diabetics Hypertensives NYHA III NYHA II	67+8 72% 23% 45% 38% 62%	67+8 74% 25% 41% 32% 68%
Patients at 3 month Heart Rate at 3 months Systolic Blood Pressure at 3 month Patients requiring unplanned visits/hospitalisations/increased diuretic therapy	236 61+6 118+16 2	369 66+11* 124+25* 14

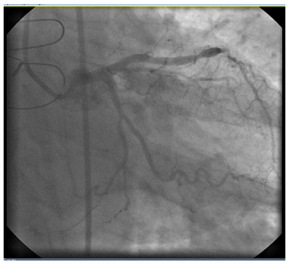
* = p < 0.02Heart rate (bpm) - Blood pressure (mmHg)

P1094

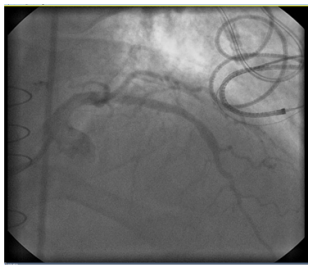
Initial experience with sirolimus in cardiac transplant patients with graft vasculopathy

L Lavanya Saiva[1]; S Murphy[1]; N Boyle[1]; C Halley[1]; N Mahon[1]; J O'neill[1]
[1]*Mater Misericordiae University Hospital, Heart and Lung Transplant Unit, Dublin, Ireland*

Background: Cardiac allograft vasculopathy (CAV) is the leading cause of graft loss in heart transplant recipients. Sirolimus is an immunosuppressant drug with potent anti-proliferative and anti-migratory effects and is used to reduce progression of CAV. We present our initial experience with sirolimus in patients with CAV.
Methods and Results: We retrospectively analyzed all our patients in whom sirolimus was commenced for CAV. Baseline characteristics of patients, indications for sirolimus, benefits and adverse effects of sirolimus were studied.
At our center total 9 patients with CAV (diagnosed by coronary angiogram) were commenced on sirolimus. The mean age of the patients was 48.8 years ± 11.8 years (range 28-62 years), 44% (n= 4) of patients were female, and 55% (n= 5) were male. The median time from heart transplant to diagnosis of CAV was 10.9 years ± 1.77 years (range 9-14 years).
All patients on sirolimus were also on tacrolimus for maintenance immunosuppression. Mycophenolate mofetil or Azathioprine was discontinued prior to starting sirolimus. The average combined tacrolimus and sirolimus levels in our patients was 11.4 ± 2.0 and median time to achieve target levels was 44.8 ± 28.7 days. The average duration of therapy on combined sirolimus and Tacrolimus was 52.8 ± 12.6 weeks.
Sirolimus was well tolerated by all 9 patients. Repeat coronary arteriography was performed in 6 patients. There was no progression of CAV in 5 patients and in 1 patient there was marked regression of CAV. No Rejection episodes (ISHLT2R or 3R) were reported during sirolimus therapy.
With regards to side-effect profile, Peripheral odema (n = 1), herpes zoster (n = 1) and oral ulcers (n = 1) were reported. No patient had to discontinue sirolimus due to side-effects.
Conclusion: We conclude that sirolimus is a safe and well-tolerated, viable treatment option for patients affected by CAV, with disease stabilization in all patients and significant regression in one patient



Left anterior descending artery (LAD) disease prior to sirolimus



LAD disease regression post sirolimus

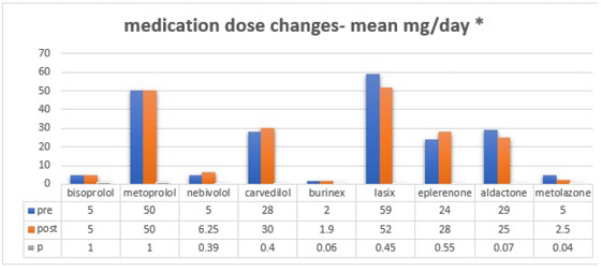
P1095

Reduced thiazide diuretic use in hfref patients taking sacubitril/valsartan (arni)

T Mannion[1]; L O Connor[1]; B Mcadam[1]; S James[1]; J Kelly O Haire[1]; G O Gara[1]
[1]*Beaumont Hospital, Supportive Heart Service, Dublin, Ireland*

Background: Post-hoc analyses from PARADIGM-HF have shown treatment with ARNI was associated with dose reductions in diuretics compared to Enalapril. Purpose To examine clinical & medication changes in HFrEF patients following treatment with ARNI.
Methods: Using a Pre-Test Post-Test Design data was collected on 43 HFrEF patients prior to initiating ARNI & post achieving max tolerated dose (mean 18 months range 2 -36). Indices of cardiac function were recorded including Left Ventricular Ejection Fraction (LVEF) vital signs (Systolic & Diastolic Blood Pressure) biochemical measures (BNP NT pro BNP renal function & electrolytes), functional capacity (NYHA Class) & changes in cardiac medications. Paired sample t-test was used to assess for statistically significant changes.
Results: Use of metolazone reduced by 12.6% (p0.04), but no significant dose changes were found in other cardiac medications (figure 1). A statistically significant change was found in LVEF with a mean increase of 7.5% (±10.5% p0.00) but there was no significant change in NYHA Class (p0.32) or QRS Duration (p0.07). Systolic BP reduced by mean 5.7mmHg (±17.6mmHg p0.04). NT pro BNP levels reduced from mean 2900pg/mL to 1662pg/mL (mean reduction of 1238pg/mL p0.04) but no significant change was found in BNP levels. Sodium levels increased by a mean of 0.9mEq/L (±2.4mEq/L p0.02) but no significant changes were found in other electrolytes/renal function (table 1)
Conclusion(s): In this small study use of ARNI was associated with more thiazide diuretic dose reduction & cessation (n = 4) but no change in loop diuretic use. There was a non-significant increase in serum sodium levels & renal function remained stable. This data suggests that treatment with ARNI results in reduced use of thiazide diuretics but does not appear to affect doses of loop diuretic/MRA in this cohort despite a modest increased in LVEF.

*note metolazone dose mg/week



Dose changes post ARNI fig 1

P1096

Disease management programs in austian heart failure patients

CM Brandstetter[1]; C Claudia Stoellberger[1]
[1]*Rudolfstiftung Hospital, Department of Internal Medicine II, Vienna, Austria*

Background: Nowadays there are multiple ways to improve the prognosis of heart failure including pharmaco- and device therapy. Nevertheless, decompensated heart failure is still common and hospitalization rates in patients with heart failure are high. To better control patients' well-being as well as their daily drug intake, Disease Management Programs (DMPs) have been developed and are recommended as class IA in the European Society of Cardiology heart failure guidelines. In Austria, discrepancies in the acceptance of DMPs have been observed which are, so far, not clarified. We hypothesized that patients in rural and urban regions may have different attitudes toward DMPs.
Methods: In a prospective study, patients hospitalized because of heart failure were asked by using a preset questionnaire comprising 40 questions about their opinion on DMPs and about their knowledge and attitude about heart failure management. Two different groups were defined: one consisted of patients hospitalized in a rural area, the other comprised patients living in a big city. The survey results between the rural and urban patients were compared.
Results: Sixty patients (females n = 26, mean age 76, range 40-94 years) were included, 30 each in a hospital in a rural area and in a big city. Significant differences between rural and urban patients were found regarding the acceptance of nurse-based DMPs (p= 0.029) which was higher among rural patients. The level of willingness to be included into a telenursing-based program was the same for both groups (p = 0.441). Patients from rural areas tend to accept nurses more likely in their private surroundings than patients living in an urban environment (p = 0.114). While the patients' knowledge of heart failure is similar in both population groups and overall adequate, their views on the current medical treatment vary: According to 50% of the rural patients the primary care physician is responsible for the follow-ups, whereas urban patients would rather go see a specialist for their follow-ups; 36,7% of urban patients chose that option.
Conclusion: Nurse-based DMPs seem to be more accepted by patients from rural areas than by patients living in big cities. DMPs for urban patients have to be developed according to their special needs.

P1097

Tolerability of sacubitril/valsartan when initiating/uptitrating in real-life patients. Initial experience in two centres.

C Goena Vives[1]; C Gomez Ramirez[2]; L Quintas Ovejero[1]; R Garcia Martin[1]; I Luis Serret[1]; R Natividad Andres[2]; I Sagasti Aboitiz[2]; M Campana Lazaro[2]
[1]*Mendaro's Hospital, Cardiology, Mendaro, Spain*; [2]*Cruces University Hospital, Cardiology, Barakaldo, Spain*

Introduction: PARADIGM-HF demonstrated the benefits of sacubitril/valsartan (SV) in patients with heart failure and reduced ejection fraction.

Purpose: Assess the tolerability of initiating/uptitrating SV and causes of no achieving the target dose in a real world registry.
Methods: Retrospective, non-protocolized study in non-selected outpatient patients with LVEF = 40% which start SV between october 2016-august 2017.We evaluated:clinical profile, tolerability, adverse effects (death, hospitalization, cardiovascular event or ventricular arrhythmias),the cause of treatment disruption or not achieving de 200mg b.i.d. dose.
Results: SV was initiated in 90 patients with mean age:66 years (43-92), 71 male (78.8%).The mean follow up time was 204 days (minimum 30 days).In our cohort the percentage of ischaemic disease was 48.8%.The mean LVEF was 27.8% (10%-40%).42.2% had LBBB with QRS duration >130 ms and 56,6% were carriers of devices:ICD, CRT-D or CRT-P.The mean basal NT-proBNP level was 2055 pg/mL (186-10989) with mean GFR of 69.44 (34 -133), mean Creatinine 1.10 mgr/dL (0.47-1.96) and mean potassium levels of 4.62 mEq/L (3.2-5.6).68.8% of patients were NYHA II/II-III, 13.3% III/IV and there is no patient NYHA I/I-II before treatment was started.Despite not achieving target SV dose there was a significant improvement in the NYHA situation when the trial stopped:12.2% NYHA I/I-II and 86.6%NYHA II/II-III.In most of the cases de initial SV dose was 50mgr b.i.d.The low dose of 50 mgr b.i.d. was the one selected for starting in most of the cases (just 13.3% (N = 12) started directly 100 mg b.i.d.).93.3% (N = 84) of patients continue with the treatment. 34.5% (N= 29) achieved and maintained the SV 200 mg b.i.d. dose and 28,6% (N= 24) the SV 100 mg b.i.d. without dose interruption/down-titration. 23.8% (N= 20) were treated with low-dose SV 50 mg b.i.d. and 13.1% (N= 11) underwent a SV dose not described in the pivotal study (1 patient with 24/26 + 49/51 and 10 with 49/51+ 97/103 mg).The treatment was discontinued in 6 patients. The main causes of not achieving the target dose were: symptomatic SBP <95 mmHg (34%, N = 19) and still titration (32.1%, N = 18).Significant renal impairment and hyperkalemia were documented in 9 and 4 patients respectively. Adverse events are infrequent.There are no angioedema, VT/FV or cardiovascular events. There are 8 cases of decompensation requiring hospital admission (1 patient was included in a palliative care home hospitalization program) and 2 died (a sudden death and a cardiogenic shock with contraindication for cardiac transplantation).
Conclusions: Initiation/uptitration of SV had a tolerability profile in line with other treatments. However, not all patients are able to tolerate the doses recommended due to dose-related adverse effects. In our initial experience with real-life patients (more symptomatic and more users of devices comparing to Paradigm),SV has an accurate security profile and improves quality of life and exercise tolerance.

P1098

ARNI treatment in hfref patients with and without pre-existing renal dysfunction-results from initial experience in single centre.

T Mannion[1]; L O Connor[1]; B Mcadam[1]; S James[1]; J Kelly O Haire[1]; G O Gara[1]
[1]*Beaumont Hospital, Supportive Heart Service, Dublin, Ireland*

Background: PARADIGM HF demonstrated the favorable cardio-renal profile in patients with HF with ARNI when compared to Enalapril with and without renal dysfunction.
Purpose: To examine clinical & biochemical changes in HFrEF patients, with & without pre-existing renal dysfunction after initiation of ARNI.
Methods Using a Pre-Test Post-Test Design data was collected on 43 Heart failure with reduced ejection fraction (HFrEF) (35 male 8 female mean LVEF 24.5% ± 6.7% & mean NYHA Class II) prior to initiating ARNI & following max tolerated dose (mean 18 months range 2-36). 66.7% had a cardiac device insitu (35.4% CRTD 29.2% ICD 2.1% PPM). Indices of cardiac function were recorded including LVEF, vital signs, biochemical measures (BNP NTproBNP renal function & electrolytes) while functional capacity was determined based on NYHA Class. Changes in cardiac medications over time were recorded. Patients were then categorized based on degree of renal dysfunction at baseline prior to initiating ARNI (Normal GFR >90, mild renal dysfunction GFR = 60-89 & moderate renal dysfunction GFR = 30-59).
Results For all patients assessed, mean baseline eGFR was 69.3 with no significant change in mean eGFR (2, p0.51) after 18 months therapy. Maximum tolerated dose of ARNI achieved, categorized by renal dysfunction is presented in figure 1. All patients were maintained on treatment for the duration of review with 1 patient requiring down titration of ARNI due to hypotension. There were no significant changes in creatinine/ eGFR in the patients between the different categories of renal function. Nor was there any significant change in plasma electrolytes between groups. Interestingly there was statistically significant change in LVEF with a mean increase of 7.5% (over the 18-month period). This finding remained statistically significant among groups categorized based on renal dysfunction. There was no appreciable changes in vital signs (see table 1) but there was an increase in BNP from baseline (from mean of 393pg/mL to 570, mean increase of 177pg/mL ± 189 pg/mL) in patients with moderate renal dysfunction following max titration of ARNI. No significant change was found in NTproBNP levels in this cohort. There was no change in mean doses of concomitant HF treatments.
Conclusion(s): Overall these findings indicate that ARNI does not compromise renal function in HFrEF patients even in those with pre-existing renal dysfunction. Pre-existing renal dysfunction at baseline did not preclude titration of ARNI to maximal dose. These findings confirm that ARNI can be safely used in HFrEF patients with mild-moderate renal dysfunction & there was no adverse impact on hemodynamics. The observed significant increase in BNP in HFrEF patients with moderate renal dysfunction, is a known pharmacological effect of ARNI but there was no change in NTproBNP levels in this cohort. In this small observational study we observed a small increase in LVEF following treatment with ARNI.

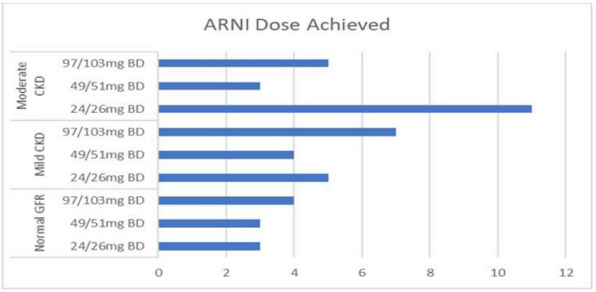


Figure 1

P1099

Effect of combination therapy of azilsartan and metoxipoliethylenglicol epoietin beta two-year survival of patients CHF with anaemia hospitalized because decompensated heart failure

K Kamala Zahidova[1]; FA Guliyev[1]
[1]*The Azerbaijan State Advanced Training Institute for Doctors , Baku, Azerbaijan*

On behalf of: Heart Failure and anaemia

Backround: The implementation into clinical of new therapeutic strategies that could improve the prognosis of patients with heart failure(HF) with reduced EF (HFrEF) with anemia remains relevant. Innovative approach is to restore imbalances of neurohumoral systems by inhibiting angiotensin II receptor.
Purpose: To asses the impact of combination therapy by angiotensin-II reseptor blockers azilsartan and Metoxipolyethylenglicolepoitin beta (MEB) of prognosis of patients CHF with anemia of hospitalized decompensated HF.
Methods. We analyzed data of hospital register of decompensated HF which comprised information on 840 patients with HFrEF ishemic aethyologi and anemia consecutively admitted in 2016-2017 years. Median follow-up was 1970 days. The level of Hb was Hb < 10 g/dl. It should be noted that in patients decompensated HF with anemia hypoerythropoietinemia was noted up to 2,3 ± 1.1 IU/ml. The 390 (46,4%) patients from them have received treatment by azilsartan in dose 20-40 mg in day and MEB in dose 50 IU in day in one months. The remaining 450 (53,6%) patients of decompensated HF combination by azilsartan and MEB did not receive. The register included cases of hospitalization in association with symptoms of HF whose severity corresponded to NYHA III-IV class and also patients in CHF with NYHA II class only in the presence of a clinical picture of acute pulmonary edema following ingestion.In the multivariate analysis of the prognosis and survival, the logistic regression method and the Cox model were used, the data are presented in the form of odds ratio (OR) and 95% confidence intervals (95%CI).
Results: The absence of combination treatment by azilsartan and MEB in 450 (53,6%) patients of decompensated HF with anemia was associated with increased risk of death: during the index hospitalization due to acute decompensated HF (HR 1.6, 95%CI 1,2-2.9), within 12 months (HR 1.3, 95%CI 1,2-1.9).The present of treatment by azilsartan in dose 20-40 mg in day and MEB in dose 50 IU in day in one months by 390 (46,4%) patients of acute decompensated HF with anemia, was associated with decreased risk of death.The mortality in it investigation was above 8,2 % -(68 patients died), which corresponds to the level of mortality in acute decompensated HF accordance with the European registers.The mortality in the group of patients in acute decompensated HF with anemia who did not receive combination therapy was above 6,4 % -(54 patients died). The mortality in the group of patients in acute decompensated HF with anemia, who receive combination therapy by azilsartan in dose 20-40 mg in day and MEB in dose 50 IU in day in one months was above 1,6 % -(14 patients died).
Conclusion: According to the Cox model, a decrease in Hb < 10 g/dl is a predictor of death.The absence of correction of anemic syndrome and appropriate therapy of angiotensin-II reseptor blockers azilsartan in patients in CHF increases risk of death of acute decompensated HF.

P1100

A retrospective observational study assessing the utilisation of sacubitril-valsartan in a single centre in the Eastern Province in Saudi Arabia

MM Alqaseer[1]; D Abdulhadi[1]; H Alrammah[1]; M Ibrahim[1]; U Ismail[1]; VJ Nambiar[1]; M Kharasani[1]; B Mushannen[1]
[1]*King Fahad Specialist Hospital, Cardiology Department, Dammam, Saudi Arabia*

Background: The landmark PARADIGM-HF trial had rapidly shifted our therapeutic approach to patients with heart failure with reduced ejection fraction (HFrEF). Within a year of the release of the trial, sacubitril-valsartan had become a cornerstone therapy in patients with symptomatic HFrEF who had not shown a marked improvement with angiotensin converting enzyme inhibitors (ACE-i) in the absence of any major contraindications to sacubitril-valsartan. In this paper, we will describe a single center's experience of utilizing this agent, highlighting its impact on our patients.
Methods: This is a retrospective observational study looking at consecutive patients that have received sacubitril-valsartan in a single center in the Eastern Province of Saudi Arabia between February 26th, 2017 and December 1st, 2017. Basic demographic data was gathered of the patients including their comorbidities and their renal function and ejection fraction prior to initiating therapies and compared against their follow up echocardiographic and laboratory studies.
Results: 34 patients were initiated on sacubitril valsartan in the hospital. Out of these patients, 19 were male, constituting 55.9% of the patient population at hand. 56% of the patient's were diabetic, 47% were hypertensive, 65% had ischemic heart disease, 38% were dyslipidemic and 9% had atrial fibrillation. The average ejection fraction of those patients prior to initiating the therapy was 27% with an average functional class of predominantly III. The average dose administered for these patients is 200mg daily. The two main causes of inability to uptitrate to the maximum dose include are slow uptitration strategy preference by the end user and hypotension. The average eGFR prior to initiation of therapy was normal at 83. 100% of the patients were on beta blockers and had received and ACE-I or ARB prior to switching. Only a third of the patients were on MRA at baseline. At follow up, the average ejection fraction had improved to 34% with improvement of functional class by an average of I class and maintenance of the eGFR with an average value of 86.
Conclusion: The utilization of sacubitril-valsartan in our patient setting was done in keeping with the PARADIGM-HF criteria. It showed a beneficial improvement of ejection fraction with an absolute improvement of 7%, and an improvement of functional class by one level, yet maintaining adequate renal function.

P1101

The limited triple therapy prescription does not depend on clinical features of heart failure patients discharged from Internal Medicine

V Verdiani[1]; A Fortini[2]; L Masotti[3]; M Alessandri[4]; G Cati[4]; C Belcari[5]; P Fabiani[6]; S Spolveri[2]; FA Tarmum[2]
[1]*Internal Medicine, Grosseto, Italy*; [2]*Internal Medicine, Florence, Italy*; [3]*Internal Medicine, Empoli, Italy*; [4]*Internal Medicine, Massa Marittima, Italy*; [5]*Internal Medicine, Pontedera, Italy*; [6]*Internal Medicine, Viareggio, Italy*

On behalf of: SMIT Study Group

Introduction: Guidelines (GL) recommend triple therapy with angiotensin-converting enzyme inhibitor (ACEI), beta-blocker (BB) and aldosterone antagonist (AA) in symptomatic heart failure (HF) patients with ejection fraction (EF) < 35 %. Nevertheless, many patients remain untreated.
Methods and Purpose: We analyzed database of a multicenter observational study (published SMIT study) on 770 patients consecutively hospitalised for HF in 32 Internal Medicine Units of Tuscany (Italian region with 3.7 million inhabitants). We selected HF patients with EF < 35% and compared features of patients treated with triple therapy (TT) respect ones untreated to identify if there were patient-dependent obstacles to follow GL recommendations in this subset of real world HF patients.
Results: The HF patients with EF < 35% was 117. At only 46 (39,3%) had been prescribed TT at discharge. TT untreated patients were mainly women (78% vs 61.9% P = 0.06) and older (mean age 78.4 vs 77.5 years, P = 0.07). In this group there was a greater number of patients with hypertension (61.9% vs 58.6% P = 0.50), Diabetes mellitus (43.6% vs 36.9% P = 0.47), Clearence Creatinine < 60 ml/min (74.6% vs 67.3% P = 0.39), Anemia (52.1% vs 45.6% P = 0.46), Atrial fibrillation (40.8% vs 34.7% P = 0.51), although none of these differences reached statistical significance. None difference about COPD. TT untreated group had a significantly greater number of patients with deficit cognitive (25.3% vs 10.8%, P = 0.04) and a major mean length of hospital stay (10.1 vs 8.4 days, P = 0.01).
Conclusions: only at a minority of HF patients discharged from Internal Medicine units had been prescribed TT. The results of our research indicate that, compared with treated patients, untreated patients were probably sicker and more complex, but, except for deficit cognitive, none singular feature was significantly prevalent. We conclude that there is space to implement guidelines recommendation also in this group of patients.

Chronic Heart Failure - Clinical

P1102

The relation between beta-adrenergic blockade and weight changes in patients with chronic heart failure

S Shirley Sze[1]; P Pellicori[2]; S Kamzi[1]; A Anton[1]; AL Clark[1]
[1]*Castle Hill Hospital, Hull, United Kingdom*; [2]*University of Glasgow, Glasgow, United Kingdom*

Background: Weight loss is common in patients with chronic heart failure (CHF) and is associated with adverse outcome. Activation of the sympathetic nervous system has been implicated in weight loss, wasting and cachexia. However, the effect of sympathetic antagonism on weight change in patients with CHF is not well defined.
Methods: We evaluated changes in body weight, the incidence of cachexia (weight loss > 6%) and significant weight gain (<5%) in unselected patients with CHF due to left ventricular systolic dysfunction (LVSD) (LV ejection fraction (LVEF) < 40%) and studied the effect of beta-blockade on weight change.
Results: Of the 1480 patients enrolled (median NTproBNP:1651ng/L, median LVEF:31%), 86% received beta-blocker, 11% never had beta-blocker and 3% discontinued beta-blocker between baseline and 1 year.
Patients who did not have or tolerate beta-blocker were more likely to develop cachexia (23% vs 10%, p < 0.001) and less likely to have significant weight gain (22% vs 24%, p < 0.001) than patient who had beta-blocker.
During a median follow up of 1876 days (IQR: 993-3052 days), 894 (60%) patients died. Higher body mass index (BMI) at baseline, weight gain and beta-blocker therapy were associated with better outcome. Patients who had all 3 features: beta-blocker therapy, baseline BMI = 25 and significant weight gain had the best outcome (22% mortality at 5 years) (Table 1).
Conclusion: Patients with CHF due to LVSD who receive beta-blocker were less likely to develop cachexia and more likely to have significant weight gain and better outcome compared to patients who did not receive or tolerate beta-blocker.

P1101 Table 1

	Weight change and BMI categories						
BMI≥25	BMI <25						
Weight gain >5%	weight change: -6% to +5%	Weight loss >6%	Weight gain >5%	Weight change: -6% to +5%	Weight loss >6%		
Betablocker (BB) therapy at baseline (BL) & 1 year (1y)	BL & 1y: BB	22% (N = 132)	28% (N = 455)	42% (N = 67)	31% (N = 80)	39% (N = 146)	46% (N = 26)
BL: No BB;1y: BB	40% (N = 55)	34% (N = 151)	42% (N = 36)	42% (N = 52)	42% (N = 60)	46% (N = 13)	
BL & 1y: No BB	37% (N = 19)	50% (N = 70)	56% (N = 27)	56% (N = 18)	38% (N = 21)	73% (N = 11)	

Percentage 5 year mortality in patient with HeFREF according to categories of weight change, BMI and beta-blocker therapy.

P1103

UTILITY OF BIOIMPEDANCE IN THE MONITORING OF PATIENTS WITH CONGESTIVE HEART FAILURE

A M Ana Maria Campos Pareja[1]; E Gutierrez Carretero[1]; J Rosell Ferrer[2]; A Ordonez Fernandez[1]
[1]University Hospital of Virgen del Rocio, Cardiology, Seville, Spain; *[2]Polytechnic University of Catalonia, Barcelona, Spain*

Funding Acknowledgements: Talemnology

Introduction: In the management of Congestive Heart Failure (CHF), an unmet need is to detect, for at-risk patients, at an early stage, fluid retention in order to avoid the high number of hospitalizations that for this reason they generate. For this reason different mechanisms are being developed that help patients to be able to detect early decompensations of their heart disease.
Objective: and justification: Our objective is the clinical validation of a medical wearable device based on measurement of localiced bioimpedances. This device would allow an early recongnition of fluid retention
Material and Methods: Material and methods Patients admitted to the Heart Area with signs suggestive of systemic congestion have been prospectively included. They were given an "Information Sheet", and the "Informed Consent" was obtained. The measurements of localized bioimpedance were performed on a daily basis with a experimental non invasive wearable device. During patients admission, impedance were obtained daily putting a experimental device with four electrodes that are attached to skin four finger cross above the ankle. Obtained values were correlated with analytical, clinical and echocardiographic parameters associated with decompensation of chronic congestive heart failure.
Results: Eighty patients were selected (66,3 ± 12 years. 76,3 % males). 28,6% patients had impaired renal function. Mean NT-ProBNP was 5978 pg /ml at admission. 45,6% patients had edemas at admission classified as grades 2 and 3.34,6% patients had a reduced left ventricular systolic function,52,9% patients had right ventricular systolic disfunction and 41,8% patients had pulmonary hypertension. Percentiles of the bioimpedance measurements obtained at 50 Hertz were 17.6, 22, 27.1 and 45.9 ohmios. This measures were statistically correlated with right and left ventricular function (p = 0,015) pulmonary hypertension (p = 0,000), use and doses of furosemide (p = 0,000), sodium levels and lower limbs edemas grades (p = 0,000). There was no association with ages, hypertension, diabetes or obesity.
Conclusions: Bioimpedance measurement is correlated with exploratory, analytical and echocardiographyc data related to fluid retention. This preliminary results are promising in that the device could be useful as an alert to about fluid retention, allowing an earlier consultation and treatment.

P1104

Reduced muscle-derived irisin reflects low muscles mass and impaired functioning of skeletal muscles in men with heart failure with reduced ejection fraction

M Kasztura[1]; M Dziegala[1]; KA Kobak[1]; M Tkaczyszyn[1]; M Drozd[1]; K Wegrzynowska-Teodorczyk[2]; K Josiak[3]; J Bania[4]; L Kiczak[5]; W Banasiak[6]; P Ponikowski[3]; EA Jankowska[1]
[1]Wroclaw Medical University, Department of Heart Diseases, Laboratory for Applied Research on Cardiovascular System, Wroclaw, Poland; *[2]University School of Physical Education of Wroclaw, Faculty of Physiotherapy, Wroclaw, Poland*; *[3]Wroclaw Medical University, Department of Heart Diseases, Wroclaw, Poland*; *[4]Wroclaw University of Environmental and Life Sciences, Department of Food Hygiene and Consumer Health, Wroclaw, Poland*; *[5]Wroclaw University of Environmental and Life Sciences, Department of Biochemistry, Pharmacology and Toxicology, Wroclaw, Poland*; *[6]Military Hospital of Wroclaw, Cardiology Department, Centre for Heart Diseases, Wroclaw, Poland*

Funding Acknowledgements: Financially supported by National Science Centre (Poland) grant no. 2012/05/E/NZ5/00590

Background: Irisin is a circulating hormone-like myokine which regulates energy metabolism in several tissues, including adipose, bone and muscle ones. Adequately high production of irisin is related to optimal exercise capacity and metabolic homeostasis.
Purpose: We assessed the production of irisin in peripheral blood and in the blood draining exercising forearm muscles in relation to the mass and functioning of skeletal muscles in men with heart failure and healthy men.
Methods: Study population comprised of 53 men with stable heart failure with reduced ejection fraction (HFrEF) (LVEF = 40%); mean age: ± 64 years; NYHA class I-II: 87%) and 15 middle-aged healthy men. Lean mass of upper extremities were determined by DEXA (dual-energy X-ray absorptiometry). We analysed the levels of irisin in plasma samples from peripheral blood from all patients by ELISA. Further, we analyzed samples taken from antecubital veins which drain the forearm muscle before and after local physical exercise (standardized 5-minute handgrip exercise) for the aforementioned myokine.
Results: There were no differences in irisin levels measured in peripheral blood samples between HF patients and healthy controls. The levels of irisin in peripheral blood were not associated with NTproBNP, eGFR or CRP in both men with HF and healthy controls. There was a relationship between reduced irisin concentrations in peripheral samples and both decreased fat content in the four extremities (R = 0.35, p < 0.05) and low lean tissue mass of the upper extremities (R = 0.37, p < 0.05). Elevated irisin level was associated with longer distance in 6-minut walking test in HF patients (R = 0.37, p < 0.05). There was a correlation between concentrations of irisin in peripheral blood and in the forearm samples in HF patients (R = 0.54, p < 0.001) whereas it is not observed in healthy controls. HF progression expressed as NYHA class was associated with decreased level of irisin measured in forearm samples (R= -0.28, p < 0.05). Lower concentrations of irisin assessed both before and after exercise in forearm samples of men with HF were associated with lower lean tissue mass of the upper extremities (R = 0.47, p < 0.001; R = 0.39, p < 0.01). Reduced irisin was related to lower fat content both in upper extremities (R = 0.37, p < 0.01) and in all 4 extremities (R= 0.32, p < 0.05). There was no correlation between irisin and inflammatory marker IL 6 in the forearm samples in HF patients.
Conclusions: Reduced circulating irisin from the blood draining exercising muscles reflects decreased skeletal mass in patient with HF.

P1105

Reduced muscle strength and quality of life in patients with heart failure with preserved ejection fraction compared to healthy controls and patients with heart failure and reduced ejection fraction

T Bekfani[1]; S Derlien[2]; A Hamadanchi[1]; J Nisser[2]; E Froeb[1]; UC Smolenski[2]; G Lehmann[3]; G Wolf[3]; S Moebius-Winkler[1]; PC Schulze[1]
[1]University Hospital of Jena, Department of Cardiology, Jena, Germany; *[2]University Hospital of Jena, Institute of Physiotherapy, Jena, Germany*; *[3]University Hospital of Jena, Department of Endocrinology, Nephrology and Rheumatology, Jena, Germany*

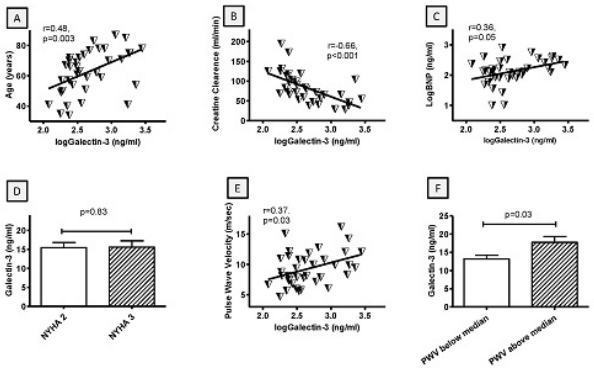
Purpose: To compare skeletal muscle function, body composition and quality of life (QoL) among symptomatic and clinically stable outpatients with heart failure (HF) with both preserved (HFpEF) and reduced ejection fraction (HFrEF) and age-matching healthy controls (HC).
Methods: 55 participants were recruited prospectively at the University Hospital Jena: 19 HFpEF, 18 HFrEF, 18 HC (Age: 71 ± 6 vs. 68 ± 9 vs. 66 ± 7 years; sex (m/f): 8/11 vs. 15/3 vs. 7/11; BMI: 28.5 ± 4.6 vs. 27.9 ± 5.3 vs. 26.1 ± 4.3 kg/m2, respectively). All participants underwent standardized tests including echocardiography, cardiopulmonary exercise test (CPET), 6-minute walk test (6MWT), muscle function tests, balance tests, blood tests, QoL assessment as well as muscle biopsies from the vastus lateralis.
Results: HFpEF patients had worse bone mineral contents in both arms and legs (p < 0.05), reduced muscle mass in the trunk (muscle mass in the trunk/BMI 0.8 ± 0.2 vs. 1.0 ± 0.3, p = 0.02) and worse muscle strength both in arms (Peak torque internal rotation of the right shoulder 150° 24.4 ± 11.9 vs. 34.6 ± 14.0 Nm, p = 0.02) and legs (Peak torque knee eccentric extension 30°/right leg lean: 12.9 ± 5.0 vs. 18.0 ± 5.9 Nm/kg, p = 0.02). Patients with HFpEF scored worse in HADS-Questionnaire (Anxiety: 5.8 ± 3.6 vs. 2.8 ± 2.8, p = 0.02). Compared to HC, skeletal muscle dysfunction in patients with both HFpEF and HFrEF develops independently of age (p = 0.1). Patients with HFpEF and HFrEF showed worse exercise capacity both in 6MWT (495.6 ± 82.7 vs. 466.8 ± 131.8 vs. 600.7 ± 59.5 m, p = 0.001) as well as in the CPET (Peak VO2: 17.1 ± 4 vs. 14.9 ± 3.7 vs. 22.5 ± 3.1 ml/min/kg, p = 0.0001), reduced walking speed (10 m walking test: HFpEF vs. HFrEF vs. HC: 6.3 ± 1.6 vs. 6.8 ± 2.7 vs. 4.9 ± 0.8 sec. p = 0.01), worse balance capacity in walking forward and backward (p = 0.02) and worse muscle function in both extremities (Peak torque internal rotation dominant shoulder 150°/body weight%: 30.0 ± 12.9 vs. 37.5 ± 12.3 vs. 41.3 ± 11.4, p = 0.02; peak torque knee eccentric extension 30°/ body weight%: 139.5 ± 55.3 vs. 181.4 ± 40.2 vs. 202.9 ± 56.0, p = 0.004). Furthermore, patients with HF reported worse QoL (VAS: HFpEF vs. HFrEF vs. HC: 67.8 ± 19.2 vs. 62.7 ± 15.6 vs. 83.4 ± 10.1; P = 0.003). Interestingly, comparing HFpEF and HFrEF patients showed no significant difference in the reported daily physical activity in spite of the reduced muscle strength in patients with HFpEF (94.4 ± 53.1 vs. 74.2 ± 42.7 MET, p = 0.2). Peak torque internal rotation of the dominant shoulder 150°/body weight % correlated stronger with Peak VO2 in HFrEF than HFpEF (p = 0.001 r= 0.69 vs. p < 0.05, r = 0.46).
Conclusion: Patients with heart failure with preserved ejection fraction have worse muscle strength and quality of life compared to both healthy controls and patients with heart failure and reduced ejection fraction. Skeletal muscle dysfunction in patients with both HFpEF and HFrEF occurs independently of age and physical activity.

P1106

Cross talk between arterial stiffening and myocardial fibrosis in patients with heart failure: The role of galectin-3

E Evagelos Oikonomou[1]; D Karlis[2]; S Tsalamandris[2]; G Siasos[2]; C Chrysohoou[2]; G Vogiatzi[2]; S Dimitropoulos[2]; G Marinos[2]; G Charalambous[2]; E Kouskouni[2]; D Tousoulis[2]
[1]*Hippokration Hospital, University of Athens, 1st Department of Cardiology, Athens, Greece*; [2]*University of Athens Medical School, 1st Cardiology Department, "Hippokration" Hospital, Athens, Greece*

Background: Cardiac performance depends on optimum ventriculoarterial coupling which is impaired in patients with heart failure (HF). Galectin-3 is a mediator of myocardial fibrosis and remodeling, and is associated with clinical status in patients with chronic HF.
Purpose: To examine the association of arterial stiffness with galectin-3 levels in patients with HF of ischemic etiology.
Methods: We consecutive enrolled 40 subjects with stable ischemic HF and reduce ejection fraction. Central aortic stiffness was evaluated non-invasively by measurement of arotid femoral pulse wave velocity (PWV). Among other factors serum levels of galectin-3 and b-type natriuretic peptide (BNP) were measured in blood samples.
Results: The median values of galectin-3 in our study population was 12.9 (10.8-18.7) ng/ml and the mean value of PWV in our study population was 9.31 ± 2.79 m/sec. There was significant association of Galectin-3 levels with age (r = 0.48, p = 0.003) with creatine clearance (r=-0.66, p < 0.001) and with BNP levels (r = 0.36, p = 0.05). Importantly there was a significant association of Galectin-3 levels with pulse wave velocity (r = 0.37, p = 0.03) and patients with PWV above median had also significant increase levels of galectin-3 compare to patients with lower values of PWV [16.1(11.8-25.2) ng/ml vs. 12.1(10.5-14) ng/ml, p = 0.03] (Figure).
Conclusions: In the present study we found that there is association of arterial stiffness and PWV with galectin-3 levels in patients with chronic HF of ischemic etiology. These findings imply an additive alternative pathway driving arterial stiffening and myocardial remodeling in HF which give insight in the mechanism determining prognosis and clinical status of patients with HF.



Figure

P1107

Relationship between body composition characteristics and endothelial dysfunction according to heart failure types

A Orea-Tejeda[1]; R Sanchez-Santillan[1]; D Gonzalez-Islas[1]; L Castillo-Aguilar[1]; C Chavez-Mendez[1]; R Olivo-Villalobos[1]; G Davila-Said[1]; V Pelaez-Hernandez[1]; A Figueroa-Herrera[1]; M Rivera-Rodriguez[1]; K Balderas-Munoz[1]
[1]*Instituto Nacional de Enfermedades Respiratorias "Ismael Cosío Villegas", Heart Failure and Respiratory Distress Clinic, Mexico city, Mexico*

Introduction: Body composition has been identified as a risk predictor morbidity and mortality in heart failure (HF) patients. However, is unknown what differences are on body changes according to heart failure type
Purpose: To evaluate the relationship between endothelial dysfunction (ED) and body composition in patients according to heart failure type.
Methods: A total of 776 outpatients older than 18 years with chronic and stable HF, from our Heart Failure Clinic, were including in a cross-sectional study. We emphasized the roll of ED in the observed changes. Body composition was evaluated by bioelectrical impedance vector analysis (BIVA). Patients were divided in 3 groups: left heart failure reduced (HFrEP) or preserved ejection fraction (HFpEF), or right heart failure (RHF). Endothelial function was assessed by photoplestimography.
ED was considered in those with a maximum amplitude / over total time of the pulse wave (MAT / TT index) > 0.30 at rest and after post ischemia period.
Results: Of the total the 53% were male with a mean age 61.34 ± 17.15 years), in HFpEF and RHF predominating females 52.15 % and 37.04 %, p = 002, respectively. Weigth: 65.95 ± 16.77, 73.01 ± 21.46, 71.98 ± 21.81, p = 0.0007; Mid-Upper Arm Circumference: 28.37 ± 4.44, 29.81 ± 5.14, 29.31 ± 6.67, p = 0.051; Total Body Water (%) 56.30 ± 35.89, 52.09 ± 7.90,51.02 ± 7.21, p = 0.003; Extracellular water (%): 24.28 ± 3.10, 23.64 ± 3.58, 23.41 ± 3.06 P = 0.06; Phase Angle: 5.26 ± 1.40, 5.02 ± 1.28, 4.95 ± 1.05, p = 0.09; MAT / TT: 0.23 ± 0.18, 0.29 ± 0.09, 0.35 ± 0.06, p = 0.013, for HFrEP, HFpEF, RHF, respectively.
Conclusions: Muscle mass strength, and membrane cell integrity were worse in RHF, suggesting a most active inflammatory process.

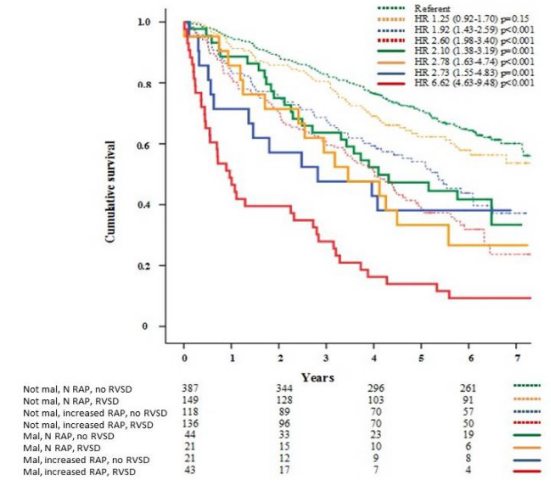
P1108

The relationship between malnutrition and congestion in chronic heart failure

S Shirley Sze[1]; P Pellicori[2]; J Zhang[3]; AL Clark[1]
[1]*Castle Hill Hospital, Hull, United Kingdom*; [2]*University of Glasgow, Glasgow, United Kingdom*; [3]*Anglia Ruskin University, Cambridge, United Kingdom*

On behalf of: n/a
Funding Acknowledgements: n/a

Background: Mechanisms leading to malnutrition in chronic heart failure (CHF) are not fully understood. CHF is a condition characterised by systemic venous congestion. We hypothesized that malnutrition in CHF is related to right heart dysfunction and congestion which predispose to bowel oedema and malabsorption, thereby leading to malnutrition.
Methods: We assessed malnutrition using the geriatric nutritional risk index (GNRI) and studied its association with congestion, assessed either clinically or by echocardiography, in a large cohort of patients referred to a community CHF clinic.
Results: Of the 1058 patients enrolled, CHF was confirmed in 952 (69% males, median age 75(interquartile range (IQR):67-81) years, median NTproBNP 1141 (IQR: 465-2562) ng/L). 39% had HF with reduced (HeFREF, LVEF < 40%) and 61% had HF with normal (HeFNEF, LVEF = 40% and NTproBNP>125 ng/l) left ventricular ejection fraction.
Overall, 14% of patients were malnourished (GNRI = 98). Clinical evidence of congestion, increasing right atrial pressure (RAP) and pulmonary artery pressure and right ventricular systolic dysfunction (RVSD) on echocardiography were associated with malnutrition. Addition of congestion variables to a model comprising of age and NTproBNP did not improve discrimination between malnourished and non-malnourished patients.
During a median follow-up of 1683 days (IQR: 1096-2230 days), 461 (44%) patients died. Malnutrition was an independent predictor of mortality. Patients who were malnourished with both RVSD and increased RAP had 6-fold increased risk of mortality compared to non-malnourished patients without RVSD and had normal RAP. (Figure)
Conclusion: Malnutrition and congestion are modestly correlated and each is independently associated with increased mortality in patients with CHF.



Figure

P1109

Prevalence of underlying gastro-intestinal malignancies in iron deficient heart failure.

P Pieter Martens[1]; L Minten[1]; M Dupont[1]; W Mullens[1]
[1]*Hospital Oost-Limburg (ZOL), Cardiology, Genk, Belgium*

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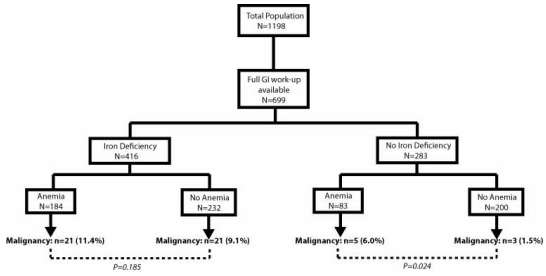
Background: Anemia and iron deficiency (ferritin < 100μg/l or 100-300μg/l with transferrin saturation < 20%) is prevalent in heart failure. Mechanistically, iron deficiency is linked to poor intestinal uptake, increased intestinal loss and chronic inflammation. However, the prevalence of underlying gastro-intestinal malignancies are not established in iron deficient heart failure with or without anemia.
Methods: Patients followed in a single-center, heart failure database with baseline registration of hemoglobin and iron-status were retrospectively evaluated. The proportion of patients undergoing upper and lower gastro-intestinal endoscopy between inclusion and censoring was determined. Afterwards the prevalence of biopsy confirmed intestinal malignancies in relation to baseline iron and hemoglobin status was determined. Anemia was defined according to WHO-criteria (hemoglobin < 12g/dl in females or < 13g/dl in males) and iron deficiency according to aforementioned criteria.
Results: Of the 1197 patients in the database, 699 (59%) patients underwent full endoscopic work-up over a mean follow-up of 50 ± 27 months. A total of 50 intestinal malignancies were identified (n = 42 [84%] in iron deficient vs n = 8 [16%] in non-iron deficient patients; p < 0.001). The prevalence of intestinal malignancies was highest in patients with iron deficient anemia (n = 21/184, 11%), however was not statically different from patients with iron deficiency without anemia (n = 21/232, 9%; p = 0.185). The prevalence was much lower in patients without iron deficiency, with (n = 5/83, 6%) or without anemia (n = 3/200, 1.5%). In patients with iron deficiency but without anemia (a group in which the role of endoscopic work-up is less established), a ferritin above 100 μg/L had a negative predictive value of 98.4% of excluding an underlying gastro-intestinal malignancies.
Conclusions: Endoscopic evaluation is warranted in heart failure patients with iron deficient anemia given the high prevalence of underlying intestinal malignancies. In patients with iron deficiency without anemia, an endoscopic workup might be reserved for patients with a ferritin bellow 100 μg/l, as a ferritin above this value carries a high negative predictive value to exclude the contribution of an underlying intestinal malignancy to the state of iron deficiency.



P1110

Hypovitaminozis d is related with inflammatory parameters in patients with heart failure

A Celik[1]; O Orscelik[1]; IT Ozcan[1]
[1]*Mersin University, Cardiology, Mersin, Turkey*

Introduction: Hypovitaminosis D has been observed to be highly prevalent in HF patients. Some data suggest that vitamin D deficiency is associated with the progression of HF and may be an independent predictor of mortality in patients with HF. Low vitamin D levels may contribute to the pro-inflammatory status present in HF, and may therefore play an important role in the development and progression of HF. Neutrophil lymphocyte ratio (NLR) is an accepted marker reflecting inflammatory status of body. In this study, we investigated the relationship between the level of vitamin D and NLR in patients with HF.
Methods: This is a single center observational study included the consecutive 57 HF patients (HFpEF, HFmrEF, HFrEF). Patients were divided into two groups according to vitamin D levels as < 20 ng/ml and = 20 ng/ml.
Results: The mean vitamin D level was 19.1 ± 12.4 ng/mL. There was no significant difference between HF types in terms of vitamin D levels (p = 0.53). Similarly, compared patients with lower and normal vitamin D levels, the properties of patients were similar (Table 1). Patients with lower vitamin D levels had significantly higher NLR and CRP value (Table 1). Vitamin D levels were significantly negative correlated with NLR levels (Figure 1).

Table 1

	Vitamin D <20 ng/mL (n = 34)	Vitamin D ≥20 ng/mL (n = 23)	p
Age, year	64.5 ± 11.8	65.9 ± 11.7	0.67
Gender, f/m	15/19	8/15	0.43
Presence of			
DM, n/%	18, % 52.9	12, %52.2	0.95
HT, n/%	24, %70.6	15, %65.2	0.66
Non-ischemic etiology	22, %64.7	12, %52.2	0.34
EF, %	33 (17-72)	39 (13-66)	0.94
Hemoglobin, g/dL	11.8 (8-17)	12.9 (7.9-17.2)	0.11
Creatine, mg/dL	1.0 (0.58-5.7)	1.1 (0.56-2.3)	0.59
CRP, mg/dL	8.9 (0.7-111)	4.2 (0.2-43.7)	0.02
proBNP, pg/mL	2518 (32-35000)	903 (3-10318)	0.25
NLR	3.7 (0.22-19)	2.7 (0.24-6.48)	0.03

The demographic and biochemical properties of patients

Conclusion: Hypovitaminosis D is associated with inflammatory status in HF patients. Vitamin D substitution may reduce pro-inflammatory parameters in HF. Further studies are needed to confirm the use of vitamin D for regression of inflammatory parameters in patients with HF.

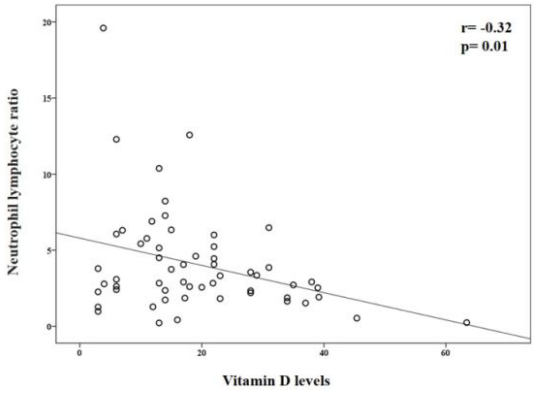


Figure 1

P1111

MIA syndrome - malnutrition, inflammation and atherosclerosis - in acute decompensated heart failure, prognosis and prevalence.

L Luisa Malvar Goncalves[1]; INÊS Pires[1]; LUÍS Abreu[1]; JULIO Pereira[1]; HUGO Antunes[1]; DAVIDE Moreira[1]; INÊS Almeida[1]; COSTA Cabral[1]
[1]*Hospital Sao Teotonio, Department of Cardiology, Viseu, Portugal*

Introduction: A strong association between malnutrition (M), inflammation (I) and atherosclerosis (A) suggests the presence of MIA syndrome, which is associated with high mortality (D). Cardiovascular disease is already associated with the 3 components (C) of MIA syndrome (MIAs). The concomitant presence of Heart Failure (HF) and MIAs should be a factor of poor prognosis.
Objective: The aim of this study was to evaluate the prevalence and prognosis of MIAs in Acute decompensated HF (ADHF).
Methods: We selected patients (P) admitted in a Cardiology ward by ADHF between 2007 and 2013. Follow-up of 24 months (m). The levels of PCR (< 0.50mg/ dL), albumin (< 3.5g/ dL), and the presence of dyslipidemia served as markers of I, M and A, respectively. The presence of MIAs was validated by the concomitant presence of 3 C (3-MIA), but the additive value of the C were also verified. Division into groups: 3-MIA, two C (2-MIA), one C (1-MIA) and zero C (0-MIA).

Results: Sample of 793 P, 50.7% male, mean age of 77.1 ± 10.2 years. 1-MIA in 42.4% (n = 336), 2-MIA in 39.3% (n = 312), 0-MIA in 11.7% (n = 93) and 3-MIA in 6.6% (n = 52). I in 78.7% (n = 624), A in 40.7% (n = 232) and M in 21.3% (n = 160). No differences in gender or age between P with 3-MIA and P without MIAs (0, 1 or 2 C). The P with 0 or 1-MIA had greater predominance of hypertension (HTA), whereas P with 2 or 3-MIA had a greater predominance of HTA and Diabetes (X2 = 17.7, p = 0.04). The higher the number of C, the more likely the P were medicated with loop diuretic (X2 = 10.3, p = 0.016) and statin (X2 = 95.3, p = 0.0001). P with 3-MIA had the lowest probability of HF diagnosis before hospitalization (X2 = 6.4, (p = 0.01), lower systolic and diastolic BP on admission (130.1 ± 26.0 vs 139.1 ± 30.9 mmHg, p = 0.02 and 76.5 ± 12.9 vs 81.3 ± 43.9 mmHg, p = 0.05, respectively), and higher mean GGT (243.9 ± 316.9 vs 95.3 ± 110.7 UI/L, p = 0.005), AST (292.3 ± 859.3 vs 49.1 ± 76.3 UI/L, p = 0.011) and ALT values (227.4 ± 597.4 vs 53.8 ± 144.5 IU/L, p = 0.023).
The presence of 3-MIA correlated with a greater interventricular septum thickness (11.7 ± 3.2 vs 13.0 ± 6.6 mm, p = 0.018) and greater number of days of hospitalization (11.3 ± 6.9 vs. 8.7 ± 6.7 days, p = 0.012). The MIAs did not correlated with rehospitalization for HF. The highest mortality rate at 3 and 6 months was found in P with 3-MIA, followed by 2-MIA, and finally the P with 0 or 1-MIA (Kaplan-Meier: X2 = 9.99, p = 0.019 and X2 = 9.52, p = 0.023, respectively). The multivariate analysis verified that the mortality was independent of the differentiating characteristics between the groups.
Conclusion: The presence of MIAs is common in HF and it is an independent factor of poor prognosis. An assessment of the presence of MIAs in practice will allow a more individualized approach, more rigorous follow-up and research of new therapeutic targets.

P1112

Chronic heart failure in liver transplant recipients: etiology, frequency, management.

A Babich[1]; H Kosmacheva[1]
[1]*the Scientific Research Institute-Regional Clinical Hospital 1 , Krasnodar, Russian Federation*

Background: Cardiovascular diseases are among the most frequent causes of patient death after liver transplantation. Due to recent improvements in survival of liver transplant, there is only few data available analyzing the prevalence and management of chronic heart failure (CHF) in liver recipients.
Purpose: The aim of this retrospective clinical study was to estimate the etiology, frequency and management of chronic heart failure before and after liver transplantation. A total of 115 patients who had undergone successful liver transplantation between 2010 and 2016 at the Scientific Research Institute-Regional Clinical Hospital ?1 were studied.
Results: Mean age was 53 ± 13 years and 66 (57.4 %) were men. Chronic heart failure was verified in 20.9% of patients before liver transplantation, among them NYHA class I - 37.5%, NYHA class II- 50%, NYHA class III - 12.5%. Chronic heart failure was considered to develop due to arterial hypertension in 58.3% of patients, due to coronary heart disease (CHD) in 37.5%, among them six patients had a combination of CHD and arterial hypertension. One case of anteroseptal myocardial infarction (CHF - NYHA class II), 3 new cases of CHF were registered as a complication of arterial hypertension 6 months after liver transplantation. Over 1 year, we observed elevation of new-onset CHF (13%) compared with preoperative, among them NYHA class I had 63.3%, NYHA class II - 36.4% (arterial hypertension and CHF - 90.9%, coronary heart disease and CHF - 9.1%).
Beta-blockers were administrated in 75%, among them 88.9% received nonselective agents - propranolol, 11.1% - bisoprolol before liver transplantation. 24 patients without cardiac pathology and CHF were assigned to propranolol, which is probably associated with portal hypertension in patients before liver transplantation. Retrospective analysis revealed that only 7.1% of recipients with CHF received beta-blockers after 6 months and 7.7% after one year transplantation. ACE inhibitors were received in 16.7% of patients before surgery, after 6 months and after one year - 3.6% and 10.3%, respectively.
Conclusions. The development of chronic heart failure arises after transplantation. We suggest that it is vitally important to manage transplant-related CHF effectively by paying our physicians' attention to administration of ACE inhibitors and beta-blockers.

P1113

Chronic kidney disease in diabetic chronic heart failure patients

EV Reznik[1]; VA Lazarev[1]; MS Komissarova[1]; ED Presnova[1]; IG Nikitin[1]; AV Salikov[2]
[1]*Russian National Research Medical University, Internal Disease 2 Department, Moscow, Russian Federation*; [2]*12 Moscow's Clinical Hospital, Moscow, Russian Federation*

Introduction and Purpose: ?omorbidities are common in chronic heart failure (CHF) and associated with increased mortality and morbidity risk, increased complexity of clinical management, increased disability and poor quality of life. Our purpose was to study chronic kidney disease in patients with chronic heart failure (CHF) and type 2 diabetes mellitus (T2DM).
Methods: We analyzed 1629 CHF patients who were hospitalized in multifield Moscow's Clinical hospital during 3 years. Left ventricular ejection fraction (LVEF, Simpson) < 45% was in 20.4% of CHF patients. 23.4% of CHF patients had T2DM. 47.2% of them had permanent atrial fibrillation. We estimated renal function (glomerular filtration rate - eGFR, CKD-EPI formula) and proteinuria in 137 patients with CHF and LVEF < 45% and T2DM (CHF-T2DM) without primary renal and oncological diseases. Median (interquartile range) of age was 61.0 (60.0-74.0) years; LVEF - 32.5 (23.0-42.0) %; HbA1c - 7.4 (6.4-8.3) %; NT-Pro-BNP 4430 (3570-12000) ng/l; 54.7% males. All patients received medical therapy in accordance with contemporary guidelines. Oral hypoglycemic drugs were prescribed to 35.8%, insulin - 28.2%, combination of oral hypoglycemic drugs and insulin - in 6.1% of CHF-T2DM patients. Duration of hospitalization was 9 (7-11) days.
Results: 95.4% and 83.2% of patients had arterial hypertension and myocardial infarction in anamnesis respectively, 15.3% had postinfarction aneurysm with thrombus in 42.9%. I NYHA class was in 2.7%, II - in 11.1%, III - in 80.3%, IV - in 5.9% of CHF-T2DM patients. eGFR was 50.9 (38.9-64.8) ml/min/1.73m2. Proteinuria was in 38.7% and its level was 0.5 (0.3-1.0) g/l. Chronic kidney disease 2 stage was in 26.2%, 3a - in 27.7%, 3b - in 28.5%, 4 - in 9.2%, 5 - in 3.1% of CHF-T2DM patients. Hemoglobin level was 134 (119-150) g/l. The death rate during follow-up was 23.6%. Mortality was higher in patient with lower eGFR (p = 0.007) and more severe CHF (higher NYHA class, p = 0.038) but wasn't associated with LVEF, NT-Pro-BNP, HbA1c.
Conclusions: 94.6% of patients with systolic chronic heart failure and type 2 diabetes mellitus have chronic kidney disease. Clinical severity of CHF and low renal function are associated with mortality risk in these patients. Future studies of mechanisms of cardiorenal syndrome and effective treatment methods are required to improve survival of patients with chronic heart failure and type 2 diabetes mellitus.

P1114

Persistence of periodic breathing/Cheyne-Stokes respiration after tilt table test during short term respiratory monitoring in patients with systolic heart failure

C Chiara Borrelli[1]; F Gentile[2]; F Rossari[1]; P Sciarrone[2]; C Passino[3]; G Mirizzi[3]; F Bramanti[3]; G Iudice[3]; M Emdin[3]; A Giannoni[3]
[1]*Sant'Anna School of Advanced Studies, Pisa, Italy*; [2]*University of Pisa, Pisa, Italy*; [3]*Gabriele Monasterio Foundation, Pisa, Italy*

Background: Although periodic breathing (PB: hyperventilation/hypopneas) and Cheyne-Stokes respiration (CSR: hyperventilation/apneas) are usually considered to occur in lying and sleeping conditions in patients with heart failure (HF), there are recent evidences that both phenomena may spread throughout the 24-hour.
Purpose: We aim to evaluate whether PB/CSR may be observed in awake and orthostatic conditions in patients with systolic HF.
Methods: A total of 202 chronic systolic HF patients on optimal guideline-recommended treatment (left ventricular ejection fraction of 33 ± 9%; 66 ± 12 years of age; 79% males) underwent beyond echocardiography, pulmonary function test, 24-h electrocardiographic and respiratory recording and neurohormonal evaluation (natriuretic peptides, plasma norepinephrine, renin activity and aldosterone levels), a short term attended respiratory monitoring during tilt table testing (10 minutes in clinostatism and 10 minutes in orthostatism). A short term scoring from 0 to 3 was created, with 0 being normal respiration, 1 and 2 being respectively PB and CSR disappearing in orthostatism and 3 being PB/CSR persisting in orthostatism.
Results: The prevalence of scores 0-1-2-3 were 54%, 12%, 22% and 11%, respectively. The score was predictive of apnea-hypopnea index severity at the 24-h recording (all p <0.001), both during daytime (from 0 to 3: 7 IR 2-15, 10 IR 3-15, 16 IR 8-25, 26 IR 12-33 events/h), nighttime (20 IR 6-29, 19 IR 13-31, 25 IR 18-36, 37 IR 25-48 events/h) and the 24-hour (13 IR 5-21, 13 IR 9-20, 21 IR 12-29, 32 IR 20-36 events/h). At univariate, logistic multinomial analysis predictors of persistence of PB/CSR in orthostatism were moderate to severe mitral regurgitation (MR), left atrial volume and baseline atrial fibrillation (AF), while at multivariate analysis only MR (OR 3.5, CI 1.04-11.8, p = 0,043) and AF (OR 4.4; CI 1.3-14.7; p = 0.017) resulted as independent predictors.
Conclusions: In HF patients, a short term recording performed during tilt testing is able to stratify the severity of PB/CSR both during daytime, nighttime and the 24-hour, with MR and AF being independently associated with persistence of PB/CSR in awake/orthostatic conditions.

P1115

Cognitively impaired versus cognitively non-impaired chronic heart failure patients: which distinctions?

A Anastasiia Solonovych[1]
[1]*NSC Institute of Cardiology M.D. Strazhesko, Heart Failure Department, Kiev, Ukraine*

Background: Cognitive dysfunction (CD) is one of the most common disorders in cardiovascular patients (pts). In chronic heart failure (CHF) CD is observed in more than half of pts and closely correlates with age, severity of disease and quality of life. Nevertheless, evidence of association between cognitive function (CF) and other clinical characteristics in CHF patients is still lacking.
Purpose: To compare the spectrum of clinical variables in CHF patients in relation to presence of CD.
Methods: 94 stable CHF pts, NYHA II-IV with left ventricular ejection fraction (LVEF) < 40% were examined. CF was evaluated by using standard MMSE and Shulte tests. Cognitive dysfunction was defined as MMSE= 26 points. Besides routine examination, the 6-minute walk test, quality of life evaluation by The Minnesota Living with Heart Failure Questionnaire (MLHFQ), interview by HADS questionnaire and flow-mediated vasodilatory response (FMVR) examination by standard cuff test were performed.
Results: CD (abnormal MMSE and Shulte tests) was observed in 60 (63.8 %) patients. There was no impact of gender, LVEF, hemoglobin level, diabetes on the results of CF tests. Simultaneously, CD in patients with CHF was associated with higher NYHA class (p = 0.0001), history of hypertension and coronary heart disease (CHD) (p = 0.004 and p = 0.001 respectively). Patients with cognitive impairment were significantly older (p = 0.0001), had worse MLHFQ score (p = 0.018), higher HADS depression score (p = 0.001), lower glomerular filtration rate (GFR) (P = 0.001), lower plasma iron (p = 0.046) and worse FMVR (p = 0.013) compared to non-CD patients.
Both MMSE score and results of Shulte test significantly correlated with the 6-minute walk test (r = - 0.492, p = 0.0001 and r = 0.464, p= 0.0001, respectively), with MLHFQ (r = -0.268, p = 0.018 and r = 0.327, p = 0.001, respectively), age (r = -0.492, p = 0.0001 and r = 0.464, p = 0.0001, respectively), GFR (r = 0.325, p = 0.001 and r = -0.221, p = 0.033, respectively) and with HADS depression score (r = -0.256, p = 0.013 and r = 0.262, p = 0.011, respectively). Both groups showed no difference in 1-year survival rate (p= 0.219) but hospitalization rate was higher in CD-group (p = 0.026).
Conclusion: CD was observed in almost 2/3 of stable CHF patients; it associates with higher NYHA class, history of hypertension and CHD, with worse quality of life, lower GFR and plasma iron, worse FMVR, higher depression score and higher 12-month hospitalization rate.

P1116

FAR NHL FARmacology and NeuroHumoraL activation in chronic heart failure - one year prognosis

J Spinar[1]; L Spinarova[2]; J Parenica[2]; M Spinarova[2]; K Labr[2]; F Malek[3]; P Ostadal[3]; J Jarkovsky[4]; O Ludka[1]
[1]*University hospital Brno and Masaryk university, Brno, Czech Republic*; [2]*University hospital, Brno, Czech Republic*; [3]*University Hospital, Prague, Czech Republic*; [4]*Masaryk University, Brno, Czech Republic*

On behalf of: FAR NHL investzigators
Funding Acknowledgements: University hospital Brno

The FAR NHL (FARmacology and NeuroHumoraL activation) registry is a database of patients treated in 3 departments with specialized heart failure care in one country. Anamnestic data, physical examination and blood samples were collected from November 2014 till November 2015. One year prognosis - mortality and hospitalisation was evaluated till November 2016. The aim of the study is to evaluate the one year prognosis and factors influencing neurohumoral activity of Nt-proBNP and the role of disease severity and comorbidities in patients with stable systolic chronic heart failure with reduced or mid range ejection fraction. The patients should be treated for systolic heart failure (EF < 50%) and stable for at least one month. Parameters of the AHEAD prognostic score (0 = no comorbidity, 5 = five comorbidities) were used to reflect the impact of comorbidities on neurohumoral activation and prognosis.
Results: 1050 patients were included, mean age 65 years, 889 (80,8%) were male. 146 (13,3%) were classified as NYHA I, 663 (60,3%) NYHA II and 285 (25,9%) as NYHA III and 6 (0,5%) NYHA IV. The Nt-proBNP levels for the different NYHA classes were 150 resp. 489 resp. 1 085 pg/ml (p <0,001) and there where no sex differences 494 vs 456 pg/ml (for different NYHA: 153 vs 489 vs 1142 for male and 108 resp. 461 resp. 907 for female; p <0,001 for NYHA, but NS for gender).
Patients with AHEAD score 0 had Nt-proBNP 228pg/ml, AHEAD 1-2 369 pg/ml and AHEAD 3-5 654 pg/ml (p <0,001) and these differences were highly significant for all separate comorbidties. There was a highly significant difference in patients with and without atrial fibrillation 432 vs 1035 pg/ml (p <0,001) and these differences were significant in all NYHA classes (142 vs 432 vs 1126 without AF and 890 vs 1043 vs 1058 with AF, all p < 0,001 for NYHA as well as for presence of AF). There was statistically significant difference according to age 416 pg/ml (<65 years) and 623 pg/ml (above 65 years; p <0,001).There was a close correlation between Nt-proBNP and renal functions; CrCl < 50 ml/min 1153pg/ml, 50-70 764 pg/ml and > 70 365 pg/ml and this difference was partly independent on NYHA class.
The general pharmacotherapy was qood 93,% of the patients received beta blockers and 88,4% druggy blocking renin angiotensin system (ACE-I and/or ARB). But the doses of the drugs were frequently not sufficient. The main predictor for no dose or low dose for bose RAAS inhibitor and betablockers was high NYHA class, high NT-proBNP level and low creatinin celearance.
The one year mortality according to AHEAD score (p < 0,001), NYHA classification (p <0,001) and Nt-pro BNP levels (< 0,001) showed high statisticaly significant differences.
Summary: Nt-proBNP levels reflect the severity of heart failure, but are strongly dependent on the presence of comorbidities. All markers of desease severity, especially NT-proBNP levels, AHEAD score and NYHA classifications are strong predictors of one year mortality.

P1117

Heart remodeling and its prevention in patients with chronic heart failure due to coronary artery disease combined with chronic obstructive pulmonary disease

V Vladimir Evdokimov[1]; E Kovalenko[1]; E Zolotareva[1]; A Evdokimova[1]; G Voronina[1]; K Tebloev[1]
[1]*State University of Medicine & Dentistry, Moscow, Russian Federation*

Purpose: to determine structural and functional changes in the heart in patients with chronic heart failure (CHF) due to coronary artery disease (CAD) combined with chronic obstructive pulmonary disease (COPD) and the possibility of their correction with nebivolol and enalapril or losartan administration.
Methods: 158 patients (128 men and 30 women), aged 63.5 ± 4.8 years, with CHF classes II to III (New York Heart Association) combined with moderate and severe COPD (GOLD-2015) and with initial ejection fraction of the left ventricle (LVEF) less than 45%, were randomized to three groups - enalapril/nebivolol (60 patients), nebivolol/losartan (40 patients) and enalapril (58 patients) group. Patients of all groups received complex CHF treatment comprising diuretics, cardiac glycosides (subject to indications) and basic COPD therapy (long acting m-anticholinergic, inhalation corticosteroids). Patients were evaluated through echocardiography (including wide spectrum of right and left side parameters), exercise tests, 24-hour electrocardiography, respiratory function at baseline and after 6 months of treatment. The quality of life was evaluated by MYHFQ and SGRQ.
Results: At baseline of the study in all patient were established progressive changes in the processes of LV and RV remodeling with increasing of their sizes, wall thickness and myocardial mass index (MMI), with a decrease of ejection fraction and progression of diastolic dysfunction. After 6 months of therapy the improvement of clinical condition and quality of life were marked in all groups. In 1st, 2nd and 3rd group LVEF was increased by 21.5%, 19.6% and 15.2%, RVEF was increased by 6%, 6.4% and 5.2%, pulmonary hypertension decreased by 23%, 25.2% and 16.4%, MMI decreased by 15.5%, 14.8% and 8.2%, left ventricular end diastolic volume index decreased by 16.5%, 14.4% and 10.4% respectively. Patients showed statistically significant and clinically meaningful reduction of SGRQ score (8.8%, 12.2% and 11.8%) and MYHFQ score (39.8%, 44.2% and 31.6%), significant improvements in MMRC dyspnea grade (21.3%, 23.5% and 15.3% respectively). Episodes of silent myocardial ischemia decreased by 45.2%, 46.9% and 29.9%, respectively. Respiratory function tests after 6 months did not show any negative changes in all groups.
Conclusions: The nebivolol and enalapril or nebivolol and losartan inclusion in the structure of complex therapy in patients with CHF combined with COPD raises efficiency of treatment, improves quality of life, basic parameters of central hemodynamics and prevent further heart remodeling. Efficacy and safety of nebivolol/enalapril and nebivolol/losartan combinations in patients with CHF due to CAD combined with COPD are similar.

P1118

Discrepancy in prevalence of impaired glucose regulation and diabetes according to screening method in outpatients with chronic heart failure

SL Kristensen[1]; M Egstrup[1]; C Tuxen[2]; P Hildebrandt[3]; C Kistorp[4]; JJV Mcmurray[5]; L Kober[1]; M Schou[6]; I Gustafsson[7]
[1]*Rigshospitalet - Copenhagen University Hospital, Cardiology, Copenhagen, Denmark*; [2]*Bispebjerg University Hospital, Department of Cardiology, Copenhagen, Denmark*; [3]*Frederiksberg Heart Clinic, Copenhagen, Denmark*; [4]*Herlev Hospital - Copenhagen University Hospital, Department of Endocrinology, Copenhagen,*

Denmark; [5]*Cardiovascular Research Centre of Glasgow, Cardiology, Glasgow, United Kingdom*; [6]*Herlev Hospital - Copenhagen University Hospital, Department of Cardiology, Copenhagen, Denmark*; [7]*Hvidovre UniversityHospital, Department of Cardiology, Copenhagen, Denmark*

Background: Diabetes and impaired glucose regulation (IGR) are frequent among patients with heart failure (HF). Both are believed to be most accurately diagnosed by measuring fasting plasma glucose (FPG), and performing a 2-hour oral glucose tolerance test (OGTT) why we considered combining these tests as the golden standard. We analysed how measurement of glycated hemoglobin (HbA1c) compares to FPG/OGTT in estimating the prevalence of diabetes and IGR.
Methods: In a cohort of 254 outpatients with chronic HF (LVEF < 45%), mean age 69 years, 67% men and no history of diabetes, FPG and HbA1c were measured in all patients and 252 patients completed an OGTT. IGR was defined by an impaired FPG (6.1-6.9 mmol/l) and/or impaired OGTT (2hPG 7.8-11.0 mmol/l), and diabetes by a FPG = 7 mmol/l and/or 2hPG = 11.1 mmol/l. For HbA1c, IGR was defined by a measurement of 6.0-6.4% and diabetes = 6.5%.
Results: A total of 51 (20%) patients had diabetes of which 17 (33%) had an HbA1c indicating diabetes, 17 (33%) an HbA1c indicating IGR and 17 (33%) a normoglycemic HbA1c (Table 1). IGR was found in 82 (32%) patients of whom 13 (16%) had diabetes, 20 (24%) IGR and 49 (60%) normoglycemia, according to HbA1c. Finally among 121 (48%) patients with normoglycemia, HbA1c measurement indicated diabetes in 5(4%) patients, IGR in 24 (20%) and normoglycemia in 92 (76%) patients (Table 1).
Conclusion: In a cohort of outpatients with chronic HF, measurement of HbA1c only detected 1 out of 3 patients with diabetes as diagnosed by FPG/OGTT (although 2 out of 3 had either diabetes or IGR as assessed by HbA1c). Only 1 out of 4 patients with IGR were correctely identified by HbA1c although 40% had either diabetes or IGR by HbA1c criteria. Normoglycemia was more accurately identified by HbA1c measurement, although still only in 76% of patients. The estimated prevalence of diabetes and IGR is lower when using HbA1c than FPG/OGTT. It should be noted, however, that most guidelines recommend a repeated measurement, regardless of screening method, which was not performed in the current study.

HbA1c vs OGTT in screening for diabetes

		HbA1c		
OGTT (FPG + 2-h value)	Subjects	Normoglycemia (%)	Impaired glucose regulation (%)	Diabetes (%)
Total	254	158 (62%)	61 (24%)	35 (14%)
Normoglycemia	121 (48%)	92 (36%)	24 (9%)	5 (2%)
Impaired glucose regulation	82 (32%)	49 (19%)	20 (8%)	13 (5%)
Diabetes	51 (20%)	17 (7%)	17 (7%)	17 (7%)

HbA1c - Glycated hemoglobin A1c, OGTT - oral glucose tolerance test, FPG - fasting plasma glucose

P1119
Bronchial obstruction contribution to chronic heart failure in patients with permanent atrial fibrillation along with coronary artery disease and arterial hypertension

N Natalia Koziolova[1]; E Polyanskaya[1]; S Berestneva[1]; O Masalkina[1]
[1]*Medical Academy, Perm, Russian Federation*

Aim: to evaluate COPD contribution to chronic heart failure(CHF) in patients with permanent atrial fibrillation (AF) along with coronary artery disease (CAD) and arterial hypertension depending on forced expiratory volume (FEV1) after bronchodilation test in spirometry.
Methods and materials: 41 patients with COPD and CHF along with arterial hypertension and CAD were examined. Average age 60,1+9,3. FEV1 was evaluated in all the patients after bronchodilation test, as well as NT-proBNP, left ventricle ejection fraction (LV EF), E/e' (via echo). Patients were divided into 3 groups depending on FEV1 after bronchodilation test according GOLD Guidelines.
The 1st group included patients with slight COPD (FEV1>80%, n = 6, 14,6%). The 2nd group - moderate COPD (FEV1 = 50-80%, n = 29, 70,7%). The 3rd group consisted of severe COPD FEV1 = 30-50%, n = 5, 12,2%). Patients with terminal COPD excluded from the study.
Results: NT-proBNP was significantly higher in group 3, than in group 1 and group 2 (pmg < 0,001) (958,8+101,2 ng/mL, 634,7+88,1 ng/mL, 498,5+62,8 ng/mL (p1-2, p1-3, p2-3 < 0,001) respectively). LV EF presented as moderately reduced in all the groups and did not differ between of them: group 1 - 48,6+6,1%, group 2 - 45,9+7,6%, group 3 - 44,2+7,8%. Reliable difference was found in average transmitral flow velocity E/e': group 1 - 14,7+1,8, group 2 - 15,8+1,5, group 3 - 17,0+1,9 (pmg= 0,002; p1-2 = 0,033, p1-3 = 0,0008, p2-3 = 0,0002). Correlation analysis showed indirect moderate interconnection between NT-proBNP and FEV1 (r=-0,48, p = 0,010), and indirect severe interconnection between E/e' and FEV1 (r=-0,69, p = 0,008).
Conclusion: in patients with COPD and permanent AF (in presence of arterial hypertension and CAD), there was indicated a progressive increase of HF severity (estimated by NT-proBNP and E/e') along with decreasing of post-dilation FEV1.

P1120
Iron deficient versus iron non-deficient chronic heart failure patients: which distinctions?

VG Vera Gorbachova[1]; A Liashenko[1]; T Gavrilenko[1]; L Voronkov[1]
[1]*NSC Institute of Cardiology M.D. Strazhesko, Heart failure, Kiev, Ukraine*

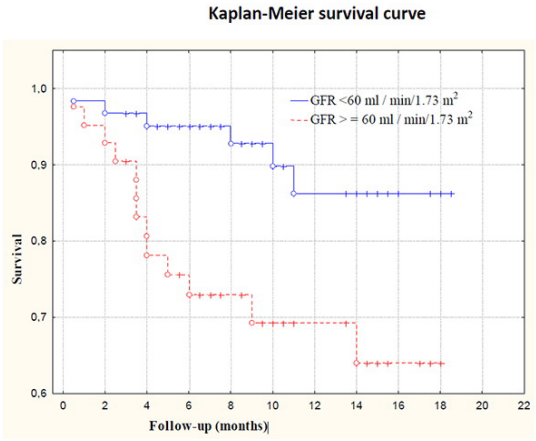
Background: According to FAIR-HF and CONFIRM-HF approach, both plasma ferritin (F) and transferrin saturation (TSAT) are considered to be an iron deficiency (ID) criteria in chronic heart failure (CHF). Nevertheless, it is still a question whether the obligate measurement of both F and TSAT is necessary in detection of ID in CHF.
Purpose: To compare clinical variables of CHF patients (pts) with ID and without ID; to evaluate the clinical significance of plasma F and TSAT in CHF patients with reduced left ventricular ejection fraction (LVEF).
Methods. 104 stable CHF patients (NYHA class II-IV, LVEF < 40%) were examined. Plasma F, IL6 and NTproBNP were determined by immunoassay, TSAT - by colorimetric assay. Beside routine clinical and laboratory examination, 6 min walk test (6MWT), standardized endurance leg extensor test and flow-mediated vasodilation (FMD) of the brachial artery were performed. Quality of life was measured with The Minnesota Living With Heart Failure Questionnaire (MLHFQ). Statistical calculations were made by Spearman's rank correlation coefficient, Student's t-criteria, Pearson's chi-squared test and Kaplan-Meyer estimator.
Results: ID was observed in 65 pts (62.5%).
No differences were observed between groups in regard to age, systolic blood pressure, heart rate, myocardium mass index, LVEF. Nevertheless, pts with ID are characterized by significantly higher NYHA class (p = 0.003), NTproBNP (p = 0.016) and IL6 levels (p = 0.040), lower Hb level (p = 0.004), lower glomerular filtration rate (p = 0.043), worse MLHFQ score (p = 0.031) and leg extensor endurance test (p = 0.024), reduced functional capacity (p = 0.007).
No correlations were found between plasma F and any main clinical variables, except Hb level. In contrast, TSAT significantly (p < 0,05) correlated with Hb (r = 0,40, p = 0,0003) and NTproBNP levels (r=-0,29, p = 0,050), 6MWT (r = 0,36, p = 0,0002), leg extensor test (r = 0,38, p= < 0,0001), MLHFQ (r=-0,27, p = 0,005) and the Duke University questionnaire (r = 0,23, p = 0,019).
All-cause mortality and combined point of mortality and hospitalization in a follow-up period of 9.5 month was significantly higher in ID group 26.1% vs 10.2% p = 0.050 and 55.4% vs 30.8%, p = 0.014 respectively.
Conclusions: Only 1/3 CHF patients do not have an ID; they are characterized by the better functional capacity, lower NTproBNP levels and better FMD response in comparison to the ID patients. Patients with ID are characterized by the lower Hb level and lower GFR, and by the higher value of IL6 and NTproBNP, higher mortality and hospitalization rate. Unlike F concentration, TSAT shows statistically significant correlations with the main parameters that represent the quality of life, patient's functional capacity and the NTproBNP level.

P1121
Renal dysfunction versus preserved renal function in chronic systolic heart failure: which patients?

A V Liashenko[1]; A E Dudnik[1]; T I Gavrilenko[1]; G V Ponomareva[1]; L G Voronkov[1]
[1]*NSC Institute of Cardiology M.D. Strazhesko, Heart failure, Kiev, Ukraine*

Background: It is known that prognosis of ?hronic heart failure (?HF) with renal dysfunction (RD) is associated with worse outcome. Finding out clinical features of patients (pts) with denoted combined pathology suggests to be useful in further understanding of the way to improve the prognosis CHF.
Purpose: To create comparative characteristics between two groups of CHF pts: with RD and preserved renal function.
Methods. 104 stable CHF pts (NYHA ??-?V, left ventricular ejection fraction (LV EF) < 40 %) were examined. According to the status of renal function, pts were divided in 2 groups: with glomerular filtration rate (GFR) <60 ml / min / 1.73 m2, and with GFR = 60 ml / min / 1.73 m2. GFR was calculated by CKD EPI formula. Daily microalbuminuria (MAU) was detected by immunoturbidimetric method. NTproBNP and interleukin-6 (IL-6) levels in plasma were determined by the immunoassay method. Plasma levels of citruline and myeloperoxidase activity were studied by spectrophotometry. Survival was analysed by the Kaplan-Meier method.
Results: Clinically relevant RD was observed in 42 pts (40,3%). There were no significant differences in both groups by: LVEF (p = 0,443), atrial fibrillation rate (p = 0,054), anemia rate (p = 0,158), heart rate (p = 0,357), systolic blood pressure (p = 0,286), NT proBNP level (p = 0,124) and activity of myeloperoxidase (p = 0,958).

Supr?s?ngly, there were no differences in MAU level (p = 0,45). At the same time, RD group demonstrate higer levels of blood urea nitrogen (BUN) (p = 0,0001), uric acid (UA) level (p = 0,0003), serum IL-6 (p = 0,0142) and serum citrulin levels (p = 0,0001). RD group was characterized by age older and higher NYHA class (p = 0,009). Pts with preserved renal function had lower rate of co-morbidities: diabetes (14% vs 43% in RD, p = 0,0012) and arterial hypertension (60% vs 86% in RD, p = 0,004). In pts with RD 1 year cumulative mortality was 30.9%, which was significantly higher than in the group without RD (11.3%) (p = 0.0125). However, there was no difference in hospitalization rate (p = 0,125).
Conclusion: Pts with CHF and reduced LVEF RD group characterized by higher rate of co-morbidities (hypertension, diabetes), higher age and NYHA class, higher UA, IL-6, BUN and citrulin levels, and demonstrate worse survival. RD was not associated with LVEF, anemia, MAU and NTproBNP levels.



Kaplan-Meier survival curve

P1122
Cognitive test results predict post-discharge rehospitalization risk among swedish heart failure patients

H Holm[1]; E Bachus[1]; L Minthon[2]; G Tasevska-Dinevska[3]; J Molvin[3]; A Jujic[1]; O Hansson[2]; K Nagga[2]; M Magnusson[3]
[1]Department of Clinical Sciences, Lund University, Skåne University Hospital, Malmö, Sweden; *[2]Lund University, Clinical Memory Research Unit, Department of Clinical Sciences Malmö, Lund, Sweden*; *[3]Lund University, Department of Cardiology, Skåne University Hospital, Malmö, Lund, Sweden*

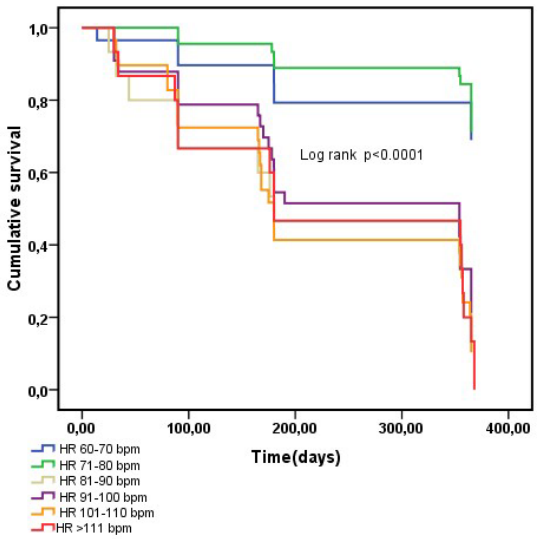
On behalf of: HARVEST
Funding Acknowledgements: The Swedish Heart and Lung foundation [2015-0322] and Wallenberg Center for Molecular Medicine, Lund University.

Background/Purpose: We aimed to assess the predictive role of four cognitive tests in regard to risk of rehospitalization in a Swedish prospective heart failure (HF) patient cohort.
Methods: 156 patients hospitalized for HF (mean age: 75 years; 29% women) had complete data on cognitive tests assessing global cognition (Montreal Cognitive Assessment (MoCA)), cognitive speed (Quick Test of Cognitive speed (AQT)), visual attention and task switching (Trailmaking A) and information processing (the digit symbol coding test (SDC)), as well as on all covariates used in the multivariate analysis. Relations between baseline cognitive test results and rehospitalization risk were assessed using multivariable Cox regression analysis adjusting for age, sex, body-mass index, systolic blood pressure, NYHA-class at hospitalization, diabetes, total cholesterol, prevalent atrial fibrillation, educational level and smoking. A two-sided p-value of 0.05 was considered statistically significant.
Results: Among the 156 HF-patients, 38 (24%) had cognitive impairment according to MoCA-score < 23 points. In the fully adjusted Cox regression analysis, readmission (n = 84, 54%, mean follow-up time 9.0 ± 8.9 months) was more likely to occur among patients with MoCA < 23 points (hazard ratio (HR) per 1SD: 1.82, 95% confidence interval (CI), 1.08-3.05; p = 0.025), AQT > 90 seconds (HR, 1.65; CI, 1.02-2.67; p = 0.041), SDC < 39 points (HR, 3.68; CI, 1.18-3.68; p = 0.025) and Trailmaking A > 70 seconds (HR, 1.88; CI, 1.15-3.06; p = 0.012). In the multivariate Cox regression analysis of continuous values of each cognitive test the MOCA-score (HR, 0.93; CI, 0.87-0.98; p = 0.014), SDC-score (HR, 0.96; CI, 0.93-0.98; p = 0.002) and Trailmaking A-time (HR, 1.01; CI, 1.00-1.01; p = 0.024) showed significant associations with risk of readmission, whereas no such association was seen for AQT-time (HR, 1.00; CI, 1.00-1.01; p = 0.231)
Conclusion: Four cognitive tests assessing global cognition, cognitive speed, visual attention and task switching as well as information processing predict rehospitalization in HF, independent of clinical and non-clinical factors.

P1123
Discharge heart rate and clinical outcomes in patients with atrial fibrillation and decompensated heart failure: data from the Optimize Heart Failure Care Program

A Grebennikova[1]; Y Lopatin[1]; H Sisakian[2]; H Hayrapetyan[3]; Z Pagava[4]; M Glezer[5]; A Chesnikova[6]; T Abdullaev[7]; G Dadashova[8]; E Tarlovskaya[9]; A Kurlianskaya[10]; S Berkinbaev[11]; A Rakisheva[11]; L Voronkov[12]; Z Kipiani[13]
[1]Volgograd State Medical University, Cardiology department, Volgograd, Russian Federation; *[2]Yerevan State Medical University Hospital 1: University Cardiology Clinic, Cardiology department, Yerevan, Armenia*; *[3]Erebouni Medical Center, Urgent cardiology department, Yerevan, Armenia*; *[4]Centre of Vascular and Heart Diseases, Cardiology department, Tbilisi, Georgia Republic of*; *[5]I.M. Sechenov First Moscow State Medical University, Cardiology department, Moscow, Russian Federation*; *[6]State Medical University of Rostov-on-Don, Department of Internal Medicine, Rostov-on-Don, Russian Federation*; *[7]Specialized Cardiology Center of the Republic of Uzbekistan, Cardiology department, Tashkent, Uzbekistan*; *[8]Scientific Research Institute of Cardiology, Cardiology department, Baku, Azerbaijan*; *[9]Nizhny Novgorod State Medical Academy, Cardiology department, Nizhny Novgorod, Russian Federation*; *[10]Republican Scientific and Practical Centre of Cardiology, Cardiology department 1 , Minsk, Belarus*; *[11]Scientific Research Institute of Cardiology and Internal Diseases, Cardiology department 1 , Almaty, Kazakhstan*; *[12]NSC Institute of Cardiology M.D. Strazhesko, Cardiology department, Kiev, Ukraine*; *[13]"New Hosps", Cardiovascular department, Tbilisi, Georgia Republic of*

Background: Optimal heart rate (HR) in patients with heart failure (HF) and atrial fibrillation (AF) is still being under discussion. The aim of our study was to investigate clinical outcomes (overall mortality and HF hospitalization) in patients with permanent atrial fibrillation (AF) and decompensated HF depending on their discharge HR. Methods. This analysis included data from the Optimize Heart Failure Care program collected over 12 months from 740 patients, of whom 170 patients (22.9%) were with HF and AF (mean age 63.7 ± 10.9 years, 70% male), NYHA II-IV (mean 2.85 ± 0.58), left ventricular ejection fraction < 40% (mean 34.1 ± 8.8%), mean heart rate 93 ± 23.8 bpm. Patients were divided into six groups depending on their discharge HR: 60-70 bpm (29 patients), 71-80 bpm (44 patients), 81-90 bpm (18 patients), 91-100 bpm (32 patients), 101-110 bpm (29 patients) and = 111 bpm (18 patients).
Results: There were no differences in demographic and clinical characteristics between groups. The prescription rates of angiotensin-converting enzyme inhibitors/angiotensin receptor blockers, beta-blockers, mineralocorticoid receptor antagonists before discharge from hospital varied from 85% to 89% in all groups, 80% of patients received digoxin. However, the proportion of patients, who received more than 50% of recommended doses of beta-blockers (BBs) was significantly lower in groups with HR 101-110 bpm and = 111 bmp (20% for BBs, p < 0.0001), compared with other groups of patients (this proportion varied from 56% to 68% for BBs in other groups). The rate of all-cause mortality and HF hospitalization was significantly higher in the groups of patients with HR 101-110 bmp and more than 111 bmp (HR 2.1, 95% CI 1.56-2.86, p = 0.0001) than in groups with HR 60-70 bmp and 71-80 bmp.
Conclusion: Despite the lack of differences in demographic and clinical characteristics between groups, patients with HR 101-110 bpm and more than 111 bmp received significantly lower doses of BBs, which was associated with significantly higher rates of all-cause mortality and HF hospitalization compared with other groups. So, some actions are needed to optimize rate control therapy and to prescribe evidence-based doses of medications in clinical practice.



Curves for overall mortality, HF hospit.

P1124

Sex differences in temporal changes in left ventricular ejection fraction among patients with heart failure -A report from the CHART-2 Study-

K Tsuji[1]; Y Sakata[1]; K Nochioka[1]; M Miura[1]; R Abe[1]; T Oikawa[1]; S Kasahara[1]; M Sato[1]; H Aoyanagi[1]; T Shiroto[1]; J Takahashi[1]; S Miyata[1]; H Shimokawa[1]
[1]Tohoku University Graduate School of Medicine, Cardiovascular Medicine, Sendai, Japan

On behalf of: the CHART-2 Investigators

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Background: We have recently reported that left ventricular ejection fraction (LVEF) dynamically changes in patients with haet failure (HF). However, sex differences in the transition of LVEF among HF with preserved LVEF (HFpEF), HF with mid-range LVEF (HFmrEF) and HF with reduced LVEF (HFrEF) remains to be fully examined.
Methods: In our Chronic Heart Failure Analysis and Registry in the Tohoku District-2 (CHART-2) Study (N = 10,219), we examined sex differences in the transition of LVEF in 3,480 consecutive HF patients. Those included 2,154 with HFpEF (LVEF = 50%, mean 71.7 yrs., male 60.8%), 596 with HFmrEF (LVEF 40-49%, mean 69.1 yrs., male 71.8%), and 730 with HFrEF (LVEF <40%, mean 66.8 yrs., male 76.7%), defined according to the 2016 ESC Guidelines.
Results: From baseline to 1-year, only a small proportion of HFpEF transitioned to HFmrEF or HFrEF in both sexes (female, 5.0% and 2.1%, respectively; male, 8.7% and 2.8%, respectively). In contrast, HFmrEF dynamically transitioned to HFpEF and HFrEF from baseline to 1-year (female, 51% and 9.7%, respectively; male, 34% and 17%, respectively), whereas HFrEF moderately transitioned to HFpEF and HFmrEF from baseline to 1-year (female, 20% and 17%, respectively; male, 14% and 21%, respectively).
In the overall population, history of ischemic heart disease (IHD) was negatively and female sex was positively associated with an increase in LVEF from baseline to 1-year (r=-0.063, P = 0.003 and r = 0.051, P = 0.014, respectively). It was noted that, regardless of HF groups at baseline, HFrEF at 1-year had increased mortality at 3-year (14.3%), as compared with HFpEF at 1-year (10.3%) and HFmrEF at 1-year (9.4%) (P for trend = 0.016). The multivariable linear regression analysis showed that HFpEF, HFmrEF, and HFrEF patients had different sets of factors associated with LVEF changes from baseline to 1-year by sex. History of IHD (r=-0.066, P = 0.002) was significantly associated with changes of LVEF only in male, while history of cancer (r=-0.018, P = 0.011) and serum albumin level (r=-0.029, P = 0.016) were significantly associated with LVEF changes only in female.
Conclusions: Sex differences were noted in the transitions among HFpEF, HFmrEF and HFrEF, where female sex, but not male sex, is associated with an increase in LVEF, which may be influenced by cancer and undernutrition.

P1125

Tachycardia-induced cardiomyopathy in children

Y Yakovleva Elena[1]; TS Loevets[1]; TL Vershinina[1]; L Butish[1]; KI Ivanova[1]; TM Pervunina[2]; DS Lebedev[3]; ES Vasichkina[1]
[1]Almazov National Medical Research Centre, Pediatric cardiovascular diseases research department, Saint Petersburg, Russian Federation; [2]Almazov National Medical Research Centre, Institute of Perinatology and Pediatrics, Saint Petersburg, Russian Federation; [3]Almazov National Medical Research Centre, Research Department of Arrhythmology, Saint Petersburg, Russian Federation

Objective: to present our clinical experience of diagnosis and treatment of the tachycardia-induced cardiomyopathy (TIC) in pediatric patients.
Methods: We enrolled 33 consecutive patients with TIC (11 girls and 22 boys). We formed 2 groups: 1st - 18 (54,5%) - frequent premature ventricular complexes (PVCs) and/or nonsustained ventricular tachycardia; 2nd - 15 (45,5%), included 13 (39,4%) had atrial ectopic tachycardia (AET), atrial fibrillation - 2 (6,1%).
Inclusion criteria were children < 18 years with idiopathic tachyarrhythmias, cardiac dysfunction (left ventricular ejection fraction < 50%), and left ventricular dilation (left ventricular end-diastolic dimension z-score = 2). Exclusion criteria were structural heart abnormalities, current inflammatory process in the myocardium.
Patients underwent a complete history, physical examination, laboratory studies (including thyroid function, CK, CK-MB, LDG, Troponin I, proBNP), echocardiography (ECHO), ECG, Treadmill test and Holter monitoring (HM). Cardiac MRI were performed according to indications and physician's decision.
The age, gender, tachycardia type, ventricular rate during tachycardia, frequency of tachycardia episodes and duration of tachycardia were studied.
All children with TIC underwent antiarrhythmic therapy (including combined treatment) and/or radiofrequency catheter ablation (RFA) of tachycardia. 1, 3 and 6 months after effective treatment of tachycardia ECHO control was performed.
Results: The mean age of diagnosis of arrhythmia was 6,78 + 6,48 (from 0 to 15) years.
The duration of tachycardia before diagnosed TIC was 32,11 + 20,48 months (range 6 to 180 months).
More often the patients complained of fatigue - 12 (36,4%), exercise intolerance - 12 (36,4%), palpitation - 11 (33,3%), shortness of breath - 6 (18,2%), dizziness - 7 (21,2%), syncope - 2 patients (6,1%).
Class of chronic heart failure was: I in 18 patients (54,5%); II - 13 patients (39,4%); III - 2 patients (6%)
NT-proBNP level was investigated in 12 children, and in 9 cases (75%) was high.
27 of 33 patients (81,8%) were obtained an antiarrhythmic therapy, 5 of them received a combination of drugs. 22 patients (66,7%) underwent RFA of tachycardia.
Long-term follow up of patients was 20,38 ± 19,14 months (range 1 to 60).
Most patients had disappeared complaints of fatigue and reduced exercise tolerance.
Heart failure resolution after effective treatment was observed in 81,8% cases (27 patients).
In all cases when the RFA was performed, follow-up with ECHO documented normalization of the heart chambers size and total recovery of ventricular function.
There were no difference between age of debut of arrhythmias, gender and duration of arrhythmias before TIC in 2 groups.
Conclusions: tachycardia-induced cardiomyopathy in children without structural myocardial defects is reversible, which underlines the importance of prompt diagnostics and control of hemodynamically significant cardiac arrhythmias.

P1126

The place of outpatient intervention program to prevent the readmissions of patients hospitalized for chronic heart failure

LG Mircheva[1]; M Rushid[1]; T Chalakova[1]; Y Yotov[1]
[1]University Hospital St. Marina, Varna, Bulgaria

Introduction: Heart failure (HF) is the leading cause of hospitalization among adults 65 years. The majority of the early readmissions could be prevented by developing disease-managing programs after discharge.
Aim: To assess the effect on rehospitalization rate of strict - ambulatory monitoring among patients with HF in out-patient HF program.
Material and subjects: We followed 198 patients with HF II-IV NYHA functional class (156 in active group and 42 in control group) for 6 months in HF out-patient program. Analysis of frequency and causes for rehospitalizations in studied patients in comparisons of control group of similar patients is made.
Results: Overall 52 patients (26,3%) have been rehospitalized. In the active group there were 33 (21,6%) events, while in the control group were 19 (42,2%), ? = 0,011. Most of them has only one rehospitalisation during follow-up. The curves' divergence starts after 30 days of follow-up. In Cox proportional regression analysis, the patients in the control group have twice higher probability to be rehospitalized during the 6-months follow-up - HR = 2,55, 95%CI = 1,44-4,53 (p = 0,001).

Conclusion: The majority of the early readmissions are prevented by developing disease-managing programs which focus on strict follow-up of the patients after discharge.

P1127

Predictors of short form-36 physical activity variables in heart failure with reduced ejection fraction

I Alexanian[1]; I Parisis[2]; V Bistola[2]; G Bakosis[2]; M Thodi[2]; F Tzifi[1]; N Karamichalakis[1]; E Rizou[1]; S Xydonas[1]; L Pappas[1]; K Letsas[1]; M Efremidis[1]; A Sideris[1]; G Filippatos[2]

[1]Evangelismos General Hospital of Athens, 2nd Department of Cardiology, Athens, Greece; *[2]Attikon University Hospital, Department of Cardiology, Athens, Greece*

Background: Quality of life reflects the multidimensional impact of a clinical condition and its treatment on patients' daily lives. It is markedly impaired in heart failure and adversely affects prognosis. Short Form -36 (SF-36) is a generic quality of life measure containing eight dimensions.
Purpose: We aimed to investigate SF-36 physical activity variables (physical function, role physical, bodily pain and general health perceptions) in patients with heart failure and reduced ejection fraction (left ventricular ejection fraction < 40%) (HFREF).
Methods: Clinical, echocardiographic and laboratory parameters were determined in 87 patients with HFREF (age: 64.81 ± 12.05, 90% male, Ischemic: 84%) visiting our outpatient clinic. Furthermore, assessment of functional capacity, quality of life and screening for depressive symptoms was performed using Duke Activity Status Index (DASI), the Kansas City Cardiomyopathy Questionnaire (KCCQ), the Minnesota Living With Heart Failure Questionnaire (MLHFQ) and the Zung self-rating depression scale (SDS). Statistical analysis was performed using SPSS 19.
Results: Median Physical function was 35.00(25.00, 70.00), median role physical was 0(0.0, 0.0), median bodily pain was 67.00(33.00,100.00) and median general health perceptions was 25.00(15.00, 42.00). Role physical correlated positively with Hgb (r = 0.363, p = 0.003), whereas it correlated negatively with NYHA (r= -0.360, p = 0.002), RV diameter (r= -0.286, p = 0.046) and logNT-proBNP (r= -0.318, p = 0.040). Bodily pain was positively associated with LVEF (r= 0.241, p = 0.046), with Hgb (r= 0.300, p = 0.014) and Na (r= 0.383, p = 0.001). General health perceptions correlated positively with LVEF (r = 0.274, p = 0.023) and Na (r= 0.288, p = 0.016) and correlated negatively with NYHA (r= -0.279, p = 0.020). Physical function was negatively associated with total score MLHFQ (r= -0.305, p = 0.008). Role physical, bodily pain and general health perceptions showed a positive association with DASI (r= 0.337, p = 0.002), (r= 0.319, p = 0.003), (r= 0.414, p < 0.001) respectively, with KCCQ overall summary (r= 0.384, p < 0.001), (r= 0.470, p < 0.001), (r= 0.406, p < 0.001) respectively and a negative association with total score MLHFQ (r= -0.319, p = 0.006), (r= -0.526, p < 0.001), (r= -0.509, p < 0.001) respectively. Physical function, bodily pain and general health perception correlated negatively with Self-rated raw score Zung (r= -0.281, p = 0.012), (r= -0.247, p = 0.027), (r= -0.493, p < 0.001), respectively.
Conclusion: NYHA, echocardiographic and laboratory parameters are significantly associated with SF-36 physical activity variables. SF-36 physical activity variables significantly correlate positively with DASI, KCCQ and negatively with MLHFQ and Self-rated raw score Zung.

P607

Targeted DNA methylation profiling of human cardiac tissue reveals novel epigenetic traits and gene deregulation across different heart failure cohorts

N Nadezhda Glezeva[1]; B Moran[1]; P Collier[2]; C Moravec[2]; A Russell-Hallinan[1]; K Mcdonald[3]; M Ledwidge[3]; J Baugh[1]; S Das[1]; C Watson[4]

[1]University College Dublin, Conway Institute, Dublin, Ireland; *[2]Cleveland Clinic Foundation, Department of Cardiovascular Medicine, Cleveland, United States of America*; *[3]St Vincent's University Hospital, Heart Failure Unit, Dublin, Ireland*; *[4]Queen's University of Belfast, Wellcome-Wolfson Institute for Experimental Medicine, Belfast, United Kingdom*

Purpose: Heart failure (HF) is a global health problem with ever increasing prevalence. Efforts to find more effective means to screen, diagnose, and treat HF must take into account the multiple aetiologies and facets that make up the complexity of the syndrome. Correct gene expression programming of the cells that form the architecture of the myocardium underlies the normal functioning of the heart. DNA methylation is a physiological process and a powerful tool for fine-tuning of gene expression in line with the needs of the body. Aberrant DNA methylation can therefore contribute to pathological cardiac remodelling. To identify novel gene-specific DNA methylation changes that may occur in different HF aetiologies, we used a focused methylation loci targeting approach to profile left ventricular myocardial tissue from patients with Left Ventricular Hypertrophy (LVH), Hypertrophic Obstructive Cardiomyopathy (HOCM), Dilated Cardiomyopathy (DCM), Ischemic Cardiomyopathy (ISCM), and age/sex-matched no HF controls.
Methods: A custom-designed SeqCap Epi Choice M kit was developed for this project to assess 18582 putative promoter and enhancer regions of coding and non-coding (nc) RNA, and 17929 CpG islands in fresh-frozen cardiac interventricular septal (IVS) tissue from 48 patients with LVH (9), HOCM (12), DCM (9), ISCM (9), and normal function controls (NF, 9). Differential methylation analysis, non-negative matrix factorisation (NMF) clustering (R software, MethylKit), and gene network analysis (Enrichr) were performed to determine methylation changes relative to gene/microRNA/long non-coding (lnc) RNA expression. Quantitative real-time PCR was carried out on a subset of methylation-sensitive genes/microRNA/lncRNA to determine changes in transcript levels.
Results: Using a 500 bp tiled approach, false discovery rate (FDR) of >0.05, and a difference in methylation of >10%, we detected 61,151 tiles with divergent methylation in the studied cohort. By comparing each HF patient group to the NF control group we identified 7 differentially methylated tiles in LVH, 5 in HOCM, 151 in DCM, and 55 in ISCM. These translated to 7 genes in LVH, 4 genes/1 ncRNA in HOCM, 131 genes/17 ncRNA in DCM, and 51 genes/5 ncRNA in ISCM. Gene ontology revealed relevance to processes and pathways implicated in HF pathogenesis. Subsequent QPCR analysis identified 10 genes (4 hyper-, 6 hypo-methylated) and 5 microRNA (3 hyper-, 2 hypo-methylated) with significantly up/down-regulated transcript levels consistent with the direction of methylation identified in the particular HF patient group.
Conclusions: Our study is the first to use a cardiovascular-specific targeted capture approach to define epigenetic signatures in HF patients with different aetiologies. We identified methylated CpG sites which affect gene expression and may contribute to disease pathophysiology. We also highlighted disease-associated genes which could be assessed as novel diagnostic or therapeutic targets.

Chronic Heart Failure - Other

P1128

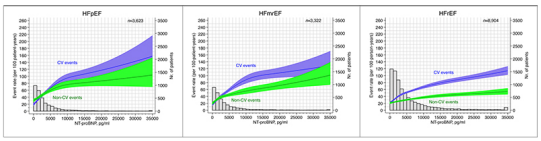
Optimizing criteria for N-terminal pro-B-type natriuretic peptide for eligibility and enrichment in trials in heart failure with preserved, mid-range and reduced ejection fraction

G Savarese[1]; N Orsini[2]; C Hage[1]; O Vedin[3]; F Cosentino[1]; G Rosano[4]; U Dahlstrom[5]; LH Lund[1]

[1]Karolinska Institute, Division of Cardiology; Department of Medicine, Stockholm, Sweden; *[2]Karolinska Institute, Department of Public Health Sciences, Stockholm, Sweden*; *[3]Uppsala University, Department of Medical Sciences, Uppsala, Sweden*; *[4]St George's University of London, Cardiovascular and Cell Sciences Research Institute, London, United Kingdom*; *[5]Linkoping University, Department of Cardiology and Department of Medical and Health Sciences, Linkoping, Sweden*

Funding Acknowledgements: Swedish Research Council [grants 2013-23897-104604-23 and 523-2014-2336], the Swedish Heart Lung Foundation [grants 20120321 and 20150557],and Relypsa

Objective: To assess the association between N-terminal pro-B-type natriuretic peptide (NT-proBNP) and cardiovascular (CV) vs. non-CV events, and between NT-proBNP and potential treatment effects, in heart failure (HF) with preserved, mid-range and reduced ejection fraction (HFpEF, HFmrEF, HFrEF) and clinically relevant sub-groups.
Background: Optimizing patient eligibility criteria in HF trials requires biomarkers that enrich for CV but not non-CV events, and select patients most likely to respond to the tested intervention.
Methods: In the Swedish HF Registry population stratified by EF category, we used: Kaplan Meier curves to estimate unadjusted CV and non-CV risk (mortality or hospitalization); Poisson regressions to calculate crude event rates of CV and non-CV events according to NT-proBNP levels; Cox regressions to calculate the adjusted hazard ratios for HF therapies according to NT-proBNP = or >median.
Results: Among 15,849 patients (23% HFpEF, 21% HFmrEF, 56% HFrEF), median NT-proBNP was 2,037, 2,192 and 3,141 pg/ml, respectively. With increasing NT-proBNP, CV event rates increased more steeply than non-CV (ranging 20-160 and 30-100 per 100 patient-years in HFpEF, 20-130 and 20-100 in HFmrEF, 20-110 and 20-50 in HFrEF, respectively). CV to non-CV ratio increased with increasing NT-proBNP in HFpEF and HFrEF, but only in the lower range in HFmrEF. The association between treatments (ACE-I /ARB and beta-blockers) and outcomes was consistent in NT-proBNP = and >median.
Conclusions: In HF trial design in different EF categories, NT-proBNP may be a useful tool for eligibility and enrichment for CV events, but its role in treatment response remains unclear. When designing HF trials, it is important to recognize that non-CV events will be higher with higher EF and potential CV treatment effect will be lower with higher EF, even if the pathophysiological treatment target is appropriate; and that higher NT-proBNP criteria will enrich for CV events but also CV to non-CV event ratios. However, it remains unknown which NT-proBNP range may have the greatest HF treatment response.



P1129

Association of phase angle and hypoxemia in patients with Heart Failure and chronic obstructive pulmonary disease

C Olivo-Villalobos[1]; D Gonzalez[1]; A Orea-Tejeda[1]; G Davila-Said[1]; C Chavez-Mendez[1]; R Sanchez-Santillan[1]; V Pelaez-Hernandez[1]; M Rivera-Rodriguez[1]; L Castillo-Aguilar[1]; K Balderas-Munoz[1]; A Figueroa-Herrera[1]
[1]Instituto Nacional de Enfermedades Respiratorias "Ismael Cosío Villegas", Heart Failure and Respiratory Distress Clinic, Mexico city, Mexico

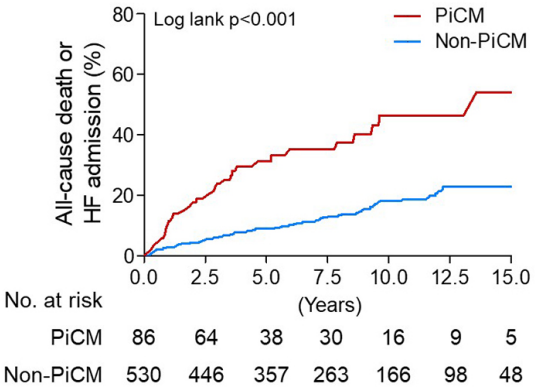
Background: Heart failure (HF) and chronic obstructive pulmonary disease (COPD) have high rates of morbidity and mortality. There is water alteration and cell damage in both pathologies and these aggravates the prognosis. The phase angle (PA), which is an indicator of the integrity of the cellular membrane and a good method of prognosis in these populations, diminished with: decrease in tissue oxygenation, in hypoxia state, which increases oxidative stress, the overproduction of peroxides and free radicals. However, there aren't studies that evaluate the relationship between hypoxia and PA in HF and COPD patients.
Purpose: To determine the relationship between hypoxia and PA in patients with HF and COPD.
Materials and Methods: Cross-sectional study was performed in 159 patients, subjects > 40 years with a diagnosis of HF and COPD were included. Those with asthma and cancer were excluded. Body composition and PA were evaluated by bioelectrical impedance vector analysis (BIVA) and hypoxia was confirmed by arterial oxygen saturation < 80%.
Results: The mean age was 67.4 ± 12 years, 58.1% were women, and 61.8% had cachexia. Subjects with hypoxia had lower PA (4.3 ± 0.84 vs 4.94 ± 0.93, p = 0.046), as well as, greater edema (89.89% vs 58.8%, p = 0.203) compared with those without hypoxia, respectively. No difference was shown between the groups in: strength, impedance index and skeletal muscle mass.
Conclusion: Subjects with HF and COPD with hypoxemia have a lower PA than the non hypoxemic group.

P1130

Clinical features, predictors, and long-term prognosis of pacing-induced cardiomyopathy

S W Cho[1]; SY Sohn[2]; KM Park[3]; YK On[3]; JS Kim[3]; SJ Park[3]
[1]Inje University, Seoul Paik Hospital, Division of Cardiology, Department of Internal Medicine, Seoul, Korea Republic of; *[2]Hospital Myongji, Division of Endocrinology, Department of Internal Medicine, Goyang, Korea Republic of*; *[3]Samsung Medical Center, Cardiology, Seoul, Korea Republic of*

Background: Right ventricular pacing sometimes have adverse effects on left ventricular (LV) structure and function. However, little is known about the clinical features, predictors, and long-term prognosis of pacing-induced cardiomyopathy (PiCM).
Methods: We reviewed 1418 patients undergoing permanent pacemaker implantation and having follow-up transthoracic echocardiography (TTE) data. PiCM was defined as less than 50% of LV ejection fraction (EF) in follow-up with = 10% decrease of EF, newly appeared regional wall motion abnormality irrelevant coronary artery disease, LV dyssynchrony, or paradoxical septal motion. The primary outcome was composite of all-cause death or admission due to heart failure (HF).
Results: Total 671 patients were enrolled and 87 (13.0%) developed PiCM, with a decrease in mean EF from 60.5% to 40.1% over a mean duration of 5.4 years. In multivariate logistic regression analysis, independent predictors of PiCM were left bundle branch block at baseline electrocardiography, wider paced QRS duration, and ventricular pacing frequencies. During the follow-up duration (mean 7.7 years), the risk of all-cause death or HF admission was significantly higher in patients with PiCM compared with non-PiCM patients (38.3% versus 54.0%, adjusted hazard ratio, 3.07; 95% confidence interval 1.90-4.94; p < 0.001).
Conclusion: PiCM showed the worse long-term prognosis compared with non-PiCM. Therefore, the patients with risk factors of PiCM should be monitored carefully and considered the biventricular pacing.



All-cause death or HF in PiCM

P1131

Differences in psychological and physical state between informal primary caregivers of patients with cardiorespiratory failure with emotional suppression or reappraising. preliminary results.

F A Figueroa Herrera[1]; V Pelaez-Hernandez[1]; B Robles-Uribe[1]; SC Torres-Montiel[1]; M Rivera-Rodriguez[1]; A Orea-Tejeda[1]; D Gonzalez-Islas[1]; G Davila-Said[1]; C Chavez-Mendez[1]; C Olivo-Villalobos[1]; L Castillo-Aguilar[1]; RN Sanchez-Santillan[1]; GK Perez-Cortes[1]; AG Navarrete-Penaloza[1]
[1]Instituto Nacional de Enfermedades Respiratorias "Ismael Cosio Villegas", Heart Failure and Respiratory Distress Clinic, Mexico City, Mexico

Background: Emotional suppression (ES) reduces health, while reappraising (RE) favours it. Patients who suppress their anger increase their physiological activity and generate hostile behaviours that hinder the relationship with their informal primary caregiver (IPC), and vice versa. In addition, the ES of a person during a social interaction increases blood pressure in both individuals. However, the impact of the ES of patients with cardiorespiratory failure (CRF) on their IPCs is unknown.
Objective: To compare psychological and physical state of IPCs of patients with CRF with ES or RE emotional regulation type.
Method: A cross-sectional study was conducted involving 12 CPIs of patients with a clinical diagnosis of cardiorespiratory failure. The patients were evaluated with the Emotional Regulation Questionnaire, according to the results their IPCs were divided in two groups: 1) IPCs of patients with ES (G1, n = 8 age: 57.75 ± 12.56, 75% women) and 2) IPC of patients with RE (G2, n = 4 age: 57 ± 9.62, 75% women).
To assess psychological state of the CPIs, the Beck Anxiety Inventory (BAI), the SF-12 health questionnaire and the Perceived Stress Scale (PSS) were used. To evaluate the physical state, the 6-minute walking test (6MWT) was performed, recording distance travelled (DIST), systolic blood pressure (SBP), diastolic blood pressure (DBP) and pulse in each of the following phases. 1) Base Line (BL), 2) Final (F) and 3) Recovery (REC).
The data was analysed with SPSS for Windows version 22 using a Mann Whitney U test.
Results: No statistically significant differences were found (p> 0.05), but clinically significant differences were found in SBP and DBP.
Psychometrics
BAI (G1 / G2): 11 ± 11.40 / 7.75 ± 6.29 (z=-.171)
SF-12 (G1 / G2): 59.68 ± 18.02 / 73.95 ± 8.03 (z=-1.191)
PSS (G1 / G2): 24.50 ± 5.73 / 30.75 ± 14.17 (z=-.937)
6MWT (BL|F|REC)
SBP (mmHg, G1 / G2): 134.75 ± 20.25 / 122 ± 14.76 (z=-1.191) | 140.38 ± 21.79 / 123.50 ± 11.81 (z=-1.531) | 133.50 ± 28.48 / 120 ± 13.44 (z=-.510)
DBP (mmHg, G1 / G2): 81.38 ± 10.87 / 80.50 ± 9.57 (z=-0.85) | 87.38 ± 15.55 / 78.75 ± 6.39 (z=-1.534) | 85 ± 13.72 / 80.25 ± 10.07 (z=-.340)
Pulse (p/min, G1 / G2): 65.25 ± 11.56 / 73.50 ± 3.69 (z=-1.281) | 68.13 ± 14.10 / 74.50 ± 10.78 (z=-.778) | 64.63 ± 13.02 / 71 ± 9.27 (z=-1.023)
Distance (meters, G1 / G2): 370.50 ± 57.25; 393.75 ± 48.03 (z=-.679)
Conclusions: The clinical differences between both groups show that the IPCs of patients with ES present an alteration of the emotional state and a diminished quality of life. They also showed a deteriorated cardiovascular response, being more reactive, presented hypertensive levels of SBP and a lower performance. This translates into greater vulnerability. An interdisciplinary health team is needed to attend to the state of health of the IPCs.

P1132

Company animals, the best friends for heart failure patients?

N G H M Nick Marcks[1]; JJJ Boyne[2]; W Robaeys[1]; MA Barandiaran Aizpurua[2]; J Merken[1]; FPH Beckers-Wesche[2]; HP Brunner-La Rocca[2]
[1]Cardiovascular Research Institute Maastricht (CARIM), Cardiology, Maastricht, Netherlands; *[2]Maastricht University Medical Centre (MUMC), Cardiology, Maastricht, Netherlands*

Purpose/Aims: Therapy adherence, physical activity, quality of life, hospitalisation and mortality are important regarding care in heart failure (HF) patients. Various means aim to improve these aspects, however little is known about the effects of pet ownership.
Methods and Results: We retrospectively investigated the Trial of Intensified vs Standard Medical Therapy in Elderly Patients with Congestive Heart Failure (TIME-CHF) population. Among the 622 HF patients, 154 owned a company animal. Pet owners were younger, more frequently men and were more often married or lived with a partner. Patients owning pets had more frequently chronic obstructive pulmonary disease (COPD) and were more frequently smokers. Systolic blood pressure and ejection fraction (EF) were lower in these patients. No significant differences were observed concerning quality of life measured by the Minnesota questionnaire (29 (± 19) vs 27 (± 19), p 0.456). Although univariate analysis demonstrated a better event free survival in HF patients with pet (HR 1.460, 95% CI 1.105-1.928, p = 0.008), adjusting for gender, age, arterial hypertension, current smoking status, history of COPD, social status, and EF unmaked this significant difference (HR 1.260, 95% CI 0.943-1.685, p = 0.119). Therapy adherence, defined as non-compliance without particular reason, showed no significant difference between groups (p = 0.209). Physical activity improved slightly in both groups over time, however without significant difference between groups (p = 0.336).
Conclusions: With this retrospective research, we could not find relevant differences in any of the investigated aspects between pet owners and non-owners.

Hazard ratios for both endpoints

	Overall survival without cancer-related deaths		
	Hazard ratio	95% CI	p-value†
Unadjusted	1.293	0.943 - 1.771	0.110
Adjusted *	1.124	0.809 - 1.561	0.485
	Combined endpoint (overall survival + HF hosp free survival)		
	Hazard ratio	95% CI	p-value†
Unadjusted	1.460	1.105 - 1.928	0.008
Adjusted *	1.260	0.943 - 1.685	0.119

* Adjusted for gender, age, hypertension, COPD, ejection fraction, relationship status and current smoking status. † p-value for pet vs. No pet. HF hosp: heart failure hospitalization; n.a. : not applicable.

P1133

Heart involvement in AA amyloidosis a prospective study on 38 patients

D Bodez[1]; S Guendouz[1]; G Grateau[2]; A Galat[1]; V Avellino[2]; M Kharoubi[1]; A Guellich[1]; E Itti[3]; JF Deux[4]; T Damy[1]; S Georgin-Lavialle[2]
[1]University Hospital Henri Mondor, Cardiology & Amyloid Research Institute, Creteil, France; *[2]Hospital Tenon, Internal medicine & CEREMAIA (national french ref center of autoinflammatory diseases and AA amyloid, Paris, France*; *[3]University Hospital Henri Mondor, Nuclear medicine & Amyloid Research Institute, Creteil, France*; *[4]University Hospital Henri Mondor, Radiology & Amyloid research institute, Creteil, France*

Funding Acknowledgements: AREMCAR, APHP

Context: AA Amyloidosis is unusually associated with cardiac amyloidosis. No systematic cardiac screening has been performed in the last decade, since new noninvasive diagnostic tools have been developed.
Aim: To determine whether AA amyloidosis is associated with a specific cardiac injury.
Methods: Thirty-eight consecutive patients with proven AA amyloidosis has been included for a systematic cardiac work-up with clinical evaluation, biomarkers, transthoracic echocardiography (TTE), cardiac MRI and bone scintigraphy.
Results: Among 38 AA patients, 11 had an inflammatory disease, 10 had an infectious disease, 10 an auto-inflammatory disease, 4 were obese, and origin of amyloidosis was unknown in 3 cases. Eleven patients were on dialysis, and 3 were already renal transplant recipients. Median age was 58.6 (51.1;67.4) years, 50% were males, 78% were in NYHA class I or II, and all presented sinus rhythm. Median troponin T us was 19 ng/l, and NT-proBNP was 382 ng/l. Median LVEF was 61%, interventricular septum thickness was 9mm, global longitudinal strain was -18%. One patient presented late gadolinium enhancement on cardiac MRI, and none patient presented myocardial bone maker fixation. Seven patients died during the study, all on dialysis with several cardiovascular risk factors.
Conclusion: None of the patients presented classical criteria of cardiac amyloidosis. A specific vascular location has to be explored with further studies.

Acute Heart Failure - Pathophysiology and Mechanisms

P1134

Orthostatic hypotension is associated with volume status changes and intensive diuretic therapy in patients with decompensated heart failure

A Soloveva[1]; M Bayarsaikhan[1]; O Lukina[1]; F Cabello Montoya[1]; S Villevalde[1]; Z Kobalava[1]
[1]Peoples' Friendship University of Russia (RUDN University), Department of Internal Diseases, Moscow, Russian Federation

Objective: Orthostatic hypotension (OH) is common among patients with heart failure (HF) and may have an adverse impact on the outcomes. Presently little is known about orthostatic reactions during hospitalisation and their associations in decompensated HF (DHF).
Methods: Systolic and diastolic blood pressure (SBP and DBP) were measured in recumbent and standing position within 3 min of assuming upright posture on admission and discharge in 72 patients with DHF (47 male, 68 ± 12 years (M ± SD), arterial hypertension 96%, myocardial infarction 46%, atrial fibrillation 65%, diabetes mellitus 40%, chronic kidney disease 32%, ejection fraction (EF) 40 ± 14%, EF < 40% 51%, NT-proBNP 3488(1359;7185)pg/ml). OH was defined as decrease of SBP = 20 mmHg and/or DBP = 10 mmHg within 3 min of active standing. The same increase of SBP and/or DPB was considered as orthostatic hypertension (OHtn). Hydration status was assessed by BIVA on admission and discharge, using resistance (R) and reactance (Xc) standardized by height (h). Mann-Whitney, McNemar tests were performed, p < 0.05 was considered significant.
Results: On admission OH and OHtn occurred in 17(23.6%) and 2(2.8%) of patients respectively. OH on admission occured in 1 min in 88% cases and was presented as isolated decrease of SBP, DBP or both in 8, 5 and 4 patients. OH and OHtn occured in 27(37.5%) and 17(23.6%) patients at discharge respectively.
OH at discharge occured in 1 min in 55.5% cases and was presented as isolated decrease of SBP, DBP and both in 15, 9 and 3 patients. In 1 patient DBP decrease was associated with postural tachycardia.
10(13.9%) patients had OH both on admission and discharge. Symptomatic OH was rare (in 12 and 7.4% cases on admission and discharge).
Patients with vs without OH at discharge received higher total dose of iv furosemide therapy during hospitalisation (500(240;860) vs 480(300;740) mg,p = 0.042) and had lower rate of hyperhydration by BIVA (29.6 vs 60%,p = 0.012) and higher R/h (308 ± 61 vs 278 ± 52 Om/m,p = 0.046) and Xc/h (31 ± 8 vs 25 ± 7 Om/m,p = 0.005) at discharge (meaning less hydration), absolute ?R/h (53 (7;69) vs 29(11;62)Om/m,p = 0.048) and ?Xc/h (6.3(1.8;10.5) vs 4.6(1.2;9.3)Om/m,p = 0.046), relative ?R/h(21.3 (2.7;30) vs 13 (2.7;17.8)%,p = 0.045) and ?Xc/h (33(8;64) vs 26(4.4;58)%, p = 0.038). Groups did not differ by baseline BIVA parameters.
OH on admission was associated with higher rate of rehospitalisation in 6 month (29.4 vs 9.1%,p = 0.034).OH at discharge had no negative impact on 6-month outcomes.
Conclusions: Orthostatic reactions in patients with DHF were diverse. OH was more frequent than OHtn both on admission and discharge.From admission to discharge incidence of OH and OHtn increase from 23.6 to 37.5% and from 2.8 to 23.6% respectively.Patients with OH at discharge had more intensive iv diuretic therapy and more pronounced decongestion by BIVA.OH on admission was associated with higher rate of 6-month rehospitalisation. OH at discharge had no impact on outcomes.

P1135

Takotsubo syndrome and hypersensitivity reaction to metals of environmental burden

M Marie Pavlusova[1]; J Manousek[1]; P Kubena[1]; P Kala[1]; J Jarkovsky[2]; L Dostalova[1]; A Zadakova[1]; J Spinar[1]; J Parenica[1]
[1]University Hospital Brno, Department of Cardiology and Internal Medicine, Brno, Czech Republic; *[2]Institute of Biostatistics and Analyses of Masaryk University, Brno, Czech Republic*

Background: Takotsubo syndrome (TS) is a rare heart pathology characterized by a sudden transient dysfunction most often of left ventricle mimicking acute myocardial infarction. The etiology is not known as yet. According to the literature and clinical observations, it appears that TS affects persons with various comorbidities.
Purpose: Our pilot project aims to determine the prevalence of comorbidities with potential pathological immune reactivity, and to evaluate the possible association between TS and delayed type hypersensitivity (type IV) reactions to metals of environmental burden assessed by lymphocyte transformation test (LTT).
Methods: A total 24 patients (23 females, 1 male, median age 65,6 years) with a history of TS acute attack and 27 healthy controls were evaluated. Hypersensitivity to metals was tested by a LTT. A questionnaire of environmental burden was used to select evaluated metals.
Results: 19 patients (79 %) had at least one condition that might potentially be associated with pathological immune reactivity (autoimmune thyroid disease, drug allergy, bronchial asthma, cancer, contact dermatitis, rheumatoid arthritis). Hypersensitivity to metals of environmental burden was identified significantly more frequently in TS patients than in healthy controls (positive reaction to at least one metal was identified in 95,8 % of TS patients and in 59,3 % of controls; p = 0,003); the difference was statistically significant particularly for mercury (45,8 % and 14,8 %, respectivelly; p = 0,029).
Conclusion: This pilot work shows that conditions with pathological immune reactivity occur frequently in TS patients, and that there in an association between TS and delayed type hypersensitivity to metals of environmental burden (mercury in particular) evaluated by LTT. Our results also suggest that apart from triggering stress factor, potential existence of other serious conditions should be considered when taking medical history of TS patients.

P1136
Right ventricular function is a strong predictor of outcome in acute heart failure

J Jack Stewart[1]; O Lazariashvili[1]; A Baltabaeva[1]
[1]*Ashford and St Peter's Hospitals NHS Trust, Cardiology, Chertsey, United Kingdom*

Funding Acknowledgements: Abbott Vascular ltd

Introduction: Acute Heart Failure (AHF) is well recognised as a growing healthcare problem with one-year mortality typically reported around 30%. Treatment strategies and prognostic markers have long been focused on the left ventricular (LV) function, despite recognition that right heart (RV) failure carries a significant mortality burden.
Purpose: In a single-centre, prospective, cross-section study, we have aimed to assess the prognostic impact of RV function markers in patients admitted with AHF or exacerbation of chronic HF (ECHF).
Methods: All consecutive patients admitted to a large district general hospital with AHF and/or ECHF over the period of 1 year had standard clinical assessment, bio-chemistry and bedside transthoracic echocardiography within 48h of recruitment. Geometric and functional parameters of cardiac function were assessed according to international guidelines. All-cause mortality was documented at 6 months post discharge.
We assessed left ventricular ejection fraction (LVEF), systolic pulmonary artery pressure (SPAP), tricuspid annular plane systolic excursion (TAPSE) and right ventricular fractional area change (RVFAC) as prognostic markers. These markers were categorised using the following cut-off values: LVEF 40%, TAPSE 1.5cm, RVFAC 32% and SPAP 45mmHg, in line with international guidelines.
Chi-square testing was used to demonstrate or refute statistical excess of mortality. Kaplan-Meier survival plots were created to demonstrate differences in survival. Individual Cox regressions were performed to obtain hazard ratios (HR).
Results: 617 patients met the inclusion criteria of whom 500 were consented and 448 were included in the study. 6-month mortality is currently available for 356 patients. 6-month mortality was 29.1%, higher than typically reported.
As expected, patients with reduced LV function (LVEF < 40%) demonstrated increased mortality compared to those with LVEF = 40% (p= < 0.05) with a HR of 1.5, (95% CI 1.0-2.2, P < 0.05).

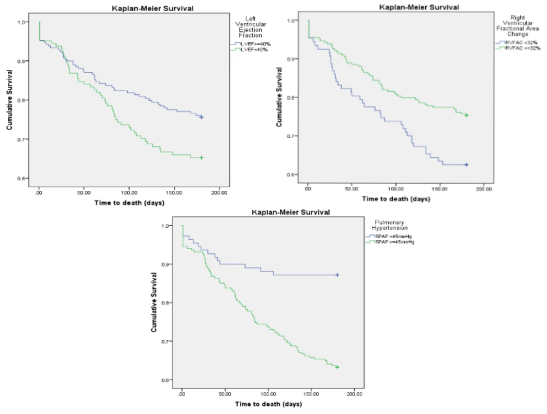


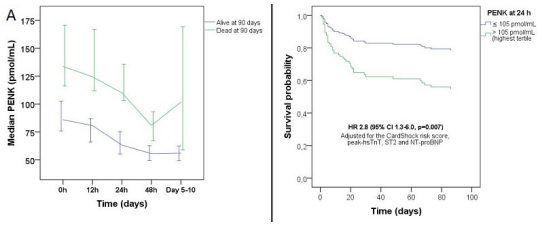
Figure 1. Kaplan-Meier survival curves

Severity of pulmonary hypertension was a strong predictor of all-cause mortality: SPAP = 45mmHg was associated with a significant increase in mortality compared to those with < 45mmHg (p= < 0.00001) with a HR of 3.2 (95% CI 1.8-5.5, p < 0.00001).
Patients with RV dysfunction as assessed by RVFAC (< 32%) showed a significant excess of mortality (p= < 0.01), with a HR of 1.9 (95% CI 1.3-2.7, p < 0.01).
TAPSE was not a significant predictor of mortality (p>0.1)
Conclusion: This study demonstrates the significance of RV failure in AHF. RVFAC is a powerful predictor of all-cause mortality in patients with AHF, as is SPAP. TAPSE is not a sensitive prognostic marker likely due to the fact that this measures longitudinal displacement not global function. Complex RV geometry should be assessed using at least 2D echo parameters. Further assessment of the right ventricle in AHF is needed, ideally using emerging and novel methods of investigating right heart function.

P1137
Prognostic value of proenkephalin in mortality prediction in cardiogenic shock

T Tarvasmaki[1]; T Jantti[1]; VP Harjola[2]; A Sionis[3]; S Di Somma[4]; A Mebazaa[5]; J Lassus[1]
[1]*Hospital District of Helsinki and Uusimaa, Heart and Lung Center, Helsinki, Finland*; [2]*Hospital District of Helsinki and Uusimaa, Department of Emergency Medicine and Services, Helsinki, Finland*; [3]*Hospital de la Santa Creu i Sant Pau, Barcelona, Spain*; [4]*Sant' Andrea Hospital, Rome, Italy*; [5]*Hospital Lariboisiere, Paris, France*

Purpose: Proenkephalin (PENK) is a small endogenous opioid peptide, which has depressive effects on cardiac and renal function. High PENK levels have been associated with worsening renal function and poor outcome in heart failure. We investigated the relationship between PENK with renal function and patient outcome in cardiogenic shock (CS).
Methods: CS patients with serial plasma samples (n = 154) from the prospective CardShock study were included. PENK along with other biomarkers, such as creatinine, hsTnT, NT-proBNP and soluble ST2, were analyzed from plasma samples at baseline (0 h), 12 h, 24 h, 48 h, and the last day in cardiac or intensive care unit between day 5 and 10. Discriminative capability was evaluated by the area under the receiver operating curve (AUROC) and optimal cutoff values for biomarkers in relation to mortality were evaluated with the Youden index. The independent association of PENK with 90-day mortality was analyzed with regression analyses adjusting for the CardShock risk score, and levels of hsTnT, ST2 and NT-proBNP.



Results: The mean age was 66 (12) years, 74% were men, and 81% had acute coronary syndrome as CS etiology. Median baseline PENK was 105 (71-167) pmol/mL and creatinine was 1.11 (0.87-1.54) mg/dl. PENK levels were highest at baseline and declined thereafter; those dead at 90 days had higher PENK levels than those alive (figure 1A). PENK was highly correlated with creatinine, eGFR and Cystatin C levels at all time points with highest correlations at 24 h (Spearman ? = 0.705, ? = 0.740 and 0.745, respectively; $p < 0.001$ for all). PENK categorized according to optimal cutoff by Youden index (low/high) was independently associated with increased 90-day mortality at 12 h and thereafter. In particular, categorized PENK at 24 h predicted dismal prognosis: 90-day mortality was 66% for high vs 18% for low PENK (see also figure 1B); the same 24-h cutoff (<105 pmol/mL) was also optimal for mortality prediction by the Youden index. Categorized PENK at 24h (below/above 105 pmol/mL) provided additive value for the CardShock risk score, peak-hsTnT, ST2 and NT-proBNP in mortality prediction ($p < 0.05$ for all comparisons of nested models). Combination of categorized PENK, ST2 (below/above 480 ng/mL) and NT-proBNP (below/above 4840 ng/L) at 24 h showed good discrimination in 90-day mortality prediction with AUROC 0.855 (95% CI 0.789-0.921, $p < 0.001$).
Conclusions: In CS, PENK is highly correlated with renal function. Its level has also a positive correlation with increased mortality and PENK at 24 h can provide additive value in risk stratification.

P1138

Predictors of long lenght of stay in elderly patients with acute heart failure: realworld evidence from the ATHENA registry

A Pratesi[1]; F Orso[1]; AC Baroncini[1]; G Biagioni[2]; F Fedeli[2]; S Parlapiano[2]; A Herbst[2]; A Lo Forte[1]; C Ghiara[1]; E Giuliani[1]; F Caramelli[1]; N Marchionni[1]; M Di Bari[1]; A Ungar[1]; S Baldasseroni[1]
[1]Careggi University Hospital (AOUC), Department of Experimental and Clinical Medicine, Florence, Italy; [2]University of Florence, Florence, Italy

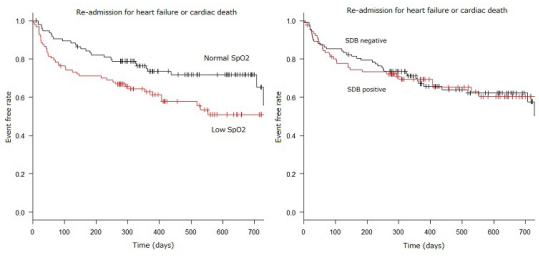
Backword: Clinical registries represent the so-called "real world" in contrast to clinical trials that are known to have a selection bias. However, heart failure (HF) registries may maintain a certain level of selection bias by including only patients hospitalized in cardiology wards. "Real world" administrative data show that only few patients (about a quarter) are hospitalized in cardiology units, while most of them are admitted to internal medicine and geriatrics wards.
Purpose: to identify the independent predictors of long length of stay of elderly patients hospitalized for acute HF in different clinical settings of care: cardiology, internal medicine and geriatrics.
Methods: data derived from the ATHENA retrospective observational study which included elderly patients (= 65 years) admitted with diagnosis of AHF (worsening or de novo) to the Emergency department (ED) of a tertiary University teaching-hospital and then transferred to the above described settings of care between 01-Dec-2014 and 01-Dec-2015.
Results: 401 patients were enrolled, 15.2% hospitalized in cardiology, 14.7% in geriatrics and 70.1% in internal medicine. Mean age was 83.5 years, and was higher in geriatrics (86.9 years) than in internal medicine (83.4 years) and in cardiology (81.0 years), $p = 0.001$. Females were 52.6%: 55.7% in cardiology, 52.7% in internal medicine and 49.2% in geriatrics ($p = 0.770$). Of those alive at discharge, mean length of stay was 9.0 days; then, we considered long length of stay (LLS) a bed rest >9 days. LLS occurred in 108 (29,6%) participants, and was longer in geriatrics (13.7 days) than in cardiology (9.9 days) and internal medicine (8.0 days), $p < 0.001$. In univariate analysis, variables related with LLS were: Charlson Comorbidity score, setting of care, NT-proBNP measured in ED, history of severe chronic kidney disease, eGFR and hematocrit in ED, cognitive impairment and Barthel index. In multivariate analysis, adjusted for age and sex, resulted independent predictors of LLS: NT -proBNP in ED - subsequently expressed as logarithm with base 10 (OR 4.12, 95%CI 2.08-8.14, $p < 0.001$), Barthel Index (OR 0.98, CI = 0.97-0.99, $p = 0.017$) and cognitive impairment (OR 3.17; 95% CI 1.40-7.18; $p = 0.006$).
Conclusion: NT-proBNP in ED, Barthel Index and cognitive impairment are independent predictors of long length of stay in a large cohort of elderly patients hospitalized for acute heart failure in different clinical setting of care.

P1139

Prognostic impact of sleep disordered breathing and nocturnal hypoxemia in patients with acute decompensated heart failure

H Hirokazu Kondo[1]; Y Obayashi[1]; M Fuki[1]; M Imanaka[1]; S Nishimura[1]; M Kuroda[1]; M Amano[1]; S Nishiuchi[1]; T Harita[1]; J Sakamoto[1]; Y Tamaki[1]; S Enomoto[1]; M Miyake[1]; T Tamura[1]; Y Nakagawa[1]
[1]Tenri Hospital, Tenri, Japan

Background: It has been reported that heart failure is frequently concomitant with sleep disordered breathing (SDB) and nocturnal hypoxemia is a worsening factor of heart failure. The purpose of this study is to evaluate prognostic impact of SDB and nocturnal hypoxemia in patients with acute decompensated heart failure (ADHF).
Methods: Consecutive 193 patients (76.9 ± 11.7 years, males, 50.2%) with ADHF emergently admitted to our hospital from September 2015 to March 2017 were enrolled and performed overnight oximetry with PULSOX®-Me300 before discharge. We examined and calculated 3% oxygen desaturated index (ODI), mean oxygen saturation (SpO2) and time with oxygen saturation <90% (T90), and defined SDB positive as 3%ODI >15, low SpO2 as mean SpO2 <95, and high T90 as T90 >6 minutes, and investigated prognosis as re-admission of heart failure and cardiac death.
Results: 3%ODI was 16.7 ± 12.5 and SDB positive were 91 patients. Median of mean SpO2 was 94.9% (93.8-96.1) and low SpO2 were 97 patients and high T90 were 100 patients. 73 patients were re-admitted for heart failure or cardiac death, and Kaplan-Meier analysis revealed that low SpO2 group and high T90 group had worse prognosis than normal SpO2 group and low T90 group, on the other hand, SDB positive was not significant (log-rank P = 0.019, P = 0.011, and P = 0.88, respectively).
Conclusions: Nocturnal hypoxemia was associated with increasing risk for re-admission and cardiac death in patients with ADHF.

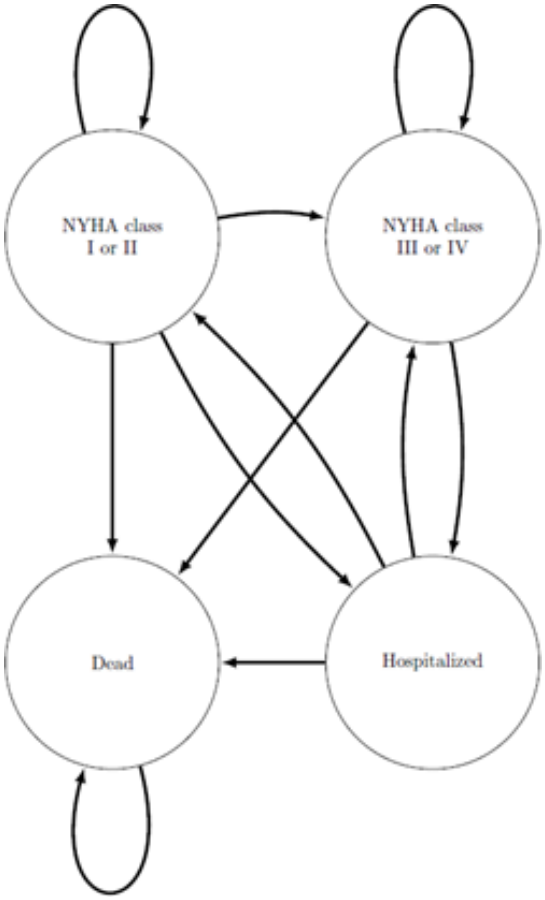


P1140

Effectiveness of heart failure care management by primary versus secondary care providers; a health state transition model.

H Henk Van Voorst[1]; AER Arnold[1]
[1]Medical Center Alkmaar, Cardiology, Alkmaar, Netherlands

Background: Heart failure reduces quality of life and life expectancy, hospital admissions are frequent and create a burden on public resources.
Purpose: The aim of this study is to quantify the differences in costs and Quality Adjusted Life Years (QALYs) of primary compared to secondary care lead heart failure follow up after an acute heart failure admission.
Methods: A health state transition (Markov) model was written with the states New York Health Association functional classification (NYHA) class I or II, NYHA class III or IV, hospitalized and dead. Transition probabilities between states were derived retrospectively from a single centre cohort of patients admitted for acute heart failure between 01-01-2013 and 31-12-2015 and available literature. 12 months of follow up data after the initial hospital admission was included in this study. QALYs in the health states were extracted from the literature. Quantity and costs of care were provided by the hospitals financial department and was only with respect to in hospital care. The treatment effect, primary versus secondary care lead follow up, was extracted from the literature. Monthly simulation steps were repeated 60 times to generate 5 years of virtual follow up data. Baseline willingness to pay was assumed € 50,000 per QALY.
Results: Primary care lead follow up decreased the costs by €137.89 and increased the QALYs by 0.22 in the baseline simulation, this resulted in a Net Monetary Benefit of € 11,227.46. Probabilistic sensitivity analysis using uniform and the most plausible distributions of parameters resulted in 86.1 % and 89.1% of the simulations favouring primary care lead heart failure follow up.
Conclusion: Involving primary care physicians in heart failure care will likely decrease costs and increase QALYs, this result was reached through a decrease of the mortality and hospitalization rate in the model.



Health state transition (Markov) diagram

P1141

Effects of beta blocker use prior to admission in patients with acute decompensated heart failure

Y Tamaki[1]; H Yaku[2]; E Yamamoto[3]; N Ozasa[2]; Y Inuzuka[4]; T Morimoto[5]; Y Nakagawa[1]; T Kato[2]; T Kimura[2]
[1]Tenri Hospital, Department of Cardiology, Tenri, Japan; *[2]Kyoto University Graduate School of Medicine, Department of Cardiovascular Medicine, Kyoto, Japan*; *[3]Massachusetts General Hospital, Cardiology Division, Boston, United States of America*; *[4]Shiga General Hospital, Department of Cardiology, Moriyama, Japan*; *[5]Hyogo College of Medicine, Department of Clinical Epidemiology, Nishinomiya, Japan*

Background: Beta blockers are guideline-recommended therapy and improve long-term prognosis in heart failure patients with reduced ejection fraction. However, whether beta blocker use before admission is beneficial in patients with acute decompensated heart failure (ADHF) remains unclear.
Purpose: The purpose of this study is to clarify the effects of beta blocker use before admission on in-hospital mortality in patients with ADHF.
Methods: This study is a physician-initiated, prospective, observational cohort study enrolling the consecutive patients who had hospital admission due to ADHF during the period between October 2014 and March 2016 in the 19 participating hospitals in Japan. After excluding 239 patients with acute coronary syndrome, 3817 patients were included in this analysis. Primary outcome measure was all cause death during hospitalization.
Results: Mean age was 78.1 years and 54.7% were male. Ischemic etiology was 28.5%. Mean left ventricular ejection fraction (LVEF) was 46.3% and 37.9% of patients showed LVEF less than 40%. Intravenous inotropes were used in 19.5%. Patients taking beta blockers before admission were 39.6%. Patients on beta blockers were significantly younger (77.6 years vs. 78.4 years, p <0.001) and had more frequently history of heart failure hospitalization (55.2% vs. 26.1%, p <0.001). Ischemic etiology was more prevalent in patients on beta blockers (36.3% vs. 23.4%, p <0.001). There was no difference in sex, prevalence of LVEF less than 40%, and use of intravenous inotropes between patients with and without beta blockers. Systolic blood pressure at presentation was lower in patients on beta blockers (143 ± 35 mmHg vs. 151 ± 35 mmHg, p <0.001). Heart rate was also lower in patients on beta blockers (92 ± 25 bpm vs. 98 ± 29 bpm, p <0.001). Patients on beta blockers showed significantly lower in-hospital mortality (4.4% vs. 7.6%, p <0.001). After adjusting for confounders, beta blocker use before admission was significantly associated with lower in-hospital mortality (hazard ratio 0.39; 95% confidence interval 0.26-0.58, p <0.001).
Conclusion: Beta blocker use prior to admission was associated with lower in-hospital mortality in patients with ADHF.

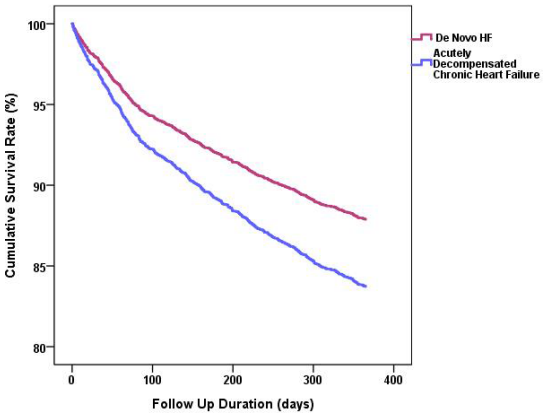
P1142

Not all acute heart failure syndromes are the same: De novo acute heart failure vs. Acutely decompensated chronic heart failure.

J-H Ju-Hee Lee[1]; WS Yoon[1]; DH Bae[1]; M Kim[1]; KK Hwang[1]; MC Cho[1]
[1]Chungbuk National University Hospital, Cardiology, Cheongju, Korea Republic of

On behalf of: KorAHF investigators
Funding Acknowledgements: This work was supported by Research of Korea Centers for Disease Control and Prevention.

Background: Acute heart failure syndromes (AHFS) can be classified into heart failure (HF) which presenting for the first time (de novo) or acutely decompensated chronic HF (AD-CHF). We compared the differences between de novo HF and AD-CHF regarding their clinical features and prognosis.
Method
We evaluated the AHFS patients hospitalized in ten regionally-representative tertiary university hospitals who registered in the Korean Acute Heart Failure (KorAHF) Registry from March 2011 to February 2014.
Results: Among the 5,625 patients who were registered at KorAHF Registry, 2,944 patients (52.3%) were classified as de novo HF and 2,681 patients (47.7%) were classified as AD-CHF. AD-CHF patients were older, more often women, and more likely to have hypertension, diabetes, ischemic heart disease, chronic kidney disease and atrial fibrillation. Regarding precipitating factors, infection, renal failure, anemia or bleeding, noncompliance and recent addition of negative inotropic drugs were predominant in AD-CHF, whereas ischemic event, severe hypertension, excessive alcohol or illicit drug use and endocrine abnormalities were predominant in de novo HF. AD-CHF patients showed lower serum sodium and hemoglobin, higher blood urea nitrogen and serum creatinine, and higher B-type natriuretic peptide level. De novo HF patients showed higher LV EF, smaller LV end-diastolic dimension and LA size, and lower RV systolic pressure. Although the use of renal replacement therapy was comparable, de novo HF patients were more frequently supported by mechanical ventilator and mechanical assisting device including IABP, PCPS and AD-CHF patients used inotropes more frequently. While in-hospital mortality was comparable between two groups (5.0% in AD-CHF vs 4.6% in de novo HF, P = 0.396), 1-year mortality was significantly higher in AD-CHF patients (22.9% vs 13.9%, P < 0.001). In multivariate analysis adjustment for 13 risk variables including age, sex, and brain natriuretic peptide, the hazard ratio for the mortality was increased in patients with AD-CHF. (Figure)
Conclusion: Independent of other key prognostic variables, AD-CHF had significantly worse prognosis than de novo HF. They also showed many differences in clinical presentation, risk factors and laboratory values. Better understanding on these differences between de novo HF and AD-CHF is needed to improve outcomes for AHFS.



P1143

Ischemic origin of heart failure is associated with worse prognosis in 3 and 12 months after acute episode

A Vinikovas[1]; R Zeimaite[2]; K Navardauskaite[2]; D Verikas[3]; D Kablucko[4]; K Stasaitis[5]; A Mebazaa[6]; A Kavoliuniene[5]; J Celutkiene[4]
[1]University Hospital Santariskiu Klinikos, Vilnius, Lithuania; *[2]Vilnius University, Faculty of Medicine, Vilnius, Lithuania*; *[3]Lithuanian University of Health Sciences, Faculty of Medicine, Kaunas, Lithuania*; *[4]Vilnius University, Clinic of Cardiac and Vascular diseases, Center of Cardiology and Angiology, Vilnius, Lithuania*; *[5]Lithuanian University of Health Sciences, Department of Cardiology, Kaunas, Lithuania*; *[6]University Paris Diderot , U942 Inserm, Hospital Lariboisiére, Paris, France*

On behalf of: GREAT network

Introduction: Ischemic origin of heart failure is associated with higher mortality rates for heart failure (HF) patients. However, the prognostic relevance of ischemic heart disease and prior coronary artery revascularization is not entirely clear.
Purpose: We aimed to analyse the impact of ischemic heart disease and history of revascularization on mortality (M) and rehospitalization (R) rates due to cardiovascular (CVR) and non-cardiovascular reasons (NCVR) in 1, 3, and 12 months (mo) in AHF patients.
Methods: A prospective two-centre observational cohort study enrolled 726 (mean age 72 years, 43% female) AHF patients admitted to an emergency department. Data, including patient history, R and M rates were grouped into non - ischemic HF (Non–Isch-HF) and an ischemic HF (Isch-HF) group, the latter was divided into 2 subgroups: with and without revascularization - (Revasc+) and non-revascularization (Revasc-) groups. Data was analyzed with binary logistic regression, SPSS v.20. Non-IscHF and Revasc- groups were used as references. Odds ratio (OR) were also adjusted to age, gender, LVEF, anemia and systolic blood pressure.
Results: 310 (42.6%) patients represented Isch-HF group, of them - 155 (50%) represented Revasc+ group. The results are presented in table below ($p < 0.05$ are marked with an asterisk *). After adjustment, only composite endpoint (M+R) due to cardiovascular reasons showed significant increase in Isch-HF group.
The history of coronary artery revascularization showed no statistically significant association.
Conclusion: Ischemic HF patients demonstrate significantly higher morbidity and mortality in 3 and 12 months after hospitalization compared to non-ischemic HF patients. On the other hand, ischemic HF patients are much less affected by non-cardiovascular rehospitalizations and mortality.

P1144

Characteristics of heart failure with preserved, mid-range, and reduced ejection fraction in patients admitted with dyspnea - impact of comorbidity

OW Nielsen[1]; N Valeur[1]; A Sajadieh[1]; A Andreas Fabricius-Bjerre[1]; CM Carlsen[1]; L Kober[2]
[1]Bispebjerg University Hospital, Copenhagen, Denmark; *[2]Rigshospitalet - Copenhagen University Hospital, Copenhagen, Denmark*

Background: The distribution of subtypes of cardiac dysfunction in heart failure (HF) including preserved ejection fraction (HFpEF), mid-range EF (HFpEF), and reduced EF (HFrEF) remains elusive, probably due to unclear diagnostic criteria, patient selection, and non-cardiac comorbidity. We studied consecutively admitted patients with dyspnea. The aim was to apply novel guidelines to describe the type of cardiac dysfunction in relation to presumed cardiac or non-cardiac cause of dyspnea.
Method: All patients with dyspnea as a main reason for hospitalization were eligible; we excluded patients with acute coronary syndrome, eGFR < 30 ml/min/1.73 m^2, and low NT-proBNP (< 35 pmol/l, i.e 296 ng/l). Patients with presumptive non-cardiac dyspnea were only included if NT-proBNP exceeded 423, 845 and 1691 ng/l, for age 40-49, 50-74 and 75+ years respectively. Novel ESC criteria for HFpEF and diastolic dysfunction were assessed in every patient with LVEF of 40% or more. Cardiac dysfunction was ranked according to the first matching abnormality: valvular heart disease (HFvhd), HFrEF, HFmrEF, HFpEF, and no cardiac dysfunction. We also adjudicated whether acute decompensated HF (ADHF) had been the primary diagnosis during admission.
Results: We included 370 patients of whom 75 had presumptive non-cardiac dyspnea. Overall, 10% (38/370) had no cardiac dysfunction. Cardiac dysfunction consisted of 18.4 % HFvhd (61/332), 30.1 % HFrEF (100/332), 10.2% HFmrEF (34/332), and 41.3% HFpEF (137/332). HFpEF was twice as common in presumptive non-cardiac dyspnea vs cardiac dyspnea (71 % vs 34%, $p < 0.0001$). HFmrEF matched HFrEF, but HFrEF was associated with higher Charlson Comorbidity index than HFmrEF and HFpEF (3.2 vs 2.3 vs 2.5, $p = 0.021$) despite lower mean age (73.2 vs 77.2 vs 77.1 years, $p = 0.011$). Adjudicated ADHF was the primary diagnosis in 80% of HFrEF, 62% of HFmrEF and 28 % of HFpEF.
Conclusion: HF according to contemporary criteria applied to 90% of patients admitted with dyspnea and elevated NT-proBNP irrespective of presumptive cause of dyspnea, of these 10% had HFmrEF and 41% HFpEF. A diagnostic and therapeutic dilemma arises for the many patients who fulfill criteria for HFpEF albeit ADHF was not adjudicated as the primary diagnosis.

P1145

Gender differences in Egyptian patients hospitalized with heart failure-Insights from the ESC heart failure long-term registry

M M Mahmoud Hassanein[1]; M Abdelhamid[2]; B Ibrahim[3]; A Elshazly[4]; MW Abouleineen[5]; H Sobhy[6]; G Nasr[7]; F Elmesseiry[8]; M Eshmawy[9]; N Farag[10]; A Youssef[11]; A Elbahry[12]; Y Elrakshy[13]; M Sobhy[14]; A Reda[15]
[1]Alexandria University, Cardiology, Alexandria, Egypt; *[2]Cairo University, Cairo, Egypt*; *[3]National Heart Institute, Cairo, Egypt*; *[4]Gamal Abdel Nasser Hospital, Alexandria, Egypt*; *[5]Zagazig University, Zagazig, Egypt*; *[6]El Menshawy General Hospital, Tanta, Egypt*; *[7]Suez Canal University, Ismailia, Egypt*; *[8]Ras Eltin Hospital, Alexandria, Egypt*; *[9]Tanta University Hospital, Tanta, Egypt*; *[10]Dar Al Fouad, Cairo, Egypt*; *[11]Assiut University Hospital, Assiut, Egypt*; *[12]Port Fouad General Hospital, Port Fouad, Egypt*; *[13]Students' University Hospital, Alexandria, Egypt*; *[14]International Cardiac Centre, Alexandria, Egypt*; *[15]Menoufeya University, Shebin Elkoum, Egypt*

On behalf of: ESC heart failure long-term registry
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Background: Women with cardiovascular disease have distinct clinical manifestations and outcome compared with males. Knowledge on relevant gender specific risk factors for HF can assist with appropriate targeted preventative interventions, diagnosis and therapeutics for each gender.
Aims: This analysis evaluates the gender differences in the Egyptian cohort of patients hospitalised for acute heart failure (AHF) in the ESC-Heart Failure long-term registry.
Methods and Results: From April 2011 to September 2014, 1634 patients hospitalised with AHF were enrolled by 20 hospitals all over Egypt. Of these patients, 1112 (68%) patients were men, mean age 60.5 ± 11.9 years, and 522 (32%) were women, mean age 60.3 ± 13.3 ($p = 0.80$). Women presented with a higher admission systolic blood pressure and resting heart rate. Compared to men, women had a higher body mass index (32.5 ± 9.0 vs 29.3 ± 4.9, $p < 0.001$), more frequent atrial fibrillation (35%vs 22%, $p < 0.001$) and anaemia defined by a haemoglobin <12 g/dl (83% vs 58%, $p < 0.001$). Women were more likely to present with heart failure with preserved ejection fraction than men (30% vs 11%, $p < 0.001$). Women had more frequent diabetes mellitus (48% vs 42%, $p < 0.05$) and hypertension (49% vs 39%, $p < 0.001$) than men whereas smoking was rare (9% vs 83%, $p < 0.005$). There was no significant difference in the primary etiology of heart failure between both sexes. ACE-inhibitors, MRA's, antiplatelets, statins and nitrates were less frequently prescribed to women, whereas they more often received digoxin, amiodarone, anticoagulants and calcium channel blockers. There was no significant difference in in-hospital (6% vs 5%, $p = 0.39$) and one- year mortality (28% vs 26%, $p = 0.48$) between both sexes. SBP (<100mmHg) and renal dysfunction (serum

P1143 Predictive value of ischemic orgin of HF

	1 month	3 months	12 months			
Outcomes	OR (C.I 95%)	Adjusted OR (C.I 95%)	OR (C.I 95%)	Adjusted OR (C.I 95%)	OR (C.I 95%)	Adjusted OR (C.I 95%)
Readmissions due to CVR	0.879 (0.6; 1.2)	0.932 (0.5; 1.6)	1.489* (1.0; 2.0)	1.285 (0.7; 2.1)	1.832* (1.3; 2.4)	1.354 (0.8; 2.1)
Readmissions due to NCVR	0.324* (0.1; 0.5)	0.610 (0.2; 1.4)	0.582* (0.3; 0.9)	1.008 (0.4; 2.3)	0.461* (0.3; 0.7)	0.582 (0.3; 1.0)
Deaths due to CVR	1.640 (0.8; 3.2)	0.545 (0.1; 1.5)	1.728* (1.0; 2.9)	1.004 (0.4; 2.3)	2.031* (1.3; 3.0)	1.313 (0.6; 2.5)
Deaths due to NCVR	0.235* (0.1; 0.6)	0.684 (0.1; 4.0)	0.349*)0.1; 0.7)	0.645 (0.2; 2.0)	0.374* (0.2; 0.6)	0.430 (0.1; 1.1)
Composite end-point (M+R) due to CVR	0.973 (0.6; 1.3)	1.922 (1.1; 3.3)	1.631* (1.1; 2.2)	1.153 (0.7; 1.8)	2.018* (1.4; 2.7)	1.401 (0.8; 2.2)
Composite end-point (M+R) due to NCVR	0.304* (0.1; 0.5)	1.445 (0.6; 3.0)	0.488* (0.3; 0.7)	1.127 (0.6; 2.0)	0.423* (0.2; 0.6)	0.2; 0.6 (0.7; 2.1)

creatinine=1.5 mg/dl) were significant predictors of in-hospital mortality. For 1-year mortality, age (one year increase in age), hemoglobin <12gm/dl, SBP <100mmHg and renal dysfunction were significant predictors.
Conclusion: Men and women with AHF differ significantly in baseline clinical characteristics, cardiovascular risk factors and management but not in adverse outcomes. These findings emphasize the importance of individualized management and need for more comprehensive recruitment of women in clinical trials.

P1146

Does the cause really matters? analysis of heart failure decompensation with or without an etiologic factor

A Alejandro Travieso Gonzalez[1]; TS Luque Diaz[1]; CN Perez Garcia[1]; D Enriquez Vazquez[1]; D Vivas Balcones[1]; C Olmos Blanco[1]; J Higueras Nafria[1]; R Bover Freire[1]; I Vilacosta[1]; C Macaya Miguel[1]
[1]*Hospital Clinic San Carlos, Madrid, Spain*

Introduction: In some acute heart failure (HF) episodes, the trigger of the event remains elusive despite a thorough investigation. Our aim is to establish if there are any differences in the clinical profile between patients with an attributable cause of the decompensation and those without it.
Methods: From July 2015 to April 2017, 336 consecutive patients were admitted to a tertiary hospital in Spain, with the diagnosis of acute heart failure. The healthcare professionals further classified them according to the presence or absence of a trigger of the event.
Results: From the 336 patients analyzed, in 281 of them a trigger for the episode was found, and in 55 it was not. Mean age was 76,2 for the first group, 73,8 for the second (p = 0,133). Slight differences in gender were seen (72,7% men without it, 51,6% women with it, p = 0,001). No significant differences were reported in other cardiovascular risk factors (Table 1).
In the complementary explorations, patients without a cause of the episode had lower values of left ventricular ejection fraction (LVEF) (38% vs 48%, p = 0,003), and lower levels of serum ferritine (111 vs 202 ng/mL, p = 0,002).
Patients without a trigger of the episode had a trend towards longer in-hospital stay (5,05 [SD 0,89] vs 4,72 [SD 0,95] days), without statistical signification. Levels of NTproBNP were higher in the group without a cause (27.141 vs 8511 pg/mL, p = 0,01). They were also characterized by a greater use of implanted cardioverter defibrillators (ICD) (16,4% vs 5,3%, p = 0,004) and cardiac resynchronization therapy (CRT) (12,7% vs 3,2%, p = 0,002). They were more commonly derived to HF specialized units at discharge (58,2% vs 20,6%, p < 0,001).

Table 1

N = 336	Without trigger (n = 55)	With trigger (n = 281)	p
Arterial Hypertension	81,8%	81,9%	0,995
Diabetes Mellitus	41,8%	47,3%	0,453
Dyslipidemia	61,8%	63,3%	0,830
Smoking habit	7,3%	10,3%	0,487
Atrial fibrillation	52,7%	55,2%	0,740
Chronic kidney disease	32,7%	28,5%	0,525

Cardiovascular risk factors.

Conclusions: Patients with an acute heart failure without a trigger of the decompensation have a different profile from those with a recognizable one. They have lower LVEF, higher levels of serum natriuretic peptides and prevalence of iron deficiency, with a broader use of device therapies for advance HF (ICD and CRT) and referral to heart failure specialized units. No significant differences were seen in the length of in-hospital stay.

P1147

Hyponatremia is associated with worse clinical markers of congestion, anemia, renal impairment, myocardial damage, neurohormonal and inflammatory activations

Y Yuksel Cavusoglu[1]; ME Altinbas[1]; S Eraslan[1]
[1]*Eskisehir Osmangazi University, Eskisehir, Turkey*

Purpose: Hyponatremia has been established as a strong predictor for worse clinical outcomes in heart failure (HF). N-terminal pro B-type natriuretic peptide (NT-proBNP), cardiac troponin, high sensitive C-reactive protein (hsCRP), hemoglobin (Hb) or estimated glomerular filtration rate (eGFR) are also known to be of prognostic significance in HF. We aim to assess possible associations between hyponatremia and other well-established clinical markers in patients with HF.
Methods: This study included 418 patients admitted to hospital with the diagnosis of acute decompensated HF, NYHA II-IV, LVEF < 40% and >18 years of age. NT-proBNP, high sensitive cardiac troponin T (hs-cTnT), carbohydrate antigen 125 (CA-125), hsCRP, eGFR, creatinine, Hb and sodium levels have been analyzed for the assessment of possible correlations and associations. Patients were classified into two groups: patients with hyponatremia (sodium < 135 mEq/L, n = 80, 19.1%) and patients with normonatremia (sodium = 135 mEq/L, n = 338, 80.9%).
Results: Mean age of study population was 67 ± 12 years. Mean EF was 25.4 ± 7.9%, NT-proBNP was 7667 ± 9876 pg/mL, CA-125 was 86.2 ± 125.5 U/mL, hs-cTnT was 0.22 ± 0.86 ng/mL, creatinine level was 1.41 ± 0.88 mg/dL, eGFR was 62.9 ± 32.4 mL/min/1.73 m2, hsCRP was 27.4 ± 39.1 mg/dL, sodium was 138.2 ± 4.7 mEq/L and hemoglobin level was 12.4 ± 2 g/dL. When compared to patients with normonatremia, patients with hyponatremia have had higher median NT-proBNP (3197 [1093-8391] vs 6964 [2647-19902] pg/mL, p < 0.001, respectively), higher CA-125 (33.33 [15.8-96.8] vs 61.04 [25.3-172.0] U/mL, p < 0.011, respectively), higher hsCRP (10.9 [3.8-24.8] vs 27.2 [10.1-67.6] mg/L, p < 0.001, respectively), higher hs-cTnT (0.033 [0.016-0.064] vs 0.044 [0.021-0.086] ng/mL, p < 0.05, respectively), higher creatinine (1.12 [0.9-1.4] vs 1.33 [1.0-1.9] mg/dL, p < 0.005, respectively), lower eGFR (59.7 [41.1-83.5] vs 48.2 [35.1-68.9] mg/L, p < 0.001, respectively) and lower Hb (12.8 [11.1-13.9] vs 11.3 [10-12.8] g/dL, p < 0.001, respectively). There were a significant negative correlation between sodium and NT-proBNP levels (r=-,232, p < 0.001), CA-125 levels (r=-,136, p = 0.01), hsCRP levels (r=-,267, p < 0.001), hs-cTnT levels (r=-,134, p = 0.008), creatinine levels (r=-,185, p = 0.001) and positive correlation between sodium and Hb levels (r=,255, p = 0.001) and eGFR (r=,173, p = 0.001). Hyponatremia was present in 26% of patients with anemia and in 11.8% of patients without anemia (p < 0.001), 22.4% of patients with an eGFR < 60 mL/min/1.73 m2 and in 14.3% of patients with an eGFR >60 mL/min/1.73 m2 (p = 0.036), in 21.2% of patients with high hsCRP and in 10.3% of patients with normal hsCRP levels (p < 0.05).
Conclusions: The results of this study showed that in decompensated HF patients, hyponatremia is associated with higher NT-proBNP, hs-cTnT, CA-125, hsCRP, creatinine levels and lower eGFR and hemoglobin levels, reflecting more severe clinical status of the disease in patients with hyponatremia.

P1148

Abnormal potassium level predicts long-term outcomes in patients with acute dyspnea

A Vinikovas[1]; R Zeimaite[2]; K Navardauskaite[2]; G Ziubryte[3]; S Tribusauskaite[3]; D Rimkeviciute-Vaiciuliene[4]; D Kablucko[5]; K Stasaitis[4]; A Mebazaa[6]; A Kavoliuniene[4]; J Celutkiene[5]
[1]*University Hospital Santariskiu Klinikos, Vilnius, Lithuania*; [2]*Vilnius University, Faculty of Medicine, Vilnius, Lithuania*; [3]*Lithuanian University of Health Sciences, Faculty of Medicine, Kaunas, Lithuania*; [4]*Lithuanian University of Health Sciences, Department of Cardiology, Kaunas, Lithuania*; [5]*Vilnius University, Clinic of Cardiac and Vascular diseases, Center of Cardiology and Angiology, Vilnius, Lithuania*; [6]*University Paris Diderot , U942 Inserm, Hospital Lariboisiére, Paris, France*

On behalf of: GREAT network

Introduction: As plasma potassium (K) level imbalance is associated with higher mortality risk, K is included in some clinical risk scores to assess the prognosis of acute heart failure (AHF) patients. The importance of hypo-/hyperkalemia in prediction of outcomes in a wide population of dyspneic patients is less clear.
Purpose: We aimed to evaluate the prognostic value of abnormal blood K levels in prediction of long-term mortality (M) and readmissions (R) in dyspneic patients.
Methods: Prospective observational cohort study enrolled consecutive patients admitted to the emergency department (ED) with acute dyspnea due to AHF and other reasons. Blood K levels at the time of admission and number of M and R due to cardiovascular (CVR) and non-cardiovascular (NCVR) reasons in 12 months of follow up were collected. Data of 1414 study patients (mean age 72 years) were included in the analysis. Patients were divided into 3 groups by plasma K level: group 1 consisted of 1243 (87.9%) patients with normal plasma K level (3,8-5,2 mmol/L); hypokalemia group - 98 (6.9%) patients with plasma K level up to 3,8 mmol/L; 73 (5.2%) patients with plasma K level higher than 5,2 mmol/L were included into hyperkalemia group. Data were analyzed using SPSS v23 with binary and multivariable regression.
Results: With binary logistic regresion, long term M and R due to CVR showed statistically significant results in hyperkalemia group: R due to CVR - OR = 1.548, C.I. 0.9; 2.4, p = 0.007; M due to CVR - OR = 2.159, C.I. 1.2; 3.8, p = 0.009. Multivariable regression's results are presented in the table below. Univariate predictors included hyperkalemia, blood urea level, chronic kidney disease (CKD), non-usage of ACE inhibitors and aldosterone inhibitors. In a multivariate analysis hyperkalemia was found as the most critical prognostic factor (adjusted OR 6,49, 95% CI 1,23-34,33; p = 0,028).
Conclusion: Patients with hyperkalemia at the time of admission have greater chances of death and readmissions due to cardiovascular reasons in a 12-month

period, compared to patients who arrived at the ED with normal blood K levels or hypokalemia.

Multivariate analysis results

Variable	Univariate analysis		Multivariate analysis	
	OR	C.I. 95%	OR	C. I. 95%
Plasma potassium level: elevated vs normal[a]	1,04	0,88-1,25	6,49*	1,23-34,33
Angiotensin-converting enzyme inhibitor: : non-use vs use[a]	0,24	0,98-1,56	1,57*	1,09-2,25
Plasma urea level: increased vs normal[a]	1,02*	1,01-1,04	1,03*	1,00-1,06
Aldosterone antagonist: non-use vs use[a]	0.83	0.64-1.07	0.89	0.63-1.27
CKD: diagnosed vs. not diagnosed [a]	1,08	0,81-1,44	1,21	0,081-1,81

a- referent; * - $p < 0.05$;

P1149

ESC guidelines for management of acute heart failure: fact vs reality, one year later

N Sahdev[1]; A Pulikal[1]; R Rajay Narain[1]; A Saidmeerasah[1]; L Ruscoe-Price[1]; N Soni[1]; J Kathirgamachelvam[1]; R Ray[1]; N Shanmugam[1]; L Anderson[1]
[1]St George's University of London, Cardiac and Vascular Sciences Research Centre, London, United Kingdom

Background/Introduction: In 1997 heart failure (HF) was said to be an emerging epidemic and twenty years on, it is at the forefront of global disease with a world prevalence of more than 23 million. Under new European Society of Cardiology (ESC) guidelines in 2016, patients with AHF with pulmonary oedema with respiratory failure should be referred to coronary care/intensive care unit within 120 minutes.
Purpose: This study aims to observe the implementation of the new ESC pathway for management of acute heart failure in a busy tertiary hospital. The study observes time periods before and after the ESC 2016 guidelines were incorporated into the hospital ED guidelines to observe if the new pathway was being competently followed.
Methods: In September 2016, we met with the ED team to draw up a pulmonary oedema pathway in line with the new ESC guidelines for AHF (referral to cardiology andtransfer of patients with pulmonary oedema and respiratory failure to CCU/HDU within 120 minutes. Patients presenting to ED and admitted to the hospital with AHF from February-June 2016 and October 2016-December 2016 who were detected by the heart failure team were extracted from the National Heart failure audit. To ensure validity in both data sets, the x-ray of each patient was reviewed by two independent cardiologists and corroborated with radiology report for pulmonary oedema. The patients that were agreed to have AHF with CXR evidence of frank pulmonary oedema were extracted. The patient notes were searched for details including: A&E diagnosis, referral pathway, final admitted ward, discharge date, HR, BP and co-morbidities.
Results: Prior to the ESC guidelines being implemented within the hospital (Feb 2016-June 2016), 26 patients admitted with AHF with pulmonary oedema were identified (11% of the total admitted AHF patients). Of these 26 patients, 9 (35%) were referred to cardiology immediately in A&E. Of these 9, 7 were transferred onto a cardiology ward [LA1] and 2 were treated on a medical ward.
Following the introduction of the ESC guidelines into hospital guidelines (Oct-Dec 2016) of the 27 patients who were admitted with AHF and frank pulmonary oedema on CXR (18% of the total admitted AHF), 13 were referred to cardiology (48%). 100% of these patients were transferred to CCU within 120 minutes.
Therefore, following the implementation of the new guidelines the percentage of patients directly referred to cardiology increased from 35% to 48%.
Conclusion(s): Following ESC 2016 guidelines more AHF patients with pulmonary oedema presenting to A&E are being referred directly to cardiology. Once referred they were transferred to a level 2 (CCU) bed within the suggested timeframe. The new guidelines allow clinicians to make more clear decisions. Although an increase in patients referred to cardiology is encouraging, further work is needed on this pathway to ensure the percentage of pulmonary oedema patients transferred to cardiology improves further.

P1150

The examination of clinical features about congestive heart failure with ischemic heart disease in cases used original clinical pathway.

Y Kato[1]; K Hayashi[1]; M Hasegawa[1]; N Matsuo[1]; T Fujiwara[1]; M Tanimoto[1]; K Kagawa[1]; Y Nakano[2]; N Onishi[1]; A Atsushi Takaishi[1]; M Ueeda[1]; S Hirohata[2]
[1]Mitoyo General Hospital, Kanonji, Japan; *[2]Okayama University, Graduate School of Health Sciences, Okayama, Japan*

Background: We introduced the clinical pathway(CP) for congestive heart failure(CHF) cases required admission from August 2015, and reported its usefulness previously. From past epidemiologic point of view, there seems to be the clinical features about age range, left ventricular function or various data of lipid and fatty acid in CHF cases with ischemic heart disease(IHD) compared in CHF cases with other underlying disease.
Purpose: We investigated the clinical features about CHF cases with IHD who ware introduced our original CP.
Method: We enrolled 197 CHF cases admitted in our hospital and introduced CP for the first time from August 2015 to July 2017(mean age 81+/-11 years old, male/female 112/85). We divided them into two groups, IHD-group(CHF with any IHD required any treatment: 62cases) and NIHD-group(CHF without IHD: 135cases), and investigated their various factors about clinical course and blood data on admission about lipid and polyunsaturated fatty acid(PUFA). Between two groups we examined the difference about each factor.
Results: In IHD-group compared in NIHD-group mean age was higher(78+/-11 vs 82+/-10 years old; $p < 0.05$), the man ratio was higher(69 vs 51%; $p < 0.05$) and the prevalence of dementia was lower(21 vs 42% $p < 0.01$). About left ventricular function the ejection fraction by echocardiography was lower(44+/-19 vs 54+/-19%; $p < 0.05$) and the value of Brain Natrium Peptide in blood on admission was higher(962+/-710 vs 734+/-645 pg/mL; $p < 0.05$) in IHD-group. The various lipid data(blood concentration of triglyceride, high density lipoprotein, low density lipoprotein or oxidized low density lipoprotein) was not different between two groups. About PUFA, in comparison except all cases administered EPA preparation, although the blood concentration of arachidonic acid(AA) and docosahexaenoic acid(DHA) on admission ware not different between two groups, the value of eicosapentaenoic acid(EPA) tended to be higher (61+/-27 vs 53+/-34 mg/dl; NS) and the ratio of cases with high EPA/AA value(= 0.3) was higher(63 vs 47%; $p < 0.05$) even in IHD-group. Although the mean hospitalization period was shorter in IHD-group(14+/-11 vs 18+/-13 days; $p < 0.05$), the ratio of cases with the history of CHF admission within past 3 years before admission was higher(37 vs 21%; $p < 0.05$) and the ratio of re-admission cases with CHF within 1 year after discharge was higher(33 vs 20%; NS) in IHD-group.
Conclusion: About clinical features in CHF cases with IHD, the result about patient characteristics or cardiac function was predictable. But we found that their hospitalization period was shorter and they tended to admit repeatedly. And we found that the EPA concentration of blood on admission among PUFA in IHD-group was higher rather than that in NIHD-group. It seemed that there was another imvolvement of influence to metabolism of PUFA in CHF cases compared in general ischemic heart disease cases.

P1151

Causes of death after hospital discharge are similar between heart failure patients with and without worsening renal function

P P M Spineti[1]; L A Feijo[2]; M I Garcia[2]; S S Xavier[2]; A S Sousa[2]
[1]Rio de Janeiro State University (UERJ), Cardiology, Rio de Janeiro, Brazil; *[2]Federal University of Rio de Janeiro (UFRJ), Cardiology, Rio de Janeiro, Brazil*

Background: Worsening renal function (WRF) is associated with higher mortality after hospital discharge in patients with decompensated heart failure (DHF).
Objectives: To describe the causes of death after discharge from patients with a previous admission for DHF. To compare the causes of death between patients with and without WRF.
Methods: Patients admitted for DHF in our university hospital, between 01/01/06 and 12/31/11, were included in a cohort study. Deaths after discharge were identified through record linkage with the state mortality database. ACRS was defined as an absolute increase in serum creatinine = 0.3mg/dL anytime during hospitalization. Causes of death were coded and grouped according the 10th International Disease Classification (IDC).
Results: 394 patients were admitted for DHF; 53.3% were men, with mean age of 64 +/- 14 years, 83.15% had systolic dysfunction and 37.6% ischemic aetiology. The incidence of WRF was 43.3. 29 patients died during the hospitalization and 248 after discharge. The accuracy of deaths search was 99.44%. The main group of death causes was diseases of the circulatory system, accounting for 58.5% of deaths. Among the diseases of the circulatory system, 45% of deaths were due to other forms of heart disease (IDCs I30 to I52), 29% to ischemic heart diseases, 12% to hypertensive diseases and 6% to rheumatic diseases. The codes referring

to heart failure (I11, I50.0 - I50.9) were cited as the underlying cause of death in 48 patients (19.35%). When all lines of the death certificate were analyzed, the codes referring to HF were cited in 99 of the 248 deaths (39.92%). If the codes referring to myocardiopathies and cardiomegaly were associated with HF codes, HF would be identified as the basic cause of 63 deaths (25.4%). Genitourinary tract disorders accounted for only 4% of deaths. The distribution of death causes was similar between groups, with the exception of death from cardiovascular causes that was higher in the ACRS group.
Conclusion: The main cause of death between DHF patients are the circulatory system diseases. The distribution of death causes was similar between patients with and without WRF.

P1152
Heart failure diagnostic after evaluation of more than surgical 1700 patients

P Losada Mora[1]; A M Alfonso Miguel Garrido Castro[1]; JL Carrillo Linares[1]; L Morcillo[1]
[1]*University Hospital Virgen de la Victoria, Cardiology, Internal Medicine, Malaga, Spain*

Introduction: Consultation are a widely used resource among the different units of a hospital. Specifically, those from Orthopedic Surgery and Traumatology (OST) and Vascular Surgery (VS) are the most frequent.
Objectives: Analyze the most frequent consultations on patients admitted to OST and VS to a team (T) assigned to the control of medical pathologies, composed of medical professionals form Internal Medicine and Cardiology.
Material and Methods: Descriptive analysis of consultations on patients admitted to OST and VS who suffered some type of medical decompensation that required to be notified to T.
Results: From June 2008 to November 2014, the following consultations were sent:
- 1486 from the OST. The most frequent consultation was "dyspnea" in 371 cases (25%), followed by "control of pluripathology" in 163 (11%), "control of diabetes" and "blood pressure" both with 124 (8.3%) and 123 (8.3%) consultations. The digestive pathology was 10.5%. 4% of the consultations were due to "analytical alterations". 48.7% of the dyspnea were of respiratory origin. 41% of the dyspnea were of cardiological origin, being the most frequent cause without evident trigger (66%, most developed an accompanying respiratory picture), while 13.6% corresponded to volume overload, 11.3% to anemia secondary to the intervention and another 11.3% to uncontrolled atrial fibrillation. The rest of dyspnea were mainly due to anxiety (4.7%). In 3.7% of the cases, dyspnea was not observed.
- 173 from the VS. The most frequent consultation was "dyspnea" in 62 cases (35.8%), followed by "control of pluripathology" in 18 (10.4%), "decrease in the level of consciousness" in 13 (7.5%), fever 13 (7.5%) renal failure 7 (4%) and "control of blood pressure" 7 (4%). 43.5% of the dyspnea were of respiratory origin. 33.8% of the dyspnea were of cardiological origin, being the most frequent cause without evident trigger (28.6%, most of them developed an accompanying respiratory picture), along with 28.6% due to volume overload, 19% to uncontrolled atrial fibrillation, 14% valvulopathy and 9.5% to hypertensive crisis. In 11.3% of cases, a specific diagnosis of dyspnea was not established.
Conclusions: Dyspnea is the most frequent consultation by these two surgical services. A quarter of the consultations for medical decompensation in patients admitted to OST and more than a third in patients admitted to VS also correspond to dyspnea correspond to dyspnea, of which almost half are respiratory and somewhat less of cardiological origin. A significant percentage of these are due to intrahospital processes like volume overload. An early evaluation of these patients could be beneficial in terms of decrease morbidity.

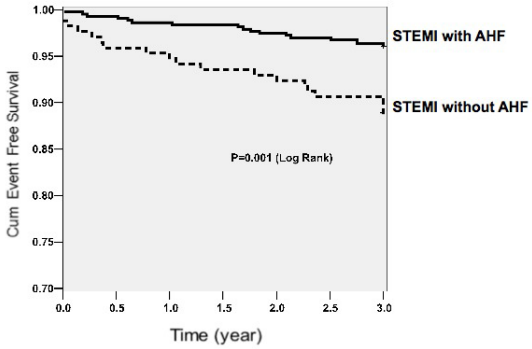
P1153
Acute heart failure in patients with ST-segment elevation myocardial infarction: prognostic significance of mid-range left ventricular ejection fraction

S Sergey Kozhukhov[1]; A Parkhomenko[1]; N Dovganych[1]
[1]*NSC "Institute of Cardiology", Kiev, Ukraine*

Background: The prevalence and clinical outcomes of acute heart failure (AHF) with mid-range left ventricular ejection fraction (mrEF) after ST-elevation myocardial infarction (STEMI) have not been well elucidated. According to the new European Society of Cardiology guidelines we allocated AHF patients (mrEF; 40% to 49%) as a distinct group.
Objective: To analyze the prevalence of AHF, clinical profile, in-hospital outcomes and and long-term survival of STEMI patients with mrEF.
Methods: We conducted a retrospective study of 606 consecutive patients with STEMI (age 54.1 ± 0.4 years) hospitalized within 12 hours of symptoms onset (4.1 ± 0.2 hours), who had echocardiographic examination performed on admission. Based on sign and symptoms of AHF (Killip II-III) within 24 hours patients were divided into two groups: with AHF - 171 and without AHF - 435 patients. Main outcome was cardiovascular mortality with a median follow-up of 3 years.
Results: Patients with AHF were likely to be older, have history of ischaemic heart disease and previous MI. On admission AHF patients presented higher level of glycemia and C-reactive protein, lower glomerular filtration rate in compare to patients without AHF. During in-hospital stay AHF patients had significantly higher rate of ventricular fibrillation/tachicardia and early left ventricle aneurism. Kaplan-Meier survival curves demonstrated that incidence of cardiovascular death in AHF patients was higher in comparison with those without AHF at long-term follow-up (Figure 1).
Conclusions: AHF is a frequent complication in STEMI even in patients with mrEF and is a powerful and independent predictor of 3-year's survival. AHF patients had higher long-term risk, required special attention and monitoring during follow-up.

Event free survival in STEMI patients with mrEF and AHF

Kaplan-Meier



Acute Heart Failure - Diagnostic Methods

P1154
Relationship between brain natriuretic peptide, high-sensitivity cardiac troponin I and kidney function in predicting worsening renal function and prognosis in acute heart failure

Y Horiuchi[1]; N Wettersten[1]; P Murray[2]; A Maisel[1]
[1]*University of California San Diego, Division of Cardiovascular Medicine, San Diego, United States of America*; [2]*University College Dublin, Department of Nephrology, Dublin, Ireland*

Funding Acknowledgements: Abbott Laboratories and Alere, Inc.

Background: In acute heart failure (AHF), relationships between brain natriuretic peptide (BNP), high-sensitivity cardiac troponin I (hscTnI) and renal function have not been fully elucidated, especially in terms of worsening renal function (WRF).
Purpose: We aimed to investigate relationships between BNP, hscTnI and creatinine and its predictive values for in-hospital mortality and WRF.
Methods: The Acute Kidney Injury NGAL Evaluation of Symptomatic heart fallure Study (AKINESIS) was a prospective, international, multicenter study of AHF. We retrospectively analyzed 886 patients for the relationships between admission BNP, hscTnI and creatinine and in-hospital death, severe WRF (sWRF), non-severe WRF (nsWRF) and WRF with clinical deterioration. sWRF was a sustained increase of = 0.5 mg/dl or 50% in creatinine and nsWRF was non-sustained increase of = 0.3 mg/dl or 50% in creatinine. WRF with clinical deterioration means nsWRF with in-hospital death, renal replacement therapy, inotrope use or mechanical ventilation.
Results: BNP, hscTnI and creatinine had significant but weak to moderate correlations ($r < 0.400$). Increased mortality was associated with both higher BNP and hscTnI (Figure 1A). WRF correlated better with hscTnI than BNP (Figure 1B, 1C and 1D). hscTnI predicted each definition of WRF after adjustment for creatinine and other confounders, while these relationships were not observed with BNP (log hscTnI; sWRF, adjusted OR 1.75, 95% CI 1.12-2.71, $p = 0.013$, nsWRF, adjusted OR 1.43, 95% CI 1.07-1.91, $p = 0.017$, WRF with clinical deterioration, adjusted OR 2.21, 95% CI 1.42-3.45, $p < 0.001$).
Conclusions: hscTnI was a significant predictor for worse in-hospital outcomes including sWRF, nsWRF and WRF with clinical deterioration.

Figure 1. Rates of clinical endpoints stratified by BNP and hscTnI above and below the median

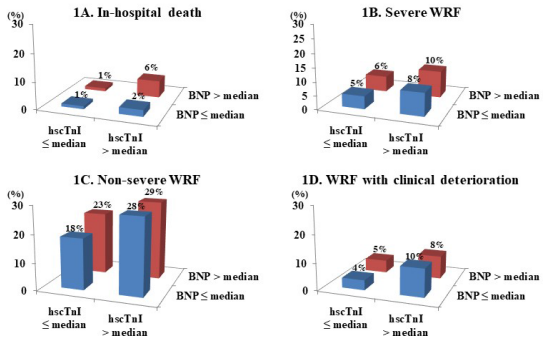


Figure 1

P1155

How to predict Heart Failure readmission

M Michael Kleiner Shochat[1]; A Shotan[1]; I Kleiner[2]; JM Weinstein[2]; M Kazatsker[1]; A Asif[1]; I Dahan[1]; S Meisel[1]
[1]Hillel Yaffe Medical Center, Heart Institute, Hadera, Israel; [2]Saroka Medical Center, Cardiology, Beer Sheva, Israel

Background: Readmission for heart failure (HF) are a major burden. We aimed to assess whether the extent of improvement in pulmonary fluid content (?PC) during HF-hospitalization evaluated by lung impedance (LI), or indirectly by other clinical and laboratory parameters, predicts readmission.
Methods: The present study is based on predefined secondary analysis of the IMPEDANCE-HF extended trial comprising 266 HF patients at NYHA class II-IV and LVEF = 35% randomized to LI-guided or conventional therapy during long-term follow-up.
Results: LI-guided patients were followed for 58 ± 36 months and the control patients for 46 ± 34 months (p <0.01) accounting for 253 and 478 HF hospitalizations, respectively (p <0.01). LI, NT-proBNP, weight, radiological score, NYHA class, lung rales, leg edema or jugular venous pressure were measured at admission and discharge on each hospitalization in both groups with the difference defined as ?PC. Average LI-assessed by ?PC was 12.1% vs. 9.2% and time to HF-readmission was 659 vs. 306 days in the LI-guided and control groups, respectively (p <0.01). LI-based ?PC predicted 30 and 90-day HF readmission better than ?PC assessed by the other variables (p <0.01). The readmission rate for HF was lower if ?PC> median compared with ?PC= median for all parameters evaluated in both study groups with the most pronounced difference predicted by LI (p <0.01). Net reclassification Improvement analysis showed that adding LI to the traditional clinical and laboratory parameters improved the predictive power significantly.
Conclusion: The extent of ?PC improvement, primarily the LI-based, during HF-hospitalization, and study group allocation strongly predicted readmission and event-free survival time.

P1156

CA-125, a biomarker in acute-decompensated heart failure. Preliminary study.

M Ababei[1]; A Campeanu[1]; D Nistorescu[1]; O Zaharia[1]; T Nanea[1]
[1]University of Medicine and Pharmacy Carol Davila, Internal Medicine "Prof. Th. Burghele" Hospital, Bucharest, Romania

Background: CA-125 is a tumor antigen expressed on the surface of ovarian cells, used to monitor treatment of ovarian cancer (with normal upper limit of 35U/mL), but that also seems to have a role as a biomarker in heart failure (HF). CA-125 is secreted secondary to stimuli as mechanical stress, oxidative stress or inflammation, pathophysiological mechanisms well known in heart failure decompensation (ADHF).
Aim: To determine CA-125 changes in ADHF patients.
Method: The study group included 110 patients (mean age 72 ± 10 years, 63% men) with ADHF caused by ischemic cardiomyopathy. The subjects were clinically, ecocardiographically and biologically (NT-proBNP, CRP, serum uric acid (sUA), CA-125) evaluated.
Results: CA-125 level at admission was 53 ± 33 U/mL and decreased at discharge to 34 ± 17U/mL. The table below shows the significant differences in the CA-125 level (U/mL) depending on the followed parameters.

The CA-125 level correlated with LVEF (R = -0.221, p = 0.02), with myocardial strech marker -NT-proBNP (R = 0.371, p < 0.001), with the inflammation marker - CRP (R = 0.284, p = 0.003) and oxidative stress marker - sUA (R = 0.234, p = 0.015).
There was a significant difference between NT-proBNP at admission in obese versus normoponderal patients, which was maintained at discharge. The CA-125 level did not have the same dynamics.
Conclusions: The wide availability of this biomarker, the relatively low cost, the unchanging level with age, weight or renal function, the correlation with known prognostic factors in HF and the additional information brought outside the classical biomarkers make CA-125 a biomarker that can be used in monitoring ADHF patients.

Followed parameters

Followed parameters	YES	NO	p
Male	55±34	51±32	0.69
Pleural effusion	63±25	43±19	0.02
Reduced LVEF heart failure	57±21	35±20	0.013
Increased LV filling pressures	61±24	37±18	0.005

P1157

Combination of ST2 and BNP in diabetic patients with acute heart failure: relation with ventricular stiffness and outcome

A Alberto Palazzuoli[1]; G Ruocco[2]; I Evangelista[2]; R Nuti[2]
[1]Santa Maria Alle Scotte Polyclinic, Siena, Italy; [2]University of Siena, Cardiovascular Diseases Unit, Department of Internal Medicine , Siena, Italy

Background: Diabetes is a common complication of HF and its relationship to this syndrome is bimodal: diabetes has a causative role in systolic and diastolic dysfunction, and diabetic patients have a worse outcome compared to non-diabetic patients. Moreover, diabetes is simultaneously a causal factor and a comorbidity. Recently, a novel biomarker, soluble ST-2, a member of interleukin-1 receptor family formally known as interleukin-1 receptor like 1 (IL1RL-1), demonstrated greater prognostic power with respect to traditional biomarkers in patients with HF
Purpose: In this study we sought to: 1- evaluate levels of ST-2 and B-type natriuretic peptide (BNP) in groups with HF with reduced ejection fraction (HFrEF) and HF with preserved ejection fraction (HFpEF) and in those with/without diabetes; 2- analyze the prognostic impact of ST-2 in terms of death and re-hospitalization for cardiovascular causes during a 6-month follow-up period.
Methods: we performed an echocardiographic examination and measured ST-2 and BNP within 12 hours of hospital admission. Patients were classified as HFrEF [LVEF < 50%] or HFpEF [LVEF = 50%]. We defined diastolic function according to recent guidelines, and we calculated LV Stiffness with the following formula: ratio E/e' (index of LV filling pressure) and left ventricular end diastolic diameter (LVEDD) (index of left ventricular volume). Patients were followed up for 6 months after discharge. Composite outcome was considered the sum of death and re-hospitalization for cardiovascular causes.
Results: Of 121 patients enrolled, 60 patients showed HFrEF and 61 HFpEF. We found a significant correlation between ST-2 and BNP; in particular, this relationship was more significant in patients with HFpEF with respect to patients with HFrEF (r = 0.50; p < 0.001 vs. r = 0.42; p = 0.001). We found a significant correlation between ST-2 and BNP, greater in diabetic patients (r = 0.50; p < 0.001) with respect to non-diabetic patients (r = 0.40; p = 0.001). ST-2 showed also a more significant correlation with LV stiffness in patients with diabetes (r = 0.56; p < 0.001) with respect to patients without (r = 0.29; p = 0.04). Univariate analysis demonstrated that both ST-2 and BNP were associated with adverse events occurring within 6 months (respectively: HR 2,73[1,46-5,09], p = 0.002; 2,48[1,49-4,74], p = 0.006.). After adjustment for potential confounding factors, multivariable analysis showed that only ST-2 levels greater than 50 pg/mL were correlated with a poor prognosis (2,15[1,10-4,19]; p = 0.02).
Conclusions: ST-2 confirmed its prognostic power in patients with diabetes as well as those with HFpEF. However the mechanism related to ST-2 increase remains to be completely understood, although increased cardiovascular stiffness and impaired filling of the left ventricle seem to be the most important causative factors. Its prognostic role appears to be additional to BNP.

P1158

Prognostic value of hyponatremia, hypochloremia and hypokalemia in patients with dyspnea admitted to the emergency department

A Arnas Rimkus[1]; I-M Saule[1]; A Mebazaa[2]; J Celutkiene[3]
[1]*Vilnius University, Faculty Of Medicine, Vilnius, Lithuania*; [2]*University Paris Diderot , U942 Inserm, Hospital Lariboisiére, Paris, France*; [3]*Vilnius University, Clinic of Cardiac and Vascular diseases, Center of Cardiology and Angiology, Vilnius, Lithuania*

On behalf of: GREAT network
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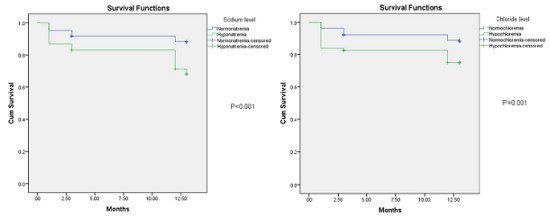
Introduction: The prognostic value of hyponatremia, hypochloremia and hypokalemia in a wider population of patients with acute dyspnea (AD) is unknown. Aim: To assess if low serum sodium, chloride and potassium levels had a significant value in predicting short and long-term rehospitalizations (RH) and mortality of patients with AD admitted to the emergency department (ED).
Methods: Prospective observational cohort study enrolled consecutive patients admitted to the ED with AD due to decompensated heart failure, pneumonia, pulmonary embolism and other reasons. Concentration of blood electrolytes on admission, mortality rates, RH at 1, 3 months, 1 year were collected. Hyponatremia was defined as a sodium level < 134 mmol/l, hypochloremia - chloride level < 98 mmol/l, hypokalemia - potassium level < 3.8 mmol/l. Data was analyzed using SPSS v23 and Cox proportional-hazards regression analysis.
Results: The study group consisted of 699 patients, 44.2% women, 55.8% men, mean age 68.60 ± 12.32 years. On admission 7.6% of patients had hyponatremia, 12.2% - hypochloremia, 8.7% - hypokalemia. Hyponatremic and hypochloremic patients results are summarized in the table. Hypokalemic patients were RH more times during 3 months due to cardiovascular (CV) causes (HR = 1.86 (1.11-3.11),p = 0.018), during 1 year due to all and CV causes (HR = 2.03 (1.15-3.59),p = 0.014; HR = 2.16 (1.10-4.25),p = 0.025).
Conclusion: Hyponatremia, hypochloremia are significant short and long-term predictors of outcomes in AD patients admitted to the ED. Hypokalemia had no prognostic value of mortality, but it was related with higher short and long-term RH rates.

	Hyponatremia HR (95% CI)	P-value	Hypochloremia HR (95% CI)	P-value
1 month RH (all causes)	2.12 (1.15-3.86)	0.027	1.80 (1.07-3.03)	0.028
1 month RH (CV)	1.87 (0.89-3.90)	0.097	1.91 (1.04-3.49)	0.036
1 month RH (non-CV)	2.74 (1.14-6.56)	0.024	1.58 (0.66-3.79)	0.306
3 months RH (all causes)	1.93 (1.21-3.08)	0.006	1.54 (1.01-2.34)	0.043
3 months RH (CV)	2.10 (1.23-3.63)	0.007	1.63 (0.97-2.67)	0.052
1 month mortalities (all causes)	2.74 (1.21-6.23)	0.016	4.20 (2.17-8.12)	0.000
1 month mortalities (CV)	1.82 (0.54-6.13)	0.332	3.15 (1.30-7.66)	0.011
1 month mortalities (non-CV)	5.59 (1.94-16.09)	0.001	4.35 (1.58-11.98)	0.004
3 months mortalities (all causes)	2.12 (1.04-4.30)	0.037	2.44 (1.37-4.37)	0.003
3 months mortalities (non-CV)	4.17 (1.66-10.52)	0.002	3.16 (1.31-7.62)	0.010
1 year mortalities (all causes)	3.25 (1.72-6.15)	0.000	2.77 (1.56-4.94)	0.001
1 year mortalities (non-CV)	5.48 (2.08-14.42)	0.001	3.35 (1.27-8.81)	0.014

HR-Hazard ratio; CI-Confidence interval; RH-rehospitalizations; CV-Cardiovascular



P1159

Neutrophil gelatinase-associated lipocalin is an early biomarker of acute kidney injury in acute decompensated heart failure

MV Lediakhova[1]; IV Zhirov[1]; SN Nasonova[1]; TM Uskach[1]; VP Masenko[1]; SN Tereshchenko[1]
[1]*National Medical Research Center for Cardiology, Moscow, Russian Federation*

Background: the incidence of acute kidney injury (AKI) is high in patients with acute decompensated heart failure (ADHF) and is linked to worse prognosis and quality of life. Early predictive biomarkers of AKI could allow early intervention and improve outcomes in AKI.
Purpose: to evaluate the value of serum neutrophil gelatinase-associated lipocalin (NGAL) concentrations for early diagnosis of AKI in patients with acute decompensated heart failure with reduced systolic function.
Methods: the study was a prospective, single-centre, randomized trial. We enrolled 60 patients hospitalized with ADHF. The patients had reduced systolic function (left ventricular ejection fraction (LVEF) <40%), increased levels of brain natriuretic peptide > 500 pg/mL and systolic blood pressure >125 mmHg. The exclusion criteria were: acute coronary syndrome; sustained ventricular tachycardia or ventricular fibrillation; severe aortic or mitral regurgitation; uncorrected obstructive valvular disease; hypertrophic obstructive cardiomyopathy; restrictive cardiomyopathy; estimated glomerular filtration rate (eGFR) < 30 mL/min/1.73m2. AKI was defined according to Kidney Disease: Improving Global Outcomes (KDIGO) Clinical Practice Guidelines. We measured of serum NGAL concentrations by a quantitative sandwich enzyme immunoassay technique (RD systems, DLCN20, USA). Statistical significance was defined as P <0.05.
Results: a total of 60 men hospitalized with ADHF were included. Average age was 62.0 ± 11.1 years and mean LVEF was 27.97 ± 6.57%. Serum NGAL concentrations were significantly higher in patients with AKI 171.2 (159.0-241.2) ng/mL compared without AKI 136.8 (108.2-163.0)ng/mL P < 0.001. For predicting AKI, the area under the receiver-operating characteristic (ROC) curve (AUC) of serum NGAL on admission for all participants in the test set was 0.83 (95% confidence interval: 0.73 to 0.93; P <0.001). A cutoff of 157.35 ng/mL yielded good sensitivity (0.83) and specificity (0.74).
Conclusion: serum neutrophil gelatinase-associated lipocalin can serve as an early biomarker for diagnosis of acute kidney injury in patients with acute decompensated heart failure with reduced systolic function.

P1160

ST-segment elevation in ECG combined with elevated high sensitive troponin-I is associated with worse long-term prognosis in ICU patients

T Javanainen[1]; R Cinotti[1]; K Cerlinskaite[1]; S Ishihara[1]; E Akiyama[1]; N Vodovar[1]; E Gayat[1]; A Mebazaa[1]
[1]*Hospital Lariboisiere, Inserm UMR-S 942 and Anesthesia and Critical Care Department, Paris, France*

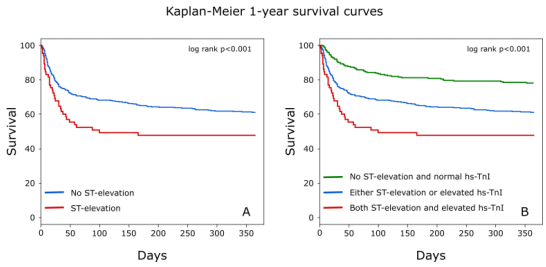
Background: In critically ill patients, ST-segment elevation (STE) in ECG has been poorly described and its association with long-term outcome is unknown.
Purpose: The aim was to investigate the incidence of STE and its association with 1-year mortality in Intensive Care Unit (ICU) patients.
Methods: The FROG-ICU (NCT 01367093) is a prospective, observational study in 2087 patients, conducted in 21 ICUs in 14 European hospitals. In this sub-study, patients with at least one ECG available during the first 3 days after ICU admission were included. ECGs were analysed digitally and STE was defined according to the Third Universal Definition (1). High sensitive troponin-I (hs-TnI) was measured at inclusion. Three groups of patients were created: 1) No STE and normal hs-TnI. 2) Either STE or elevated hs-TnI. 3) Both STE and elevated hs-TnI.
Cox multivariate regression analysis for 1-year mortality was conducted and the final adjusted model included Simplified Acute Physiology Score II (SAPS II), Charlson Comorbidity Index, gender, hs-TnI at inclusion and cardiac arrest as cause for ICU admission.

Results: In the 738 included patients, 93 (13%) displayed STE. Patients with STE were older (64 years (±18) vs. 59 years (±17), p = 0.009), more often male (n = 72 (77%) vs. n = 425 (66%), p = 0.036) and had more comorbidities. Cardiac arrest or cardiogenic shock as cause for ICU admission was more common in STE and hs-TnI was higher (64 ng/l (14-348) vs. 26 ng/l (8-177) p = 0.023) (Table). One-year mortality was higher in patients with STE (n = 45 (49%) vs. n = 206 (32%), p < 0.001, Figure A) and STE was associated with mortality in the adjusted cox model (HR 1.52-IC95% (1.09-2.11), p = 0.013). Patients with both STE and elevated hs-TnI had two-fold mortality in comparison with no STE and normal hs-TnI (n = 25 (49%) vs. n = 98 (27%), p < 0.001, Figure B).
Conclusions: STE is associated with increased long-term mortality in ICU patients. Combined STE and elevated hs-TnI define patients with the highest mortality risk.
1. Thygesen K et al Third Universal Definition of Myocardial Infarction. J Am Coll Cardiol. 2012 Oct 16;60(16):1581-98.

Table

	No ST-elevation n = 645	ST-elevation n = 93	p
Age, years (SD)	59 (17)	64 (18)	0.009
Male gender, n (%)	425 (66)	72 (77)	0.036
Charlson Comorbidity Index, pts (SD)	2.9 (2.4)	3.7 (2.5)	0.007
SAPS II, pts (SD)	47 (19)	51 (18)	0.021
Cardiac arrest or cardiogenic shock, n (%)	76 (12)	22 (24)	0.003
hs-TnI, ng/L (IQR)	26 (8-177)	64 (14-348)	0.023

Baseline characteristics



Figure

P1161

The predictive value of plasma biomarkers in heart failure patients: do they maintain their value in elderly population?

M Mauro Feola[1]; M Testa[2]; C Ferreri[3]; GL Rosso[4]
[1]Cardiovascular Rehabilitation-Heart Failure Unit, Fossano, Italy; *[2]Cardiology Division, Mondoví, Italy*; *[3]School of Geriatry University of Turin, Turin, Italy*; *[4]Emergency 118 ASLCN1, cuneo, Italy*

Galectin-3 demonstrated to be a robust independent marker of cardiovascular mid-term (18-month) outcome in heart failure (HF) patients. The objective of this study was to analyse the value of a pre-discharged determination of plasma galectin-3 alone and with plasma BNP in predicting mid-term outcome in elderly (<70 yers old) patients discharged after an acute decompensated HF (ADHF) episode.
Methods: all elderly HF subjects discharged alive after an ADHF were enrolled. All patients underwent a determination of BNP and galectin-3, a 6-minute walk test (6MWT) and an echocardiogram within 48 hours upon hospital discharge. Death by any cause, cardiac transplantation and worsening heart failure requiring readmission to hospital were considered cardiovascular events.
Results: patients (males, age 77.5 ± 5.9 ys old) were analyzed (mean follow-up 16.2 months; range months). During the follow-up events (53.6%) were scheduled (18 cardiac deaths, 27 re-hospitalizations for ADHF). HF patients who suffered an event demonstrated more impaired ventricular function (p = 0.04), higher plasma BNP (p = 0.02) and Gal-3 at pre-discharge evaluation (p = 0.05). Choosing adequate cut-off points (BNP = 500 pg/ml and Gal-3 = 17.6 ng/ml), the Kaplan-Meier curves depicted the powerful stratification using Galectin-3>17.6 ng/ml alone (log-rank 13.22; p = 0.0003) and adding BNP+Gal-3 the result was even better (log-rank 17.96; p < 0.00001).
Conclusion: in elderly population, adding Gal-3 to BNP, a single pre-discharge strategy testing seemed to obtain a satisfactorily predictive value in alive HF patients discharged after an ADHF episode.

Table 1. Main clinical features.

	NO-Event Group (39 pts)	Event Group (45 pts)	p
Age [years]	77.5±0.8	77.6±0.9	0.97
Sodium [mEq/l]	139.8±0.6	139.7±0.4	0.94
Haemoglobin [g/dl]	12.8±0.3	12.5±0.3	0.60
Creatinine [mg/dl]	1.3±0.1	1.6±0.2	0.08
eGFR [ml/min/1.73m^2]	53.3±3.6	48.6±3.5	0.35
BNP [pg/ml]	844.5±160.8	1431.9±178.1	0.02
Galectin-3 [ng/ml]	21.7±2.4	28.1±2.2	0.05
LVEF [%]	41.6±2.7	34.1±2.5	0.04

P1162

Predictive criteria for acute heart failure in emergency department patients with acute dyspnea: the PREDICA trial.

J Roncalli[1]; F Picard[2]; N Delarche[3]; I Faure[4]; C Pradeau[5]; M Thicoipe[5]; M Galinier[1]; S Charpentier[6]
[1]University Hospital of Toulouse, Cardiology, Institute CARDIOMET, Toulouse, France; *[2]University Hospital of Bordeaux, Cardiology, Bordeaux, France*; *[3]Hospital Center of Pau, Cardiology, Pau, France*; *[4]University Hospital of Bordeaux, Urgences, Bordeaux, France*; *[5]University Hospital of Bordeaux, SAMU, Bordeaux, France*; *[6]University Hospital of Toulouse, Urgences, Toulouse, France*

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Introduction: Early identification of patients with Acute Heart Failure Syndrome (AHFS) among patients admitted to the emergency department for dyspnea can quickly help implement the appropriate treatments. At a time when diagnostic tools (clinical ultrasound, biomarkers) are developing, knowing the performance of clinical and anamnestic data would make it possible to propose diagnostic strategies. The objective is to evaluate the diagnostic predictive value of various anamnestic and clinical signs for the diagnosis of AHFS in emergencies.
Method: PREDICA is an observational, prospective, multicentre study for construction of a diagnostic model. Inclusion of patients admitted to emergency department for non-traumatic acute dyspnea and data collection at admission were recorded by the patient's emergency physician. Criteria for judgment was assessed for AHFS after double expertise by pairs of cardiologists and emergency physicians. Construction of a model of prediction by logistic regression step by step. Sensitivity, specificity and area under the ROC curve of the model.
Results: Among 341 patients consecutively included in 3 centres, 149 (44 %) presented AHFS. The predictive factors of AHFS are shown in Table 1. The area under the ROC curve of the model is 0, 86. The sensitivity is 73% and the specificity is 81%.
Conclusion: The performance of clinical and anamnestic signs is high and should contribute to the development of diagnostic strategies in emergency departments.

	Odd ratio	Confiance interval 95%
> 80 years old	1.99	1.12-3.56
Bronchodilatator treatment	0.51	0.26-0.98
More than 3 cardiac treatments	2.24	1.13-4.41
Paroxysmal dyspnea	3.62	1.28-10.29
Jugular turbulence or hepatic jugular reflux	2.53	1.31-4.87
Oedema of the lower limbs	3.74	2.01-6.83
Crackling rales	4.13	2.32-7.36
Normal ECG	0.35	0.18-0.62

P1163

Relationship between pulmonary pressures and right ventricular mechanics in patients undergoing mitral valve surgery: initial results of the PREPARE-MVR study

B K Lakatos[1]; M Tokodi[1]; Z Toser[2]; AA Molnar[1]; S Szigeti[3]; KB Koritsanszky[3]; V Berzsenyi[3]; E Kispal[1]; K Racz[3]; AV Soltesz[3]; B Merkely[1]; E Nemeth[3]; A Kovacs[1]
[1]Semmelweis University Heart Center, Budapest, Hungary; [2]Argus Cognitive Inc., Dover, DE, United States of America; [3]Semmelweis University, Department of Anaesthesiology and Intensive Therapy, Budapest, Hungary

Severe mitral regurgitation is associated with significant changes not only in left ventricular, but also in right ventricular (RV) morphology and function. One of the major cause of RV remodelling is pulmonary hypertension, which could be reversible by mitral valve repair (MVR). Following MVR, characteristic and instant alterations in RV mechanics can be established, which may be related to the hemodynamic changes in the pulmonary vasculature. The PREPARE-MVR study (PRediction of Early PostoperAtive Right vEntricular failure in Mitral Valve Replacement/Repair patients) aims to determine parameters with added value in perioperative risk stratification to predict acute RV failure.

In this preliminary analysis, we sought to investigate the relationship between pulmonary pressures and resistance, and pre- and postoperative RV mechanics in patients undergoing MVR.

Our study group consisted of 22 MVR patients (mean age: 64 ± 10 years, m/f: 14/8). Transthoracic 3D echocardiography was performed before the operation, and at intensive care unit discharge. 3D beutel model of the RV was created and RV end-diastolic volume (EDV) along with RV ejection fraction (RVEF) were calculated using commercially available software. For in-depth analysis of RV mechanics, we have decomposed the motion of the RV using the ReVISION method to determine longitudinal (LEF) and radial ejection fraction (REF). The ratio of LEF or REF to RVEF quantifies the relative contribution of longitudinal or radial (bellows effect) wall motions to global function. Right heart catheterization measurements were performed preoperatively and 24 hours after the procedure to determine mean pulmonary artery pressure (mPAP), pulmonary arterial wedge pressure (PAWP) and pulmonary vascular resistance (PVR).

Based on EDV, RV morphology was similar after the surgery (pre- vs. postoperative; 160 ± 42 vs. 155 ± 50 mL, p = NS). RVEF decreased slightly after the MVR (48 ± 8 vs. 43 ± 8%, $p < 0.05$), however, RV motion pattern has markedly changed. Before the surgery a higher LEF/RVEF ratio was seen compared to lower REF/RVEF (0.48 ± 0.11 vs. 0.37 ± 0.10, $p < 0.001$), while after MVR, the radial motion became the dominant component of RV mechanics (0.35 ± 0.07 vs. 0.54 ± 0.07, $p < 0.0001$). Preoperative mPAP and PAWP inversely correlated with preoperative LEF ($r=-0.67$, $p < 0.01$; $r=-0.52$, $p < 0.05$). Preoperative REF/RVEF ratio showed relationship with the postoperative decrease in PVR ($r=-0.49$, $p < 0.05$). Moreover, patients with elevated preoperative PVR (72%) had significantly lower REF compared to those who had normal resistance (14 ± 6 vs. 21 ± 5, $p < 0.05$).

MVR results in complex hemodynamic changes in the pulmonary vascular bed which may have significant role in the development of postoperative alterations in RV mechanics and subsequent RV failure. Novel parameters of RV mechanics show relationship with invasively measured pulmonary pressures and resistance and may predict postoperative complications and outcome.

P1164

Simplified pulmonary ultrasound in heart failure

M Tsverava[1]; D Tsverava[2]
[1]Tbilisi State Medical University Iv.Javakhishvili (TSU), Internal Medicine, Tbilisi, Georgia Republic of; [2]MediClubGeorgia Tbilisi Clinic, Medicime, Tbilisi, Georgia Republic of

Pulmonary oedema (PE), due to fluid retention and redistribution is the cardinal manifestations of acute and exacerbation of heart failure (HF). The aim of this investigation was to study the effectiveness of simplified thoracic sonography in diagnosis of PE

Material and Methods: 420 patients with acute or exacerbated chronic HF (115 patients with diastolic and 305 with systolic HF). The control group consisted of 170 patients with different heart diseases (CHD, Hypertension, Aortic valve diseases),but without HF. Sonographic examination of a lung was done with 3,0-4,0 MgHz convex or sector probe, from 10 points on thoracic wall (cross points of midclavicular line with II, IV and V intercostal spaces and anterior axilar line with IV and V intercostal spaces), which corresponded to the projection of lower, middle and upper lobes of right lung and upper and lower lobes of left lung.

Results: During ultrasound examination 94.5% of patients with HF had "Comet tail phenomenon" (CTPh), which was registered only in 35,5% patients without HF ($p>0,001$). In DHF group CTPh was registered in 90,5% and in systolic HF group in 95,9% patients. In 91% of patients with HF CTPh was registered from 3 and more registration points. In control group CTPh was registered from more than 3 points only in 2 (1,3%) patients. The best results in diagnosis of DHF can be achieved if we take "3 and more registration points" as a reference point for diagnosis of pulmonary congestion (sensitivity - 0,911, specificity - 0,942, positive predictive value 0,975). The time of examination by simplified method for evaluation of CTPh and pleural space took 3-4 minutes.

Conclusion: In patients with HF during pulmonary ultrasound examination significantly often was registered CTPh. The count of registration points from the thoracic wall of CTPh 3 and > is sensitive and specific sign of HF. The simplified thoracic ultrasound is highly effective in diagnosis of PE in patients with HF

P1165

Right ventricle free wall strain predicts post-surgical low cardiac output syndrome in patients undergoing aortic valve replacement surgery.

K Karla Balderas-Munoz[1]; H Rodriguez Zanella Hugo[1]; JF Fritche Salazar[1]; A Jordan[1]; JA Arias Godinez[1]; MBA Gaxiola Macias[1]; A Orea Tejeda[1]
[1]National Institute of Cardiology Ignacio Chavez, Echocardiography, Mexico City, Mexico

Background: Severe aortic stenosis (AoS) represents a common entity for which surgical aortic valve (SAVR) replacement remains the treatment of choice. Low cardiac output syndrome after SAVR is related with increased mortality and treatment related costs. Recently strain imaging has been shown to be useful for prognosis in AoS, and its value remains beyond left ventricular ejection fraction. However its role for predicting low cardiac output syndrome (LCOS) has not been previously assessed.

Purpose: The aim of the present study was to evaluate whether echocardiography-derived right ventricle free wall strain (RVFWS) predicts the occurrence of postoperative LCOS in patients undergoing SAVR.

Methods: We prospectively enrolled patients with symptomatic severe aortic stenosis with LVEF > 30%, NYHA Class I and II, without other significant valvular lesion. A complete echocardiographic examination was perfomed before SAVR. Right ventricle free wall strain was measured in all patients before surgery. Patients were followed up during hospital stay. The main outcome was the occurrence of LCOS.

Results: A total 32 patients were included. Baseline clinical characteristics were similar between groups.

RVFWS was significantly lower in patients with LCOS than in patients without LCOS (12.8 ± 4.3 vs. -17.1 ± 3.9) before surgery and it was independently associated to the occurrence of low cardiac output [$p = 0.005$]. ROC curves to evaluate the utility of RV free wall strain to predict LCOS occurrence yielded a sensitivity of 81.2% and specificity of 71.4% , +LR of 2.86 of and −LR of 0.25 for a cut-off point of -15.

Conclusion: Right ventricle free wall strain is a useful parameter for risk stratification in patients with Sever AoS without severely depressed LVEF, and is independently associated with LCOS occurrence. The role of right ventricle in the genesis of LCOS is never contemplated and could explain its development in patients with preserved LVEF. This is an open field to extend research.

Right ventricle free wall strain

Variable	Without Low output	With low output	p
Basal RV free wall strain(%)	-16.4±4.0	-13.3±6.4	0.103
Middle free wall RV strain (%)	-18.4±5.5	-12.5±4.7	0.0056
Apical RV freewall strain (%)	-17.4±6.0	-13.9±5.1	0.110
Global Right ventricle free wall strain (%)	-17.1±3.9	-12.8±4.3	0.0081

RV: Right ventricle

P1166

Pulmonary acceleration time in non acute coronary syndrom pulmonary edema - prognostic value

V Vasilica Enache[1]; A-C Nechita[1]; I Badulescu[1]; S-C Stamate[1]
[1]University of Medicine and Pharmacy Carol Davila, Emergency Hospital St. Pantelimon, Bucharest, Romania

P1166 Table

	In-hospital mortality	30 days mortality	1 year mortality							
APE group	Ischemic	Valvular	Hypertensive	APE group	Ischemic	Valvular	APE group	Ischemic	Valvular	
PAAT	p <0.01	p <0.01	NS	p <0.01	p <0.01	p = 0.02	p = NS	p <0.01	NS	p = 0.04
COV	92ms				95ms			98ms		

PAAT-pulmonary acceleration timeCOV-cut off valueNS-non statistically significant

Introduction: Modified peripheral systemic vascular resistance as etiopathogeny of APE is a theory that has already been accepted. Can be non-invasive echocardiographic assessment of high pulmonary vascular resistance (PVR) helpful in understanding the pathophysiology as well as in establishing the prognosis?
Purpose: Identifying the prognostic value of pulmonary acceleration time in pulmonary artery(PAT) in Acute Pulmonary Edema outside of an acute coronary syndrome (non ACS APE) of diversified ethiologies.
Methods: 92 patients with non-ACS APE consecutively hospitalized in our clinic between 01.01-31.12.2015, distributed and analyzed according to three etiologies, based on anamnesis, clinical and paraclinical data: ischemic, primary valvular and hypertensive (with preserved LVEF, without significant valvular or documented coronary artery disease). An echocardiography was performed on admission. We assessed also PAT. We assumed that this echo parameter when has semnificative decresed values, can express high pulmonary vascular resistance and does not depend on RV systolic function. We correlated this parameter, when pathological modified, with short, medium and long-term prognosis for entire group and according with ethiology. We identified cut-off values with prognostic value using a ROC curve analysis.
Results: In the entire group 63% patients have PAT < 105 ms. PAT has been statistically significant (SS) associated with short, medium and long term prognosis in the whole group($p < 0.01$)with cut off value(COV) 92ms, 95ms and respectivly, 98ms. The prognostic value changes depending on substrate and on the end-point term:SS for in hospital mortality($p < 0.01$) for ischemic and hypertensive substrate; for 30 days mortality for ischemic($p = 0.02$) and for valvular ethiology ($p = 0.04$) for 1 year mortality.
Conclusions: A decreased PAT was present in more than 50% of pts with non ACS APE and has proven an important prognostic value for short($p < 0.01$), medium($p < 0.01$) and long- term mortality($p < 0.01$) in entire group with COV of 92ms, 95ms and 98 ms. The prognostic role changed according with etiology and endpoint term. High pulmonary vascular resistance play an important in role in APE patophysiology and PAT can be an usefull echo-parameter with diagnostic and prognostic value.

Acute Heart Failure - Treatment

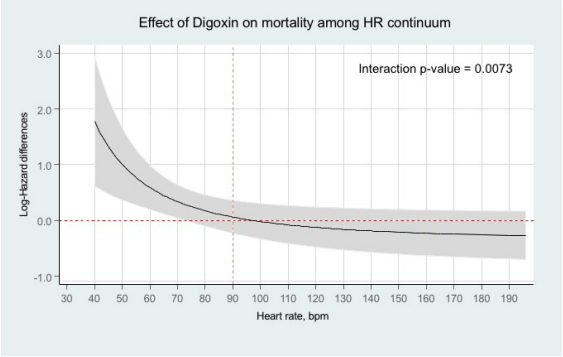
P1167

Digoxin and Prognosis of Heart Failure in Older Patients with Preserved Ejection Fraction: Importance of Heart Rate

P Pau Llacer[1]; J Nunez[2]; A Bayes-Genis[3]; A Conde Martel[4]; J Perez Silvestre[5]; J Diez Manglano[6]; P Alvarez Rocha[7]; LL Soler Rangel[8]; O Aramburu Bodas[9]; JC Arevalo Lorido[10]; JC Trullas Vila[11]; F Epelde Gonzalo[12]; JM Cepeda Rodrigo[13]; L Manzano Espinosa[14]; M Montero Perez-Barquero[15]
[1]Manises Hospital, Internal medicine, Valencia, Spain; *[2]University Hospital Clinic of Valencia, cardiology, Valencia, Spain*; *[3]Germans Trias i Pujol Hospital, Cardiology, Badalona (Barcelona), Spain*; *[4]University Hospital Dr Negrin, Internal medicine , Las Palmas De Gran Canaria, Spain*; *[5]University General Hospital of Valencia, Internal medicine , Valencia, Spain*; *[6]University Hospital Miguel Servet, Internal medicine , Zaragoza, Spain*; *[7]Hospital de Clinicas Dr. Manuel Quintela, Internal medicine and cardiology, Montevideo, Uruguay*; *[8]University Hospital Infanta Sofia, Internal medicine, Madrid, Spain*; *[9]Hospital Universitario Virgen Macarena, Internal medicine, Sevilla, Spain*; *[10]Zafra County Hospital, Internal medicine, Zafra, Spain*; *[11]Hospital d'Olot i Comarcal de la Garrotxa, Internal medicine, Olot. Girona, Spain*; *[12]Hospital Parc Tauli, Emergency Support Service, Internal Medicine, Sabadell. Barcelona, Spain*; *[13]Vega Baja Hospital, Internal medicine , Orihuela, Spain*; *[14]University Hospital Ramon y Cajal de Madrid, Internal medicine , Madrid, Spain*; *[15]University Hospital Reina Sofia, Internal medicine , Cordoba, Spain*

On behalf of: RICA register. SEMI

Background: The value of digoxin in heart failure (HF) remains controversial, particularly in patients with preserved ejection fraction (HFpEF). This study evaluated the 1-year risk of events after digoxin treatment for acute heart failure (AHF) in patients >70 years old with HFpEF.



Digoxin and mortality across heart rate

Methods: 1883 patients were included in this analysis (mean age, 82 years). The main endpoints were all-cause death and the composite of death and/or HF re-admission within 1 year. Cox regression analysis was used to evaluate the association between digoxin treatment and prognosis.
Results: 401 patients received digoxin treatment; of these, 86% had atrial fibrillation. The mean baseline heart rate was 86 ± 22 bpm. At the 1-year follow-up, 375 patients (20.5%) died and 684 (37.3%) had composite endpoints. Patients treated with digoxin showed higher rates of death (3.21 vs. 2.44 per 10 person-years, $p = 0.019$) and composite endpoint (6.72 vs. 5.18 per 10 person-years, $p = 0.003$). After multivariate adjustment, digoxin treatment remained associated with increased risks of death (HR = 1.46, 95% CI: 1.16-1.85, $p = 0.001$) and the composite endpoint (HR = 1.35, 95% CI: 1.13-1.61, $p = 0.001$). A distinctive prognostic effect of digoxin was found across the heart rate continuum; the risks for both endpoints were higher at lower heart rates and neutral at higher heart rates (p of the interactions = 0.014 and 0.028, respectively).
Conclusions: In older patients with HFpEF discharged after AHF, digoxin treatment was associated with increased mortality and/or re-admission, particularly in patients with lower heart rates.

P1168

Elegibility for sacubitril/valsartan utilization in acute heart failure

LCSP Luiz Carlos Passos[1]; TM Trindade[2]; WN De Carvalho[2]; AGQ De Jesus[2]; VRS Souza[3]; EOM Andrade[3]; YM Lira[4]; EL Garrido[3]; NFC De Oliveira[4]; AMP De Lima[2]
[1]Federal University of Bahia, Internal Medicine, Salvador, Brazil; *[2]Ana Nery Hospital, Salvador, Brazil*; *[3]Federal University of Bahia, Faculty of Nursing, Salvador, Brazil*; *[4]Bahiana School of Medicine and Public Health, Salvador, Brazil*

On behalf of: EPICO

Background: Sacubitril/Valsartan represents a major breakthrough in the set of heart failure treatment, since it has improved risk of death and re-hospitalization after more than a decade without new perspectives. Despite of this, PARADIGM-HF trial has not investigated benefits of utilization among acute decompensated patients during their hospital phase.
Purpose: We sought to investigate and describe the proportion of elegible patients and reasons for non-elegibility for sacubitril/valsartan utilization among patients admitted for acute decompensated heart failure.
Methods: Cohort data from 543 patients admitted in a tertiary cardiac referral centre for acute systolic heart failure compensation (left ventricular ejection fraction <50%). All the data was collected from medical records. Heart failure was defined according the European Society of Cardiology (ESC) guidelines.
Results: The main reason for non-elegibility was left ventricular ejection fraction = 35% (34%; 171 individuals). 31.1% (155) of the patients had previous intolerance to angiotensin converting enzyme inhibitors or angiotensin receptor blockers and 7% (37) had hypotension during hospital stay (systolic blood pressure <90mmHg). Likewise, 37 patients (7%) had need for dialysis. At the end of the analysis, 36.5% (198) of the patients remained elegible for sacubitril/valsartan initiation during hospital phase.

Conclusion: Although there is no evidence for sacubitril/valsartan implementation during hospital phase of acute heart failure, our data suggest that more than one third of the patients could be elegible for such implementation even before of the hospital discharge.

P1169

Efficacy of Tolvaptan for the first hospitalized patients with acute decompensated heart failure

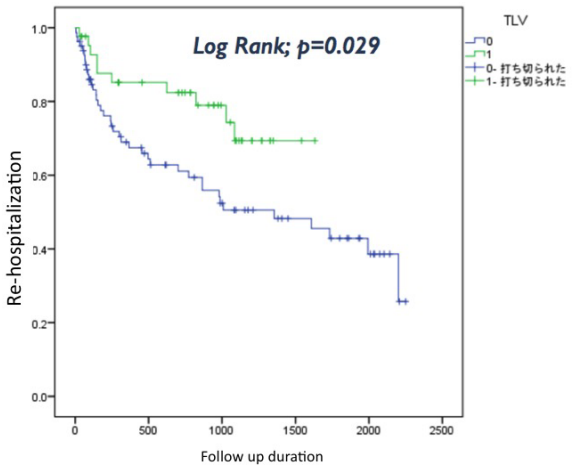
Y Yoriyasu Suzuki[1]; A Murata[1]; S Tsujimoto[1]; Y Ochiumi[1]; M Ehara[1]; T Ito[1]
[1]*Nagoya Heart Center, Nagoya, Japan*

Aim: the purpose of this study is to evaluate the efficacy of tolvaptan (TLV) for the initially hospitalized patients with acute decompensated heart failure (ADHF).
Methods: From 2015 to 2017, consecutive 124 patients initially hospitalized with a diagnosis of ADHF (clinical scenario 2/5) at Nagoya Heart Center. They were treated with or without TLV (TLV (-); n = 81, TLV (+); n = 43). We retrospectively analyzed the clinical outcome of these patients.
Results; the results are shown in the table and figure. 39.5% of cases were re-hospitalized and In the group treated with TLV, there was significantly fewer re-hospitalization (TLV(+) vs. TLV(-); 23.3% vs. 48.1%, Log rank p = 0.029). In the re-hospitalized cases, the incidence of WRF was significantly higher (TLV(+) vs. TLV(-); 0% vs. 14.8%, p = 0.004).
Conclusion: the treatment with TLV could shortened the duration of bed-rest and prevent WRF and re-hospitalization. The results of this study suggest tolvaptan initiated for acute treatment of patients initially hospitalized with ADHF had effect outcome in daily clinical practice.

Table

	TLV(+), N = 43	TLV(-), N = 81	p-value
male, %	58.1	56.9	0.520
age	79.5	76.2	0.354
Etiology, %			<0.0001
IHD	25.6	22.2	
VHD	32.6	23.5	
DCM	9.3	9.9	
EF, %	40.5	47.0	0.095
Cr, mg/dl	1,48	1.13	0.005
CCU stay, day	2.1	3.6	<0.001
WRF, %	0	14.8	0.004
Re-hospitalization, %	23.3	48.1	0.005

IHD; ischemic heart disease, VHD; valvular heart disease, DCM, Dilated cardiomyopathy, WRF; worsening renal function



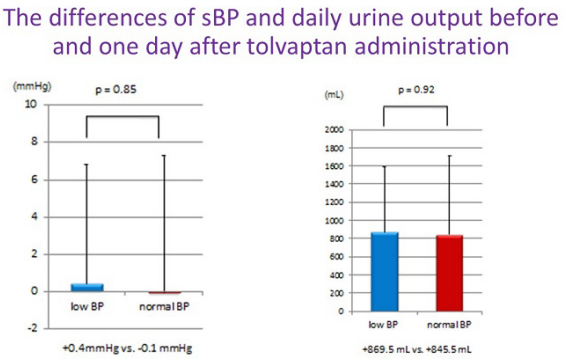
Figure

P1170

Safety and efficacy of tolvaptan administration in patients hospitalised for acute decompensated heart failure due to moderate or severe aortic stenosis

R Reo Hata[1]; Y Kawase[1]; T Tada[1]; K Kadota[1]
[1]*Kurashiki Central Hospital, Cardiology, Kurashiki, Japan*

Background: The administration of loop diuretics for the treatment of acute decompensated heart failure (ADHF) due to moderate or severe aortic stenosis has been reported to decrease blood pressure. Recently, tolvaptan, a selective vasopressin V2 receptor antagonist, has been reported to stabilise haemodynamics in patients with heart failure.
Purpose: We evaluated the short-term safety and efficacy of tolvaptan administration in patients hospitalised for ADHF due to moderate or severe aortic stenosis.
Methods: We analysed consecutive patients who had been hospitalised for ADHF due to moderate or severe aortic stenosis and treated with tolvaptan because of inadequate urine output response to loop diuretics between December 2011 and December 2014. The major outcome measures were defined as blood pressure and daily urine output before tolvaptan administration and one day after tolvaptan administration. The patients were classified into two groups on the basis of a systolic blood pressure (sBP) before tolvaptan administration: sBP <110 mmHg (low sBP group) and sBP = 110 mmHg (normal sBP group).
Results: Data on 44 patients were available for final analysis. The average age was 85.2 ± 6.3 years, the mean left ventricular ejection fraction was 49.5 ± 11.1%, and the mean estimated glomerular filtration rate on admission was 37.7 ± 21.5 ml/min/1.73m2. The average maximal aortic peak velocity was 3.48 ± 1.11 m/s, and the mean aortic valve area was 0.82 ± 0.28 cm2. Although the average daily urine output one day after tolvaptan administration was significantly increased compared with that before tolvaptan administration (1249.0 ± 627.5 ml vs. 2106.5 ± 1118.5 ml, p <0.01), the average sBP and diastolic blood pressure remained unchanged before and one day after tolvaptan administration (114.4 ± 17.5 mmHg vs. 114.6 ± 18.4 mmHg, p = 0.88 and 60.0 ± 12.7 mmHg vs. 59.1.6 ± 14.9 mmHg, p = 0.59, respectively). There were 22 patients in the low sBP group and 22 patients in the normal sBP group. Between the low and normal sBP groups, no significant differences were observed in the differences of sBP and daily urine output before and one day after tolvaptan administration (0.4 ± 6.4 mmHg vs. -0.1 ± 7.4 mmHg, p = 0.85 and 869.5 ± 723.1 ml vs. 845.5 ± 870.7 ml, p = 0.92, respectively) (Figure).
Conclusion: Tolvaptan administration to patients hospitalised for ADHF due to moderate or severe aortic stenosis may not affect their haemodynamics and is likely to be effective in obtaining adequate urine output.



Figure

P1171

Effects of low dose levosimendan on renal function in patients with advanced heart failure

R Riet Dierckx[1]; W Heggermont[1]; S Verstreken[1]; M Goethals[1]; M Vanderheyden[1]
[1]*OLV Hospital Aalst, Cardiovascular Center, Aalst, Belgium*

Background: The cardiorenal syndrome is a common problem in patients with advanced heart failure (AdHF) and is linked to poor prognosis. Levosimendan is an inodilator that improves hemodynamics and has a beneficial effect on neurohormone levels. Hypotension is a common side effect and can limit the use of higher doses in patients with AdHF.
Aims: To evaluate if administration of low dose Levosimendan in patients with decompensated AdHF can improve renal function.

Methods and Results: Between March 2016 and January 2017, 29 patients hospitalized with decompensated AdHF were treated with Levosimendan. Six patients received repetitive infusions, yielding a total of 41 Levosimendan treatments (12-hours intravenous infusion of 0.05 ug/kg/min, without bolus). Renal function was assessed before and after administration.
Most patients had ischemic cardiomyopathy (62%) and were severely symptomatic (10% New York Heart Association (NYHA) class II, 55% NYHA class III, 34% NYHA class IV). Medical treatment was often suboptimal because of history of hypotension and/or renal dysfunction: only 34% of patients were treated with ACE-inhibitors/angiotensin II-receptor blockers, 83% with beta-blockers, 93% with mineralocorticoid receptor antagonists and 3% with sacubitril/valsartan. Mean age was 68 ± 11 years, median N-terminal pro brain natriuretic peptide (NTproBNP) 6977 ng/L (IQR 4007 -16757), mean left ventricular ejection fraction (LVEF) 22 ± 8% and mean glomerular filtration rate (GFR) 38 ± 18 ml/min. All patients had pulmonary hypertension with a mean systolic pulmonary arterial pressure (sPAP) - measured by echocardiography - of 60 ± 21 mmHg.
Evaluating all 41 treatment episodes, mean pre-treatment GFR was 35 ± 17 ml/min and rose to 38 ± 18 ml/min after administration of low dose Levosimendan (p 0.03) . In 21 cases, NTproBNP levels pre-and post-treatment were available. Levosimendan infusion significantly reduced NTproBNP from 9356 ± 7547 ng/L to 6542 ± 6238 ng/L (p 0.02).
Conclusions: In patients admitted with decompensated AdHF, low dose Levosimendan significantly improves renal function.

P1172

Using Levosimanden in place for unresponsive acute decompensated heart failure to dobutamine

M-T Ming-Ting Chou[1]; CY Chiang[1]
[1]*Chi-Mei Medical Center, section of Cardiology, Tainan, Taiwan ROC*

Background: Levosimanden improves hemodynamics and symptom in acute decompensated heart failure(ADHF) at a much higher cost than dobutamine use
Purpose: To evaluate a cost-effective use of Levosimanden in ADHF unresponsive to dobutamine
Methods: Twenty-five consecutive patients admitted through emergency room due to ADHF and remained dyspnea at rest despite treatment with intravenous diuretic and /or intravenous vasodilator. They all had reduced ejection less than 35% evaluated by echocardiography. These patients first received intravenous dobutamine for 24 to 48 hours, if the symptom is not improved then they will shift to 24-hour levosimanden infusion. At 24h and after 2,3 and 5 days after infusion, patients were asked to evaluate in overall clinical status and in dyspnea. Also NT-pro-BNP level were measured at ER and after 24h and 5 days.
Results: 23 patients improved after levosimanden infusion, in which 15 patients felt markedly improved. The improvement persisted for 5 days and only 2 patients got worse.
The NT-proBNP level decreased significantly(- 30.2 ± 15.3%, $P < 0.01$).
Conclusion: In patients with ADHF unresponsive to dobutamine treatment, levosimanden provides rapid and durable symptomatic relief. This may be a more cost-effective use of this costly medication.

P1173

Outcome of temporary mechanical circulatory support bridging to left ventricular assist device

H S Hoong Sern Lim[1]; H Ahmed[1]; A Ranasinghe[1]; J Mascaro[1]; N Howell[1]
[1]*Queen Elizabeth Hospital, Birmingham, United Kingdom*

Background: Temporary mechanical circulatory support (tMCS) is increasingly used to bridge patients with severe heart failure (HF) and cardiogenic shock (CS) to durable left ventricular assist devices (LVAD).
Purpose: To compare the 1-year survival of patients with LVAD with and without bridging with tMCS.
Methods: Single-centre study of 105 consecutive patients (25 with and 80 without tMCS bridging) with advanced HF and CS who underwent LVAD implant.
Results: Patients bridged with tMCS had more severe HF and more likely to require multi organ support (Table). Acute myocardial infarction was the cause of HF in 14 (56%) vs 4 (5%) of cases with tMCS vs no tMCS. The 25 tMCS were: 10 intra-aortic ballon pumps, 5 Impella CP, 3 veno-arterial extracorporeal membrane oxygenation (VA ECMO), 4 surgical temporary VADs and 3 patients had multiple modalities with Impella, VA ECMO and surgical VADs. LVADs included Heartmate 2 in 10 (40%) vs 40 (50%) and Heartmate 3 devices in 15 (60%) vs 40 (50%) in patients with and without tMCS respectively (p = 0.382). 7 (28%) and 9 (11%) patients required right ventricular assist device or VA ECMO support post-LVAD implant (p = 0.046). 6 and 12-month survival for patients with and without tMCS were 84% vs 83% and 84% vs 79%, respectively (log rank test, p = 0.603).

Table (mean ± SD or median (IQR)

	tMCS (n = 25)	notMCS(n = 80)	p
Age (years)	50.5±5.3	54.8±2.3	0.095
Males	21 (88%)	70 (84%)	0.653
LVEF (%)	15 (10-20)	10 (10-15)	0.362
TAPSE (mm)	14.9±2.2	15.3±1.6	0.805
MAP (mmHg)	74±5	82±2	0.001
RAP (mmHg)	10 (8-20)	11 (8-14)	0.919
CI (L/min/m2)	1.5 ± 0.3	1.7±0.1	0.059
INTERMACS 1	10 (40%)	2 (2.5%)	<0.001
Pre-op ventilation	11 (44%)	3 (4%)	<0.001
Pre-op CVVH	7 (28%)	3 (4%)	<0.001

LVEF: left ventricular ejection fraction; TAPSE: tricuspid annular systolic excursion; MAP: mean arterial pressure; RAP: right atrial pressure; CVVH: continuous veno-venous hemofiltration; CI: cardiac index

Conclusion: Despite more severe HF and CS pre-operatively, and greater need for post-operative support, 1-year survival in patients with LVAD bridged with tMCS were comparable to patients without tMCS.

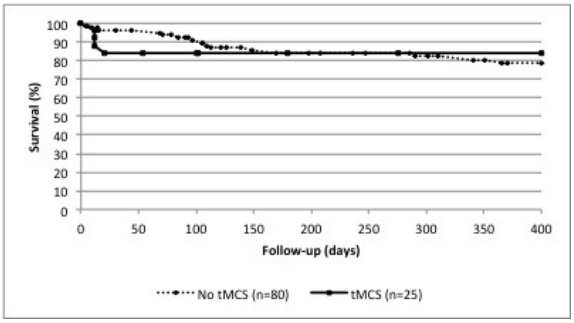


Figure: Kaplan Meier survival curves

P1174

Percutaneous implantation of extracorporeal life support for refractory cardiac arrest or cardiogenic shock complicating acute coronary syndrome: the CareGem registry.

D Domenico D'amario[1]; C Sorini Dini[2]; I Porto[1]; A Mattesini[1]; R Vergallo[1]; R Della Bona[1]; C Trani[1]; F Burzotta[1]; PG Bruno[1]; C Di Mario[2]; M Massetti[1]; S Valente[2]
[1]*Catholic University of the Sacred Heart, Institute of Cardiology, Rome, Italy*;
[2]*Careggi University Hospital (AOUC), Florence, Italy*

Background: Refractory cardiogenic shock (RCS) or refractory cardiac arrest (RCA) complicating acute coronary syndrome (ACS) is associated with extremely high mortality rate. Veno-arterial extracorporeal life support (VA-ECLS) represents a therapeutic option to stabilize patients' condition before or at the time of emergency revascularization.
Methods: We analyzed 29 consecutive patients with RCS or RCA complicating ACS, and implanted with VA-ECLS in two centers who have adopted a similar, structured approach to ECLS implantation. Data were collected from January 2010 to Dicember 2015 and ECLS had to be percutaneously implanted either before (within 48 hours) or at the time of attempted percutaneous coronary revascularization (PCI). We investigated in-hospital outcome and factors associated with survival.
Results: Twenty-one (72%) were implanted for RCA, whereas 8 (28%) were implanted on ECLS for RCS. All RCA were witnessed and no-flow time was shorter than 5 minutes in all cases but one. All patients underwent attempted emergency PCI, using radial access in 10 cases (34.5%), whereas in 3 patients a subsequent CABG was performed. Overall, 10 patients (34.5%) survived, 9 of them with a good neurological outcome. Life threatening complications, including stroke (4 pts), leg ischemia (4 pts), intestinal ischemia (5 pts), and deep vein thrombosis 2 pts), occurred frequently, but were not associated with in-hospital death. Main cause of death was multi-organ failure. PCI variables did not predict survival. Survivors were younger, with shorter low-flow time, and with ECLS mainly implanted for RCS, as opposed to RCA. At multivariate analysis, levels of lactate at ECLS implantation

(OR 4.32, 95%CI:1.01-18.51, p = 0.049) emerged as the only significant variable to predict survival.
Conclusion: In patients with RCA or RCS complicating ACS, who are percutaneously implanted with ECLS before or at the time of coronary revascularization, in hospital survival rate is higher than 30 %, generally with good neurological outcome. Level of lactate at ECLS implantation seems to be the most important factor to predict survival.

P1175
Investigating the relationship between heart failure clinical nurse specialist input and readmissions in patients hospitalised for heart failure: is there evidence of a recency effect?

M Nandakumar[1]; RR Shah[1]; T Godec[2]; J De Courcey[1]; S Piper[1]; T Mcdonagh[1]; D Bromage[1]
[1]King's College Hospital, London, United Kingdom; *[2]London School of Hygiene and Tropical Medicine, London, United Kingdom*

Background: Heart failure (HF) Clinical Nurse Specialist (CNS) intervention is known to reduce HF readmissions. However, the impact of the timing of inpatient HF CNS input is unknown.
Purpose: We aimed to analyse whether the interval between patients' last HF CNS review and their discharge date affects readmission. We hypothesised that there is a recency effect; that is, that patients reviewed closer to discharge would have reduced readmissions.
Methods: This was a retrospective observational study of 243 patients in a tertiary HF Unit, from October 2015 to March 2016. Patient data was collected into the National HF Audit database. HF CNS Review data was collected by 2 authors and a random selection checked by a third. A review was eligible if it was face-to-face and included an educational component. The primary endpoints were readmission within 12 months, mortality and admission duration.
Results: 53 patients (22.2% of the study population) had an educational review during admission (per protocol). Compared to patients without a review, the study group were older, more female, more commonly managed on general medicine wards, had less device therapy, more hypertension, higher brain-type natriuretic peptide, lower ferritin, and more atrial fibrillation (Table 1). There was no significant association with mortality. Likewise, there was no significant association between HF CNS review or its timing and rates of readmission after adjustment for other variables significantly associated with the outcome (P = 0.096). HF CNS review was significantly associated with admission duration (P = 0.019), which is likely to be a function of reverse causality.
Conclusion: HF CNS review did not significantly reduce readmissions up to 1 year and no recency effect was evident.

P1176
Improving outcomes in patients with heart failure; reduction in mortality and readmissions achieved with reduction in length of stay

C Chokanan Thaitirarot[1]; Z Vali[1]; L Clayton[1]; I Loke[1]
[1]Glenfield Hospital, Cardiology Department, Leicester, United Kingdom

Heart failure (HF) poses a staggering clinical and public health problem associated with significant morbidity and mortality. Glenfield Hospital (GH) is one of the UK's largest tertiary cardiology centres. Over the last 5 years, our HF service has been transformed. Recent studies have raised concern that shorter length of stay (LOS) in hospital is associated with increased rates of readmission and worse outcome. We carried out detailed audits to assess the impact of the improvements made, and assessed if this trend is observed in our locally collected data.
For our initial audit, electronic discharge letters of all patients admitted to GH between 30th March and 13th April 2012 were retrospectively reviewed. Patients treated for acute HF were identified, and data was then collected for these patients. We re-audited the same period in 2017. Chi-square was used to assess statistical correlation between LOS and 6 month readmissions.
The second audit does not only show significant improvement in LOS (11 to 7 days), 30 day readmissions (29% to 17%) and inpatient mortality (14.3% to 5.5%), but also the number of acute HF admissions as a proportion of all admissions has fallen from 11.4% to 7.8% (see table 1). Furthermore, we found no statistical correlation between LOS and medical readmissions at 6 months.
Since the initial audit in 2012, several changes have been implemented to improve the inpatient HF service. These include an inpatient HF nurse team, nurse led follow-up clinics with ability to see patients urgently, creation of a dedicated HF unit with beds for direct admission from the community, weekly HF MDT meetings, regular educational sessions for junior doctors and nursing staff, and expansion of consultant cover with rapid access one-stop HF clinics. Our data found improvement in prescription of evidence based medical therapy and better patient follow up. We show that reduction in readmissions can be achieved even with lower LOS.

P1175 Table 1: Baseline Characteristics

Seen by HF nurse		Yes	No
Patient details			
Age		74 (63.0-81.0)	63 (58.0-76.0)
Gender	Female Male	84 (44.2) 106 (55.8)	19 (35.9) 34 (64.2)
Place of care	Cardiology General Medicine Other	44 (23.2) 128 (67.4) 18 (9.5)	39 (73.6) 12 (22.6) 2 (3.8)
Past medical history			
IHD AMI CABG PCI Previous device therapy Valve disease Hypertension Diabetes		75 (42.9) 44 (23.7) 1 (5.3) 6 (35.3) 40 (21.1) 53 (27.9) 153 (81.0) 76 (40.0)	20 (38.5) 12 (23.1) 5 (17.2) 8 (26.7) 22 (41.5) 16 (30.2) 28 (52.8) 20 (37.7)
Admission investigations			
Hb Urea Creatinine Sodium Potassium BNP Ferritin Iron Transferrin saturation QRS duration		116.0 (101.0-128.0) 10.4 (7.1-14.0) 111.5 (86.0-158.0) 139.0 (136.0-141.0) 4.3 (3.9-4.7) 687.5 (281.0-1660.0) 102.0 (47.0-230.0) 7.6 (0.1-12.2) 15.5 (12.0-23.0) 110.0 (90.0-140.0)	115.0 (101.0-127.0) 11.9 (7.8-19.2) 120.0 (97.0-167.0) 139.0 (135.0-141.0) 4.3 (4.0-4.9) 563.0 (288.0-1306.0) 157.0 (66.0-268.0) 11.1 (5.1-14.2) 16.0 (6.0-24.0) 118.0 (94.0-158.0)
ECG	Atrial fibrillation Other Sinus rhythm	95 (50.5) 5 (2.7) 88 (46.8)	16 (30.2) 4 (7.6) 33 (62.3)

Table 1

	Initial Audit GH 2012	Re-audit GH 2017
Proportion of admissions for acute HF	11.4% (56/492)	7.8% (73/942)
Proportion with reduced ejection fraction (HFREF)	65.1% (28/43)	62.7% (42/67)
Median length of stay (days)	11	7
30 day readmissions	29.2% (14/48)	17.4% (12/69)
6 month readmissions	44% (21/48)	39.1 (27/69)
Inpatient mortality	14.3% (8/56)	5.5% (4/73)
Mortality at 30 days after discharge	6.3% (3/48)	7.2% (5/69)
Mortality at 6 months after discharge	20.8% (10/48)	17.4% (12/69)

Results of both the initial audit in 2012 and re-audit in 2017

P1177

Patient preferences for heart failure information delivery and perceptions of patient-provider communication

SE Serra Ivynian[1]; PJ Newton[2]; M Digiacomo[1]
[1]University of Technology, Sydney, Sydney, Australia; *[2]University of Western Sydney, Sydney, Australia*

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Background: Improving health literacy is a global health goal. For people managing chronic illness such as heart failure (HF), adequate health literacy is crucial to effectively self-manage on a daily basis.
Purpose: 1) To identify HF patients' preferred sources of HF information, perceived gaps in HF knowledge, and ascertain unmet educational needs from the perspective of the HF patient; and 2) to explore perceptions of patient-provider communication, highlighting barriers and facilitators of effective health information delivery, to improve health literacy in HF.
Methods: Semi-structured in-depth interviews were conducted with 15 symptomatic HF patients at a teaching hospital. Transcripts were analysed using interpretative phenomenological analysis (IPA).
Results: Participants relied heavily on providers for HF information and support, expressed numerous unmet educational needs, and had mixed feelings about quality of communication. Credibility of information was most important and participants avoided the internet to prevent misinformation. Participants expressed the need for tailored HF information, accounting for comorbid conditions, and a preference for face-to-face information delivery. Knowledge gaps included HF pharmacotherapy, symptom appraisal and management, the cause and chronicity of HF, and a specific action plan for HF symptom exacerbation. Barriers to effective patient-provider communication included participants' memory problems, providers using complex medical terminology, lack of adequately detailed information, perceived deliberate concealment of information, and relationships that did not allow for open communication. Facilitators included patient note-taking during consultations, delivery of consistent health information, and positive patient-provider relationships.
Conclusion: Suggested topics of education and communication strategies aligned with national guideline recommendations for HF education. Gaps in knowledge and poor communication may point to inadequate availability of multidisciplinary HF management programs, and/or their fidelity to guideline recommendations.

P1178

Acute heart failure in the emergency department: current trends in management

P Patricia Alves[1]; AV Marinho[1]; JP Almeida[1]; R Baptista[1]; S Costa[1]; F Franco[1]; M Pego[1]
[1]University Hospitals of Coimbra, Cardiology, Coimbra, Portugal

Background: Although acute heart failure (AHF) remains an important public health issue, management has not changed significantly in the past decades. The initial approach in the emergency department (ED) is being increasingly emphasized.
Purpose : We studied the association of early ED management and prognosis in patients with AHF.
Methods: We retrospectively included all 870 patients admitted in our ED with AHF from November 2016 to October 2017. Baseline clinical and analytical data were collected. Outcomes regarding overall mortality, in-hospital mortality, admission and readmissions were determined. Patients were followed-up over a median period of 7 [IQR 2.8-9.9] months (all patients had a minimum follow up of one month).
Results: The mean age was 78 ± 10.5 years and 51% were male. The prevalence of valvular heart disease was 38%, coronary artery disease was 27% and atrial fibrillation 69%. Mean left ventricular ejection fraction (LVEF) was 42.5 ± 12.6% and median BNP was 500 [IQR 275-1014] pg.ml-1. At admission, 92% presented with a B profile (wet and warm), 2.4% a C profile and 1.15% a L profile, whereas 7% in acute pulmonary edema (APE). The median door-to-furosemide time was 90 [IQR 50-240] minutes; 5% received intravenous nitrates and 6% noninvasive ventilation. About 45% were discharged from the ED. Overall mortality was 21%, in-hospital mortality 13% and the all-cause readmission rates were 32% (10.5% at 30 days). BNP emerged as the best predictor of outcome (readmission and mortality) (HR 1.6, 95%CI 1.4-1.8, p <0.001). Age (OR 1.06, 95%CI 1.02-1.09, p = 0.001), BNP (OR 1.4, 95%CI 1.06-1.97, p = 0.021), creatinine (OR 1.4, 95%CI 1.07-1.9, p = 0.018), LVEF (OR 0.96, 95%CI 0.94-0.98, p = 0.002) and APE at admission (OR 2.8, 95%1.2-6.6, p = 0.028) were predictors of in-hospital mortality. No significant predictors were found for readmission. However, patients that received furosemide within the first 60 minutes of admission had a lower readmission rate than those with latter administration timings (10 vs 20%; OR 0.7, 95% 0.54-0.82, p = 0.04).
Conclusions: : In-hospital mortality and readmission rates were considerable in this cohort of elderly patients with AHF. Clinical and analytical status at admission in the ED were important predictors of poor prognosis. Rapid administration of loop diuretics was associated with smaller readmission rates.

Acute Heart Failure - Prevention

P1179

Risks of functional decline during hospitalization in patients with acute heart failure

H Hidenori Yaku[1]; T Kato[1]; Y Yoshikawa[1]; Y Inuzuka[2]; Y Tamaki[3]; T Kimura[1]
[1]Kyoto University Graduate School of Medicine, Department of Cardiovascular Medicine, Kyoto, Japan; *[2]Shiga Medical Center for Adults, Department of Cardiovascular Medicine, Moriyama, Japan*; *[3]Tenri Hospital, Department of Cardiovascular Medicine, Tenri, Japan*

Background: Previous registry data has provided limited information about the functional status of very elderly patients with acute heart failure (AHF).
Purpose: The current study sought to clarify risks for functional decline during hospitalization in patients with acute heart failure.
Methods: Using data from the Kyoto Congestive Heart Failure registry, which enrolled prospectively 4056 consecutive hospitalized patients from October 2014 to March 2016, we classified patients hospitalized for AHF into 2 groups by the change in functional status during hospitalization: those with functional decline during hospitalization (Group A) and those not with functional decline during hospitalization (Group B). Physical activity before admission and at discharge was classified as ambulatory, use of wheelchair outdoor only, and use of wheelchair indoor and outdoor. Functional decline was defined as the decline of more than one step in physical activity during hospitalization, and clinical predictors of functional decline during hospitalization were identified using multivariate logistic regression analysis.
Results: After excluding those who died in hospital (N = 271), bedridden at admission (N = 127), and missing data (N = 103), Group A and B included 528 patients and 3027 patients, respectively. Regarding the baseline clinical characteristics, Group A had significantly greater prevalence of patients with advanced age (84 ± 9 vs. 76 ± 12 years, P < 0.001), female gender (56 vs. 42%, P < 0.001), hypertension (77 vs. 72%, P = 0.02), prior stroke (24 vs. 14%, P < 0.001), chronic kidney disease (53% vs. 43%, P < 0.001), malignancy (18% vs. 14%, P = 0.006), and dementia (33% vs. 14%, P < 0.001). Regarding the clinical presentations, systolic blood pressure and heart rate was higher in Group A than in Group B [144 ± 32 vs. 149 ± 35 mmHg (P = 0.003), and 93 ± 27 vs. 96 ± 28 beat/min (P = 0.001), respectively], while left ventricular ejection fraction was higher in Group A than in Group B (48 ± 16 vs. 46 ± 16 %, P = 0.02). The median length of hospital stay was longer in Group A than in Group B (21 versus 15 days, P < 0.001). After adjusting for potential confounders, independent risk factors for the functional decline during hospitalization included age = 80 years (OR = 2.46, 95%CI 1.91-3.17), female (OR = 1.30, 95%CI 1.03-1.63), past history of stroke (OR = 1.65, 95%CI 1.27-2.14) and malignancy (OR = 1.40, 95%CI 1.06-1.84), dementia (OR = 1.97, 95%CI 1.53-2.52), hyponatremia (OR = 1.45, 95%CI 1.07-1.96), hypoalbuminemia (OR= 1.77, 95%CI 1.34-2.32), renal dysfunction (OR = 1.59, 95%CI 1.26-2.02), and New York Heart Association (NYHA) class IV at admission (OR= 1.25, 95%CI 1.01-1.55). Consequently, the proportion of patients in Group A discharged to their homes was also lower (47%), as compared with 90% of those in Group B.

Conclusions: Risk stratification for the decline in physical activity is important for the discharge to their homes in very elderly patients with AHF.

Effect of the optimize heart failure care program on clinical outcomes of HF patients at ho chi minh city heart institute in vietnam.

PHUONG Do[1]; BAN Ha[1]; DUNG Do[1]; HUAN Do[1]; MARTIN Cowie[2]
[1]Heart Institute, Ho Chi Minh city, Vietnam; [2]Royal Brompton Hospital, London, United Kingdom

On behalf of: HCMC Heart Institute OHF

Heart failure (HF) is a common public health in Europe and US but also in Asia. The HF prevalence is increasing in LMI countries with a big annual burden. The OHF program was developed in HCMcity Heart Institute to improve HF patient's awareness, to optimize HF treatment in order to improve clinical outcome.
Since October 2016, we included all of HF patients with ejection fraction (EF) <50% hospitalized . The patients received education for "HF diet", "appropriate HF exercise", "weight control", "detection of worsening HF symptoms", and optimized HF treatments. The data was collected at 2 and 6 months (M2,M6) for clinical signs, treatments and outcomes (readmission and death). We conducted a call survey at M6 to check patient's knowledge and practice.
From October 2016 to October 2017, we recruited 257 HF patients with EF <50% hospitalized. Among them, 58% are male, the mean age is 64.4 ± 15 and BMI is 22.2 ± 3.5 kg/m2. The 3 principal etiologic HF disease is IHD (64.2%), cardiomyopathy (21.8%) and valvular HD (9.3%). The key comorbidities are hypertension (48.2%), valvular HD (40.5%), dyslipidemia (33%), arrhythmia or atrial fibrillation (AF) (31%), diabetes (25.7%) and renal failure (21%).
There is a significant improvement in mean heart rate between admission (M0) vs. discharge (97.8 ± 22.2 vs 78.5 ± 11.7, p <0.001), and M0 vs. M6 (97.8 ± 22.2 vs 78.9 ± 13.6, p <0.001). The clinical signs have been improved: M0 vs. M2 and M2 vs. M6: for dyspnea (79.8% vs. 36.3%, p <0.001 and 36.3% vs. 22.2%, p = 0.002); for orthopnea (39.7% vs. 1.2%, p <0.001 and 1.2% vs. 0%, p = 0.25); and for sign of pulmonary congestion (27.3% vs. 0.6%, p <0.001 and 0.6% vs. 0%, p = 0.65). The percentage of patients with NYHA class I&II increased at M2 and M6 vs. M0 (96.8%, 99% vs. 45.3%, p <0.001 for both). The EF was also improved at M6 compared to M0 (36.5 ± 9 vs. 33.4 ± 9.3, p = 0.005).
In terms of education, 98.8% of patients were educated for "HF diet" (72.2% acquired the knowledge and 77.8% practice it); 84.8% were educated for "appropriate HF exercise" (66.7% acquired the knowledge and 62.5% practice it); 89.5% were educated for "weight control" (54.3% acquired the knowledge and 44.1% practice it) and 91.8% were educated for "detection of worsening HF symptoms", while only 55.9% remembered this education.
For HF treatment, we followed European guidelines, including at discharge: 91.4% of RAAS inhibitors, 33% of beta-blockers (but 50.3% at M6), 77% of MRA, 85.2% of others diuretics, 8.9% of ivabradine (but 18.1% at M6), 33.3% digoxin (noted 21.8% treated for AF) and 16.3% of isosorbide dinitrate.
The rate of readmission after discharge at <30 days was 8.3% and at <60 days was 12.5%. There was no in-hospital death. The mortality of 30-day was 1.2%, 60-days was 2.5% and 6-months was 10.4%.
The OHFCare Program demonstrated the benefits on clinical outcomes of HF patients after discharge. A new analysis based on dosage of HF treatment is needed to determine the target dose in Asian HF patients.

P1180

The prognostic value of B-type natriuretic peptide verus SUPER score for the onset of acute heart failure in acute heart failure unit

Y Yuan Bian[1]; FENG Xu[1]; LI-JUN Cao[1]; JIAN Zhang[1]; DAN-YU Yu[1]; RJ Lv[1]; YU-GUO Chen[1]
[1]Qi-Lu Hospital of Shandong University School of Medicine, Emergency Department, Jinan, China People's Republic of

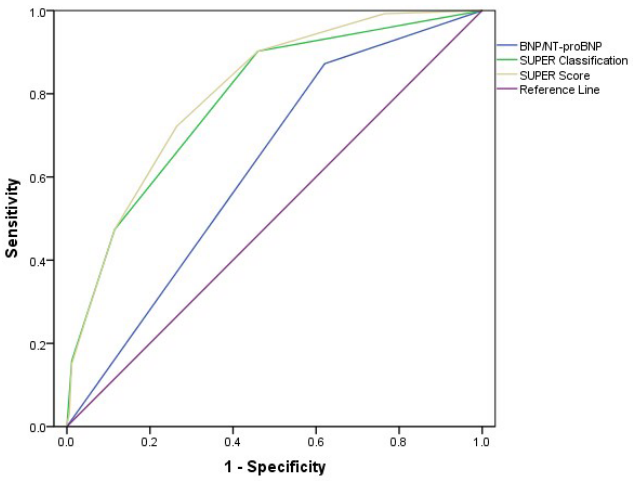
Background: Early identification of the potential risk of acute heart failure (AHF) among high-risk patients would contribute to 'time to therapy' in Acute Heart Failure Unit (AHFU). The SUPER score was an early warning scoring system for the onset of AHF, comprised of five factors: SpO2, urine volume, pulse, emotional state, and respiratory rate.

Baseline characteristics

	Negative group (n = 86)	Positive group (n = 221)	p-value
Male (n, %)	62(71.1)	118(53.3)	0.003
Age (years)	56.2±15.2	66.3±14.3	<0.001
hospitalization time (days)	6.4±8.9	8.2±7.8	0.115
ACS (n, %)	54(6208)	144(65.2)	0.693
PPCI (n, %)	44(51.2)	60(27.1)	<0.001
CAD (n, %)	58(67.4)	182(82.4)	0.006
Hypertension (n, %)	19(22.1)	56(25.3)	0.658
Diabetes (n, %)	5(5.8)	25(11.3)	0.199
Positive cTn (n, %)	55(64.0)	174(78.7)	0.009
SUPER score	1.8±1.7	2.8±1.8	<0.001
AHF onset (n, %)	17(19.8)	116(52.5)	<0.001
In-hospital Mortality (n, %)	7(8.1)	57(25.8)	<0.001

Abbreviations: ACS, acute coronary syndrome; PPCI, Primary Percutaneous Coronary Intervention; CAD, coronary artery disease; cTn, cardiac troponin; AHF, Acute Heart Failure.

Purpose: We aimed to investigate whether the predictive value for AHF of SUPER score was superior to the B-type natriuretic peptide (BNP) or N-terminal pro-BNP (NT-proBNP).
Methods: A total of 307 patients admitted in the AHFU were divided into two groups according to the level of BNP/NT-proBNP on admission: negative group (n = 86) and positive group (n = 221). The primary endpoint was the onset of AHF during hospitalization. The secondary endpoint was in-hospital all-cause mortality.



Receiver operating characteristic curve

Results: The mean SUPER score (1.8 ± 1.7 vs. 2.8 ± 1.8, p <0.001), AHF onset (19.8% vs. 52.5%, p <0.001) and in-hospital mortality (8.1% vs. 25.8%, p <0.001) was significant lower in the negative group. A binary logistic regression analysis showed the BNP/NT-proBNP (OR: 2.178, 95%CI = 1.031˜4.598, p = 0.041) and SUPER score (OR: 2.061, 95%CI = 1.695˜2.505, p <0.001) were independent risk factor for the onset of AHF. The AUC for the BNP/NT-proBNP, SUPER classification and SUPER score were 0.634, 0.785 and 0.804, respectively.
Conclusion: The SUPER score is independent predictor superiority in predicting the onset of AHF in AHFU.

P1181

Angioplasty with stenting in acute myocardial infarctions and acute coronary syndromes with 30ml contrast using cordis 6F diagnostic coronary catheters with bench testing in radial and femoral routes

MC Mark Christopher Arokiaraj[1]
[1]Pondicherry Institute of Medical Sciences, Pondicherry, India

Aims and objectives: To safely perform angioplasties in acute coronary syndromes and acute myocardial infarctions with low contrast volume using cordis infiniti 6F diagnostic catheters. To perform pushability and trackability tests on the diagnostic and guide catheters in radial and femoral paths.
Purpose: To perform safely angioplasty with low contrast volume and prevent congestive heart failure.
Methods and Results: In 327 patients (416 lesions/ 451 stents) with acute coronary syndromes angioplasty were performed with cordis 6F diagnostic catheters. 108 out of 327 patients underwent primary angioplasty. The lesions included left anterior descending (221), Left main (6), left circumflex (88), ramus (5) and right coronary artery (96) lesions, and in total 451 stents were used by this method. In 65% of cases Iodixanol was used. All contrast injections were given by hand. Regular follow-up of the patients was performed at 30 days. The patient population had 79% diabetes. All the procedures were performed in femoral route only. Pre-dilatation was performed in 83 lesions. In rest of the lesions direct stenting was used to deploy the stents. Successful revascularization of the target lesion was achieved in all cases. The mean contrast volume used per patient was 28 ml (±8 ml). Mild reversible contrast induced nephropathy was observed in three patients and no patients required dialysis. A variety of commercially available standard stents were used in the procedures. Cardiogenic shock was seen in 12 cases, and three mortality in total was observed. Of these 3 cases who expired, one patient had a large left ventricular clot, one patient had acute ventricular septal defect and the other patient presented with hypotension and severe congestive heart failure. Mild congestive heart failure was seen in 14 cases who were managed with diuretics and non-invasive ventilation. Buddy wire technique was used in 5 patients, and tirofiban was used in 99% cases in adjusted dosages. Proximal to the stent mild dissection was seen in one patient, and mild dissection distal to the stent in two patients. Coronary perforations or ruptures were not seen. Acute stent thrombosis was seen in 1 patient, who was treated with an additional stent and balloon dilatation. None of the patients required re-intervention in one month period. Bench evaluation showed balanced force transmission and flexibility parameters with diagnostic catheters compared to the guide catheters in both femoral and radial paths. There was restriction in trackability in the radial path at 81 cm which correlates wtih aorto-brachiocephalic junction. Force displacement curves showed favourable parameters with diagnostic catheters compared to guide catheters.
Conclusions: Emergency angioplasty could be performed safely in patients using Cordis 6F diagnostic catheters using low volume of contrast. Low contrast volume usage would result in lower incidence of contrast induced nephropathy and cardiac failures.

P1182
Evaluating the patient and carers perspective of the heart failure pathway following an admission with an acute decompensation of heart failure

R Ronan Kernan[1]; E Lennon[1]; J Gallagher[2]; M Walshe[2]; JP Riley[3]; C Keane[2]; PR Kalra[4]; MR Cowie[3]; K Mcdonald[2]
[1]University College Dublin, Dublin, Ireland; *[2]Heart Failure Unit, Dublin, Ireland*; *[3]Imperial College London, London, United Kingdom*; *[4]Portsmouth Hospitals NHS Trust, Portsmouth, United Kingdom*

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Heart Failure (HF) is an increasingly prevalent chronic condition accounting for a substantial proportion of hospitalisations, particularly in those > 65. This study sought to evaluate the perspective of both patients and their carers with respect to symptom recognition and management of HF pre and post admission with Acute Decompensation of Heart Failure (ADHF). In order to do so we administered a validated questionnaire to patients (n = 70) admitted to a large teaching hospital with ADHF and their carers (n = 40), prior to discharge. At three months, following an intensive disease management programme (DMP), a follow-up questionnaire was also administered to patients (n = 57) and carers (n = 22).
Of the 70 patients surveyed, 66% (46) were male. The average age was 72.9 ± 12.8. The average number of co-morbidities was 3.8 ± 2.0. Patients were divided into those presenting for the first time with HF (De Novo, DN, 56% (39)) and those with an existing diagnosis of HF in their medical records (Known, K, 44% (31)).
In the baseline patient questionnaire, breathlessness was noted as the most dominant presentation with 62% (24) DN and 81% (25) K affected, however, 70% (21) DN and 42% (11) K did not associate it with HF. Furthermore, 65% (25) DN and 68% (21) K waited >7 days before seeking help with 18% (7) DN and 15% (3) K stating they would not have sought help earlier had they had thought it was HF related.
In the 3-month questionnaire, 82% (23) DN and 71% (17) K strongly agreed with calling the doctor if their limbs swell or when short of breath, however, 30% (8) DN and 25% (6) K patients still stated that they did not recognise breathlessness as a symptom of HF. While 36% (10) DN and 33% (8) K patients disagreed/strongly disagreed with calling their doctor if they experienced fatigue.
In the carer questionnaires at baseline, 92% (22) DN and 88% (14) K had daily contact with their patient. However, 63% (15) DN and 75% (12) K carers stated that their patient was suffering for >7 days before seeking help and 30% (3) DN and 25% (4) K carers were unfamiliar with their patient's medication list.
At 3-months, 76% (10) DN and 89% (8) K recognised breathlessness as a symptom of HF and 84% (11) DN and 67% (6) K felt their relative's ability to carry out routine daily activities had improved. However, despite 92% (12) DN and 78% (7) stating that their understanding of HF is of benefit to caring for their patient, 31% (4) DN and 56% (5) K stated that they were not involved in their patient's self-care management of HF.
Conclusion: Early symptom recognition and adequate management of HF in the community is vital if early intervention is to be triggered in an attempt to prevent Emergency Department visits and hospital admissions. Our results show knowledge of HF symptoms is poor even following an intensive HF DMP. Improvement and modification in the methods of delivering impactful patient and carer education are required.

Acute Heart Failure - Clinical

P1183
Epidemiology of heart failure following ST-segment elevation myocardial infarction treated with primary percutaneous coronary intervention.

N Farre[1]; A Fort[1]; H Tizon-Marcos[1]; L Recasens[1]; B Vaquerizo[1]; R Serrat[1]; M Grau[2]; J Comin-Colet[3]; J Marti-Almor[1]
[1]Hospital del Mar, Department of Cardiology, Municipal Institute for Medical Research (IMIM), Barcelona, Spain; *[2]Hospital del Mar Medical Research Institute (IMIM), Barcelona, Spain*; *[3]University Hospital of Bellvitge, Barcelona, Spain*

On behalf of: Codi IAM Investigators

Introduction and objectives: To analyse the epidemiology and 30-day and 1-year mortality of heart failure (HF) that complicates ST-segment elevation myocardial infarction (STEMI) treated with primary percutaneous coronary intervention (PCI).
Methods: Multicentre registry of 14070 patients with STEMI treated with primary PCI from January 2010 to December 2015.
Results: Patients with HF were older, more frequently female, and diabetic and had higher prevalence of chronic ischemic heart disease. Only 10.3% of patients with STEMI treated with primary PCI had HF on admission and the majority of them had the mildest form (Killip-Kimball II 77.8%). The presence of HF was associated with high mortality (30-day mortality was 2.9% of patients in Killip-Kimball I, 9.5% of Killip-Kimball II and 17.4% in Killip-Kimball III, p <0.005, and 1-year mortality in patients who survived 30 days was 2.9%, 9.3% and 14.3%, p <0.005, respectively). Both the presence of Killip-Kimball class II and III were independently associated with 30-day and 1-year mortality in 30-day survivors. Up to 6% and 15% of patients in Killip-Kimball II and III on admission worsened to cardiogenic shock, and the onset of cardiogenic shock during hospitalization was independently associated with mortality at 30-day and 1-year follow-up.
Conclusion: Only 10.3% of patients with STEMI treated with primary PCI had HF on admission but it was associated with a higher risk of developing cardiogenic shock during hospitalization and with 30-day and 1-year mortality in 30-day survivors. In this high risk population, primary PCI and posterior medical treatment should be prioritized to avoid worsening of HF.

P1184
Cardiac troponin release is associated with higher CA 125, NT-proBNP and hsCRP levels in patients with acute decompensated heart failure

Y Yuksel Cavusoglu[1]; ME Altinbas[1]; S Eraslan[1]
[1]Eskisehir Osmangazi University, Eskisehir, Turkey

Purpose: High sensitive cardiac troponin (hs-cTn) has been proven to increase in majority of patients hospitalized with acute decompensated heart failure (HF), and referred as a potent predictor of poor prognosis. Plasma levels of carbohydrate antigen 125 (CA-125) have been shown to correlate with clinical, hemodynamic, and echocardiographic parameters in HF. Higher level of hsCRP is known to be present in the inflammatory process of HF. NT-proBNP is also a well-known biomarker of neurohormonal activation in HF. In this study, we aimed to evaluate the relationship between hs-cTn release and plasma levels of CA-125, NT-proBNP or hsCRP levels.
Methods: A total 425 patients admitted to the hospital with the diagnosis of decompensated HF, NYHA II-IV, LVEF < 40% and >18 years of age were included in this study. Plasma levels of hs-cTnT, CA-125, hsCRP or NT-proBNP levels have been measured from the blood samples at admission. hs-cTnT was considered to be abnormal if hs-cTnT was detected >0.014 ng/mL according to the assay used in this study. Patients were classified into two groups: patients with high hs-cTnT levels (n = 342, 80.5%) and patients with normal hs-cTnT levels (n = 83, 19.5%).
Results: Mean age of study population was 67 ± 12 years. Mean EF was 25.4 ± 7.9%, hs-cTnT was 0.22 ± 0.86 ng/mL, CA-125 was 86.2 ± 125.5 U/mL, NT-proBNP was 7667 ± 9876 pg/mL, and hsCRP was 27.4 ± 39.1 mg/dL. Plasma levels of CA-125 were found to be significantly higher in patients with high hs-cTnT as compared to those with normal hs-cTnT level (47.01 [18.8-130.3] U/mL vs 15.02 [11.3-30.9] U/mL, p < 0.001, respectively). NT-proBNP and hsCRP levels were also found to be significantly higher in patients with high hs-cTnT as compared to those

with normal hs-cTnT (4531 [1716-12047] pg/mL vs 651 [327-1768] pg/mL, p < 0.001 for NT-proBNP and 15.8 [6.05-35.43] mg/L vs 5.02 [3.44-12.51] mg/L, p < 0.001 for hsCRP, respectively). Furthermore, a significant positive correlation was found between hs-cTnT levels and CA-125 (r=.261, p < 0.001), NT-proBNP (r=.252, p < 0.001), or hsCRP levels (r=.326, p < 0.001).

Conclusions: The results of this study showed that majority of patients with acute decompensated HF have abnormal hs-cTn levels at admission and hs-cTn release in this group of patients is associated with higher CA-125, NT-proBNP and hsCRP levels, suggesting more severe clinical status of the disease in patients with cardiac troponin release.

P1185

In-hospital Mortality in Cardiorenal Anemia Syndrome: An Observational Data from Gulf-CARE-Registry

M Al Jarallah[1]; R Rajesh[1]; I Al Zakwani[2]; R Dashti[1]; B Bulbanat[1]; M Ridha[3]; J Al Suwaidi[4]; K Sulaiman[5]; P Panduranga[5]; W Almahmeed[6]; K Alhabib[7]; A Al Motareb[8]; H Amin[9]; N Bazargani[10]; A Alsheik Ali[6]

[1]Sabah Al Ahmad Cardiac Center, Al Amiri Hospital, Cardiology , Kuwait, Kuwait; *[2]Sultan Qaboos University , Department of Pharmacology & Clinical Pharmacy, College of Medicine & Health Sciences, Muscat, Oman*; *[3]Adan Hospital, Cardiology, Kuwait, Kuwait*; *[4]Hamad General Hospital, Cardiology, Doha, Qatar*; *[5]Royal Hospital, Cardiology, Muscat, Oman*; *[6]Sheikh Khalifa Medical City, Cardiology, Abu Dhabi, United Arab Emirates*; *[7]King Fahad Cardiac Center, Cardiology, Riyadh, Saudi Arabia*; *[8]Sana'a University, Internal Medicine, Sana'a, Yemen*; *[9]Mohammed Bin Khalifa Cardiac Centre, Cardiology, Bahrain, Bahrain*; *[10]Dubai Hospital and Rashid Hospital, Cardiology, Dubai, United Arab Emirates*

On behalf of: Gulf CARE

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Background: The purpose of this study is to analyze the in-hospital mortality associated with cardio renal anemia syndrome (CRAS) in acute heart failure.

Subjects

Demographic and clinical characteristics

Characteristic, n (%) unless specified otherwise	All (N = 4934)	CRAS	P-value	
No (n = 3615)	Yes (n = 1319)			
Age, mean±SD, years	59±15	57±15	65±14	<0.001
Male gender	3081 (62%)	2378 (66%)	703 (53%)	<0.001
Smoking	1076 (22%)	912 (25%)	164 (12%)	<0.001
Hyperlipidemia	1770 (36%)	1126 (31%)	644 (49%)	<0.001
CAD	2971 (60%)	2107 (58%)	864 (66%)	<0.001
Hypertension	3014 (61%)	1992 (55%)	1022 (77%)	<0.001
Diabetes mellitus	2449 (50%)	1560 (43%)	889 (67%)	<0.001
PVD	208 (4.2%)	102 (2.8%)	106 (8.0%)	<0.001
Stroke/TIA	399 (8.1%)	231 (6.4%)	168 (13%)	<0.001
AF	594 (12%)	408 (11%)	186 (14%)	0.007
Crea, mean±SD, µmol/L	128±110	99±64	207±159	<0.001
LVEF, mean±SD, %	37±14	36±14	38±14	0.017
PCI/CABG	353 (7.2%)	303 (8.4%)	50 (3.8%)	<0.001
Treatment course*	2224 (45%)	1519 (42%)	705 (53%)	<0.001
De novo AHF	2251 (46%)	1805 (50%)	446 (34%)	<0.001
ADCHF	2683 (54%)	1810 (50%)	873 (66%)	
NYHA III discharge	145 (3.1%)	103 (3.0%)	42 (3.5%)	<0.001
NYHA III discharge	221 (4.8%)	170 (5.0%)	51 (4.3%)	

Treatment course*, included non-invasive ventilation, intubation/ventilation, cardiogenic shock, inotrops, IABP,dialysis, atrial fibrillation, major bleeding,stroke and systemic infection

Fig. 1 Impact of cardiorenal anemia syndrome (CRAS) status on mortality (at in-hospital, at 3-month, and at 12-month) of the Gulf CARE cohort.

Mortality	Pearson's chi-squared test				Multivariate logistic regression			
	All	No CRAS	CRAS	*p*-value	Adj. OR [95% CI]	Adj. *p*-value	HL	ROC
In-hospital	308 (3.2%)	189 (5.2%)	119 (9.0%)	<0.001	1.71 [1.03-2.81]	0.036	0.341	0.91
3-month	620 (12.6%)	390 (10.8%)	230 (17.4%)	<0.001	1.36 [1.03-1.79]	0.030	0.358	0.76
12-month	998 (20.2%)	630 (17.4%)	368 (27.9%)	<0.001	1.39 [1.13-1.71]	0.002	0.695	0.73

Impact of cardiorenal anemia syndrome

Methods: We analyzed the data of patients with CRAS and divided into patients without CRAS and patients with CRAS. Multivariate logistic regression and pearson's chi-square test were utilized.

Results: In-hospital, 3 month and 12 month mortality were significantly higher higher (adjusted odds ratio (aOR), 1.71; 95% confidence interval (CI): 1.03 to 2.81; p = 0.036), 3-month (aOR = 1.36; 95% CI: 1.03 to 1.79; p = 0.030) and at 12-month (aOR, 1.39; 95% CI: 1.13 to 1.71; p = 0.002).

Conclusions: CRAS AHF patients were associated with worse mortality at not only in-hospital but at 3-month and 12-month.

Key Words: Cardiorenal Anemia Syndrome, Acute Heart Failure, Chronic Kidney Disease

P1186

Clinical characteristics of atrial fibrillation in patients with acute heart failure; insights from The Kyoto Congestive Heart Failure (KCHF) registry

K Hotta[1]; R Taniguchi[1]; Y Sato[1]; E Yamamoto[2]; H Yaku[2]; N Ozasa[2]; T Kato[2]; T Morimoto[2]; T Kimura[2]

[1]Hyogo Prefectural Amagasaki Hospital, Cardiology, Hyogo, Japan; *[2]Kyoto University, Cardiology, Kyoto, Japan*

Background: Patients with acute heart failure (AHF) frequently have atrial fibrillation (AF), but characteristics of AF in patients with AHF are unclear.

Methods and Results: The study included patients from The Kyoto Congestive Herat Failure (KCHF) registry, prospective, observational, multicenter cohort study enrolling 4,065 consecutive patients who had hospital admission due to AHF for the first time during the period between November 2014 and March 2016 in the 19 participating hospitals in Japan. AF at presentation was detected in 1,455 (35.9%) patients. Patients with AF at presentation were older than those with Sinus Rhythm (SR) at presentation (79.5 vs. 76.6, P < 0.001), had higher left ventricular ejection fraction (48.7% vs. 44.2%, P < 0.001), lower systolic blood pressure (140 vs. 153 mmHg, P < 0.001), higher ventricular rate (103 vs 93 bpm, P < 0.001). There was no difference in-hospital mortality between patients with AF at presentation and patients with SR at presentation (3.92% vs. 4.78%). All patients were divided into four groups based on rhythm at presentation and at discharge (SR-SR 56.7%, AF-AF 32.7%, AF-SR 6.3%, SR-AF 4.3%). An admission-to-discharge percentage BNP reduction of SR-SR group was greater than other groups. There was no difference in-hospital mortality and worsening heart failure during hospitalization between four groups.

Conclusions: We elucidated clinical characteristics of atrial fibrillation in patients with acute heart failure. There was no difference in-hospital mortality between patients with AF at presentation and patients with SR at presentation.

Coronary Artery Disease - Pathophysiology and Mechanisms

P1187

Clinical outcomes of early well-developed coronary collateral circulation in patients with late presentation myocardial infarction

C Carmen Collado Moreno[1]; A Gutierrez-Barrios[2]; D Canadas-Pruano[3]; T Bretones-Del Pino[2]; A Giraldez-Valpuesta[3]; M Alba-Sanchez[3]; S Gamaza-Chulian[3]; D Ruiz-Fernandez[3]; G Calle-Perez[2]; R Zayas-Rueda[2]; E Marante-Fuertes[2]; J Oneto-Otero[3]; R Vazquez-Garcia[2]

[1]Puerto Real Hospital, Department of Cardiology, Puerto Real, Spain; *[2]University Hospital Puerta del Mar, Cardiology, Cadiz, Spain*; *[3]General Hospital of Jerez, Cardiology, Cadiz, Spain*

Background: The aim of the study was to evaluate if early well-developed coronary collateral circulation (CCC) and clinical outcomes in patients with late presentation (>24 hours) myocardial infarction (MI).

Methods: Retrospective multicenter longitudinal study on 164 patients with a late presentation MI and angiographic evidence of a thrombotic occlusion (TIMI 0) of a major coronary artery from 2009 to 2016. The Rentrop and Werner score were used for the angiographic categorization of CCC.

The primary aim of the study was to assess the impact of CCC on major adverse cardiac events (MACE) at 12 months defined as cardiovascular mortality (CVM),

transplant or heart failure hospitalization. The secondary aim was to evaluate the cardiogenic shock rate at presentation and CVM on 12 months follow up.
Results: Poor CCC was detected in 46% of the patients. Patients with good CCC more commonly had a right coronary (RC) occlusion but less often had a left anterior descending occlusion (p <0.05 for both). There were no significant differences between both groups neither in baseline characteristics nor in medical treatment at discharge.
The median follow up was 3.4 years (interquartile range 1.1-5.5 years). 3 patients lost to follow up.
Patients with good CC were less often rated as Killip class III or IV at presentation (3% vs 15%, p = 0.03) and were less often presented in cardiogenic shock (9.2% vs 1.1%, p = 0.02) and consequently the systolic blood pressure (SBP) was lower and the heart rate (HR) was higher among these patients
At one-year follow-up, patients with evidence of angiographic collaterals had statistically significant lower unadjusted rates of the combined endpoint of MACE (p <0.01); CVM (p <0.01) and were less often rated at NYHA III/IV at 12 month follow-up (p = 0.02) The independent effect of CCC on 1-year MACE was confirmed by a multiple logistic regression analysis. Significant predictors on univariable analysis were: absent or poor collateral flow (Rentrop grade 0 or 1), lower Killip class at presentation, left anterior descending (LAD) culprit vessel, decreased LVEF after MI. After adjustment the absence of CCC remained an independent predictor of 1-year MACE (p <0.01).
Logistic regression analysis shows that absence of early collateralization is an independent determinant of 1-year CV mortality (p <0.01). Using the Cox proportional hazard model, the HR for the occurrence of 1-year MACE in patients who had good CC was 8.05 (95% CI, 1.73 - 37.4; P <0.01) and 1-year CVM was 6.92 (95% CI, 1.37 - 34.7, p = 0.019) compared to patients with poor collateralization at baseline. Kaplan-meier curves showed that MACE and CVM were significantly higher (p <0.01) in poor compared to early developed CCC group according to log rank.
Conclusion: An early well-developed coronary collateral circulation in patients with late presentation MI improved one-year clinical outcome rates and exerted a protective effect against cardiogenic shock at presentation.

P1188
Relationship between Monocyte Subsets, IL-6 and hs-CRP with the Severity of Coronary Artery Disease in Stable Angina Pectoris Patients

A M Abdelmohsen Moustafa Abdou Aboualia[1]; E Mokhtar[2]; B Saleh[2]; H Nageb[3]
[1]Al-Azhar University, cardiology department, cairo, Egypt; *[2]Al-Azhar University, clinical pathology, Cairo, Egypt*; *[3]Al-Azhar University, internal medicine, Cairo, Egypt*

Background: Monocytes are crucially involved in all stages of atherogenesis as cellular drivers of vascular inflammation hallmarking atherosclerotic disease. CD16+monocytes are proinflammatory cells, whose proportion is related to the occurrence of coronary artery disease (CAD), intma-media thickness and plaque stability. Interleukin-6 (IL-6) and highly sensitive C reactive protein (hs-CRP) were also closely related to atherosclerotic disease.
Objective: We investigated the relationship between the monocyte subsets, IL-6, and hs-CRP with the severity of CAD assessed by coronary angiography (CAG) in patients with stable angina pectoris (SAP) through their correlation with Gensini score.
Methods: Our study included 45 SAP patients who underwent diagnostic CAG. Thirty two patients of them who diagnosed as CAD were subdivided into 2 groups: 17 patients with multiple-vessel disease (MVD) and 15 patients with single-vessel disease (SVD). The rest thirteen SAP patients without CAD (non-CAD) were considered as a comparative group. Gensini score was used to assess the severity of CAD. Monocyte subsets were analysed by flow cytometry and serum levels of IL-6 and hs-CRP were measured by ELISA.
Results: The relative proportion of CD14+ CD16+ and CD14bright CD16+ was significantly higher in CAD patients, MVD and SVD as compared with non-CAD patients and in MVD more than SVD. Serum levels of IL-6 and hs-CRP were significantly increased in CAD patients, MVD and SVD when compared with non-CAD patients, but no significant difference between MVD and SVD. The proportion of CD14+ CD16+ and CD14bright CD16+ monocytes was positively correlated with Gensini score (r = 0.667, P = 0.000, r = 0.695, P = 0.000).
Conclusions: Elevated proportion of CD14+ CD16+ monocytes subsets was associated with the severity of CAD in patients with SAP.

P1189
Global myocardial strain of left ventricle depending on segmentary stenosis of left anterior descending artery in STEMI patients

V Valentin Oleinikov[1]; V Galimskaya[1]; A Golubeva[1]; S Kupriyanova[1]; S Skvortcov[1]
[1]Penza State University, Penza, Russian Federation

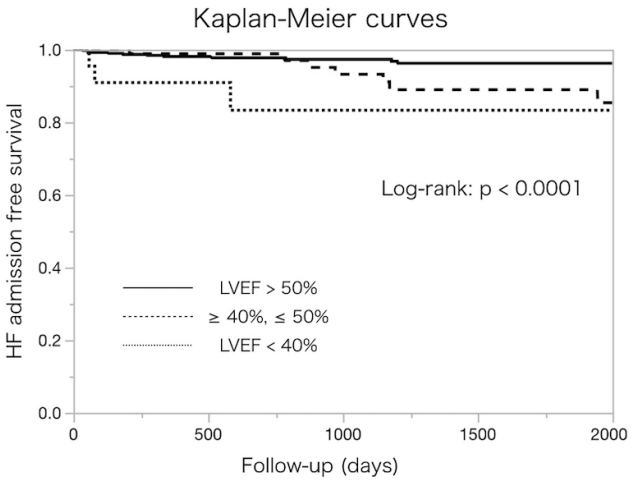
Aim: Determine the dependence of different global strain types of the left ventricle (LV) from stenosis of the left anterior descending artery (LAD) specific segments in STEMI patients.
Methods: The study included 60 patients with STEMI (51.8 ± 8.2 years), confirmed by ECG, coronary angiography (CAG), troponin I level, CK-MB. Inclusion criteria: age 35-65 years, significant stenosis only LAD (infarct-related artery), revascularized within the first hours from the cardiac pain onset, stenosis of other arteries less than 50%, the trunk of LA - less than 30%. Exclusion criterion - history of previous myocardial infarctions and other cardiovascular diseases. All patients underwent echocardiography (MyLab, Esaote, Italy) at the 6th-7th day after the disease onset. Using the X-Strain™ software, the following peak global strain parameters were determined: longitudinal (GLS), circumferential (GCS) and radial strain (GRS), as the average of 18 LV myocardium segments. The hypothesis of normality of each sample distribution is verified using the non-parametric Kolmogorov-Smirnov criterion.
Results: Taking into account the segmental location of the infarct-related LAD stenosis, patients were divided into two groups: 1 - 33 people with stenosis in the middle segment, 2 - 27 subjects with proximal segment stenosis. GLS in the 1st group was 13.8% (95% CI 11.8, 15.7), in the 2nd - 12.9% (95% CI 10.8, 14.9), (p>0.05); GCS-18.4% (95% CI 15.4, 21.3) and 15.4% (95% CI 12.2, 18.6), (p>0.05), respectively. GRS values in group 1 were 27.8% (95% CI 22.9, 32.7), in the 2nd group 24.3% (95% CI 18.9, 29.6), p>0,05).
Conclusion: Global longitudinal, circumferential and radial LV strain in STEMI patients does not depend on stenosis location in the proximal or middle LAD segment.

Coronary Artery Disease - Treatment

P1190
The influence on the onset of heart failure in patients with preserved, mid-range and reduced ejection fraction after first-time acute myocardial infarction.

R Ushigome[1]; S Namiuchi[1]
[1]Sendai Open Hospital, Sendai, Japan

Background: Left ventricular ejection fraction (LVEF) after acute myocardial infarction (AMI) is well established as an important predictor of clinical outcome. The new category of heart failure (HF), HF with mid-range LVEF (HFmrEF), has recently been propounded. The influence on the onset of HF of patients with mrEF after AMI remain unclear.
Purpose: The study sought to assess the clinical characteristics and influence on the onset of HF after primary percutaneous coronary intervention (PCI) for first-time AMI, classified by ejection fraction.
Methods: We evaluated 632 consecutive patients admitted with first-time AMI due to plaque rupture, visiting hospital within 24 hours of onset, and without a history of HF. All patients were treated with primary PCI. Patients were divided into three groups by LVEF after AMI, reduced EF (rEF): < 40%, mrEF: 40-50%, and preserved EF (pEF): >50%, and were evaluated for clinical characteristics management and onset of HF after first-time AMI.
Results: Those with rEF, mrEF, and pEF comprised 41, 126 and 465 patients, respectively. There are no significant differences in age (rEF 69yrs., mrEF 68yrs., pEF 66yrs., p = 0.07), gender distributions (Male; 88%, 72%, 76%, p = 0.11) and discharge medication, between 3 groups. In patients with mrEF, hemoglobin (13.3g/dL, 13.7g/dL, 14.3g/dL, p < 0.01), creatinine (1.1mg/dL, 0.83mg/dL, 0.80mg/dL, p < 0.01), peak creatine kinase (3964U/L, 2981U/L, 1309U/L, p < 0.01) and B-type natriuretic peptide (647pg/mL, 228pg/mL, 69pg/mL, p < 0.01) of mrEF were intermediate between pEF and rEF. Kaplan-Meier analysis revealed that the rate of onset of HF differed significantly between rEF and pEF; mrEF patients experienced intermediate rates (Figure). After adjustment with patient background, the rate of onset of HF of mrEF was significantly lower than that of rEF (adjusted HR, 6.65; 95% CI: 1.82 to 22.6, p = 0.046), while there was no significantly between mrEF and pEF (adjusted HR, 0.51; 95% CI: 0.21-1.31, p = 0.15).
Conclusion: We found that the patients with mrEF after first-time AMI represent clinically diverse group with many intermediate features compared to rEF and pEF, while mrEF patients carry a lower risk of onset of HF after MI than rEF but a similar risk with pEF.



Kaplan-Meier Curves

P1191

Predictors of hospital mortality in patients with acute myocardial infarction and reduced left ventricular systolic function

T Tanja Popov[1]; I Ivanov[1]; S Bjelic[1]; M Jarakovic[1]; M Cankovic[1]; M Petrovic[1]; I Srdanovic[1]
[1]*Institute of Cardiovascular Diseases Vojvodina, Novi Sad, Serbia*

Introduction: Modern treatment of myocardial infarction tends to faster and efficient opening of the infarct-related artery, shorter length of stay in the coronary care unit and shorten hospitalization. However, aging of the population, previous cardiovascular diseases, contribute to a growing number of patients with numerous comorbidities, reinfarction, heart failure. Mortality in these groups of patients is high, and special care must be taken to treat them. The aim of this study was to determine the predictors of in-hospital mortality in patients with acute myocardial infarction and reduced left ventricular systolic function.
Methods: This is single center, retrospective study, that includes patients who were treated in 2014/15. because of acute myocardial infarction.
Results: The study included 2665 patients (64.9% men, 35.1% women). Preserved left ventricular systolic function, EF = 50% had 1413 (53%) subjects. Hospital mortality in the group with EF < 50% was 8.6%, while in the group EF = 50% was 1.2%, p < 0.0005. Patients with EF < 50% were older (66.1 ± 11.7 vs. 61.9 ± 11.6 years, p < 0.0005), had a lower body mass index (BMI) (27.4 ± 4 , 6 vs 27.8 ± 4.4, p < 0,018), lower Jung variable (systolic blood pressure/(heart rate x age)) (0.026 ± 0.008 vs. 0.031 ± 0.009), higher dimensions of the heart chambers and regurgitation rates on the valves, p < 0.005, a higher serum glucose (10.1 ± 4.6 vs. 8.7 ± 3.9 mmol / l, p < 0.0005), creatinine (128.2 ± 80.7 vs 110.06 ± 63.38 mmol / l, p < 0.0005), lower triglycerides (1.76 ± 1.1 vs 1.92 ± 1.6 mmol / l), higher C reactive protein (66.44 ± 85.65 vs 32.41 ± 56.47 mg / dl, p < 0.0005), higher markers of myocardial necrosis and NT-pro-BNP, p < 0.0005, more frequent left anterior descending coronary artery stenosis (LAD)(53.8% vs 25.1%, p < 0.0005), fewer implanted stents during treatment (1.09 ± 0.95 vs 1.20 ± 1.0, p = 0.003), lower TIMI flows before and after intervention. The predictors of hospital mortality in the group of patients with reduced left ventricular systolic function are age, BMI, Jung variable, valvular regurgitation degree, left atrial size, serum glucose, creatinine, triglyceride, CRP, troponin, NT-pro-BNP, TIMI flow after intervention, LAD stenosis, a fewer implanted stents.
Conclusion: Ejection fraction of the left ventricle is an independent predictor of hospital mortality.

P1192

The effect of the invasive cardiology on sudden cardiac death, caused by acute heart failure

B Boris Slavchev[1]; R Ilieva[2]; T Donova[1]
[1]*University Hospital "Lozenets", Cardiology Department, Sofia, Bulgaria*;
[2]*University Hospital Tsaritsa Yoanna, Cardiology Department, Sofia, Bulgaria*

Background: Sudden cardiac death (SCD) is the third most frequent cause of death in Europe. Despite the clear reduction in the rates of SCD in the recent years through better revascularization and prevention of coronary artery disease the effect of the invasive coronary angiography on the SCD, caused by acute heart failure remains unknown.
Purpose: The aim of the study was to investigate the effect of the invasive cardiology on SCD, caused by acute heart failure.
Methods: We reviewed retrospectively the forensic department autopsy files of 1971 cases of sudden death (SD) for the period 2000-2016 in a region with population of 350 000 inhabitants. The cardiac catheterization laboratory in the region was opened in 2012 and therefore the study was divided into two periods 2000-2012 and 2013-2016.
Results: From 1971 cases of sudden death for the whole period we found 1358 cases of SCD (69%) (71 % males; mean age 64 ± 16.4 years). The SCD cases for the period 2000-2012 were 72% of all SD cases and for the period 2013-2016 were 63%. The most common reason for SCD for both periods was acute heart failure (caused by cardiomyopathy, coronary artery disease, myocarditis, valvular disease and arterial hypertension). The diagnosis was made according to the autopsy findings of acutely dilated heart, pulmonary oedema, and organ congestion and was proven histologically. The share of acute heart failure was 52.9 % of all cases of SCD for the period before the invasive cardiology introduction and 25.3% after it (p < 0.001). The significant reduction in the SCD due to acute heart failure is mainly caused by increased revascularization and decreased prevalence of chronic coronary artery disease. Better awareness of the signs and symptoms of heart failure, and the improved medical care might also have played a role.
Conclusion: SCD is the main cause of SD, with acute heart failure still comprising a huge proportion of it. In the recent years we found significant decrease in the acute heart failure SCD cases mainly due to revascularization.

P1193

Clinical, angiographic characteristics and 2-year outcome of acute coronary syndrome presenting with cardiogenic shock

A Antonio Valentim Goncalves[1]; AT Timoteo[1]; T Pereira-Da-Silva[1]; S Aguiar Rosa[1]; L Ferreira[1]; R Carvalho[1]; T Mendonca[1]; R Ilhao Moreira[1]; M Coutinho Cruz[1]; P Modas Daniel[1]; L Morais[1]; I Rodrigues[1]; R Cruz Ferreira[1]
[1]*Hospital de Santa Marta, Lisbon, Portugal*

Introduction: Among patients admitted to a catheterization laboratory with acute coronary syndrome (ACS), a minority present with cardiogenic shock (CS). Evidence for the best way to manage these patients are needed.
Aims: We aimed to assess patients' characteristics and short and long-term outcomes of CS due to ACS.
Methods: We analysed all ACS cases with CS admitted during a ten-year period in a tertiary care centre. We defined CS as systolic blood pressure <90mmHg and signs of impaired organ perfusion with need for catecholamine therapy or presenting with cardiac arrest.
At discharge, a standardized registry was performed in all cases. All patients were followed-up for two years and potencial predictors were analysed (Cox regression) for the occurrence of mortality (total and cardiovascular (CV)), CV hospitalizations and revascularization procedures.
Results: From 3283 patients admitted with ACS, 92 (2.8%) presented with CS. Mean age was 66.0 ± 12.8 years, with 64 (69.6%) males, and 60 (65.2%) presenting with STEMI. These patients presented previous ACS in 12.0%, were smokers in 28.3% and had diabetes, dyslipidemia and hypertension in 23.9%, 37.0% and 45.7%, respectively.
Angiographic characteristics are described in the table. Index-PCI was successful in 83.7% cases. Multivessel CAD was presented in 56 patients (60.9%), with complete revascularization in the index-PCI attempted in 11 patients (19.6%) and staged revascularization performed in 7 patients (12.5%). No statistical differences regarding outcomes were found between these two groups.
Mean hospitalization duration of 16.4 ± 9.5 days with in-hospital mortality of 50.0%. Unsuccessful index-PCI (p = 0.002), culprit left main coronary artery (LMCA) (p = 0.044) and reduced LVEF (p <0,001) were significant in-hospital mortality predictors. At 24 months, survival after hospital release was 91.3%, with 40.0% having at least one CV hospitalization requiring PCI in 13.0% and CABG in 4.4%.
Conclusion: CS was uncommon among ACS patients. Unsuccessful PCI, culprit LMCA and reduced LVEF were independent predictors of in-hospital mortality. Despite a very high in-hospital mortality, long-term outcome was favourable.

Coronary anatomy	Culprit vessel	CAD: Stenosis ≥70% (≥50% LMCA) Culprit or not		
n (%)	In-hospital mortality (%)	n (%)	In-hospital mortality (%)	
left main coronary artery	10 (10.9%)	80.0%	15 (16.3%)	73.3%
Left anterior descending artery	36 (39.1%)	52.8%	59 (64.1%)	47.4%
Left circumflex artery	8 (8.7%)	42.1%	42 (45.7%)	40.5%
Right coronary artery	38 (41.3%)	37.5%	57 (62.0%)	47.4%

Angiographic characteristics

P1194

Echocardiographic parametters of myocardial mechanic as potentially predictors of worse prognosis during one year follow up in STEMI patients

G Krljanac[1]; D Trifunovic[1]; M Asanin[1]; L Savic Spasic[1]; M Vukicevic[2]; I Mrdovic[1]
[1]*Clinical Centre of Serbia, Cardiology Clinic, Medical Faculty, Belgrade, Serbia*; [2]*Clinical center of Serbia, Cardiology Clinic, Belgrade, Serbia*

Parameters of left atrial (LA) mechanic as well as left ventricle (LV) could be substrate of worse prognosis and incidence of major cardiac events (MACE) defined as death, re-infarction, emergency revascularization, ventricular arrhythmias (VT and/or VF) and heart failure which need emergency re-hospitalization in STEMI patients (pts) treated with primary percutaneous interventions (PPCI). Aim: To determine mechanic parameters as predictors of MACE during 12 month follow up (FU). We studded conventional echo parameters, parameters of LV mechanics: global longitudinal strain (GLS) and LA mechanics: peack sistolic strain (S LAs) and strain rate (Sr LA).
Method: 120 consecutive STEMI pts treated with PPCI were prospectively included. Echo examination performed on day 4 ± 2 (VIVID 9GE, Echo PAC Ver 113).
Results: 15/95 (15.8%) of all pts had MACE during one year FU. Parameters of EF, LA vol and vol index, GLS and S LA were significant predictors of MACE. (table 1). The largest area under the ROC had GLS (area 0.815, cut off -11.53, Sn 66.7%, Sp 73.2%).
Conclusion: During after PPCI period the left atrial mechanic parameters could be important to predict of MACE. However, global longitudinal strain is the best prognostic parameter in PPCI STEMI patients.

Table 1. Predictors of MACE

	Pts without MACE (n = 95)	Pts with MACE (n = 15)	p
LVEF (%)	51.2±9.4	37.0±12.1	<0.001
LA vol (ml)	35.4±9.9	46.9±14.5	0.001
LA vol index (ml/m^2)	18.4±5.6	24.1±7.3	0.002
GLS	-14.6±4.3	-10.1±3.9	<0.001
S LAs (%)	20.9±8.1	16.0±7.1	0.030

P1195

Effect of atorvastiatin therapy on lipid profile and carotid intima-media thickness in patients with STEMI

I Matrosova[1]; E Melnikova[1]; N Burko[1]; V Valentin Oleinikov[1]
[1]*Penza State University, Penza, Russian Federation*

Aim: to analyze the lipid profile and carotid intima-media thickness (CIMT) in patients with ST segment elevation myocardial infarction (STEMI).
Methods: the study included 100 patients with STEMI: 90 men and 10 women; the average age is 52 ± 8.9 years. Patients were randomized into two groups. The main group received atorvastatin 80 mg/day, the comparison group was prescribed atorvastatin 20 mg/day. 51 patients (46 men and 5 women) were included in the 1st group, the average age was 51.4 ± 8.5 years. The second group consisted of 49 people (43 men and 6 women), aged 51.5 ± 9.5 years. The groups were matched by age, sex, height, BMI, office BP. All patients received atorvastatin for 48 weeks. The levels of total cholesterol (TC), high density lipoprotein (HDL), low density lipoprotein (LDL), triglycerides (TG) were evaluated.
The carotid artery structural and functional properties were evaluated by ultrasonic scanner MyLab 90 ("Esaote", Italy). The measurements were carried out using the radiofrequency (RF) analysis technology with RF-QIMT software. QIMT (μm) was evaluated at 7-9th days and after 48 weeks of therapy.
Results: Initial values of lipid profile in the 1st group were: TC - 6 ± 1,2 mmol/l; LDL - 4.1 ± 1.2 mmol/l; HDL - 1,2 ± 0,3 mmol/l; TG -1.3 (0.7, 2.2) mmol/l. After 48 weeks of treatment, there was a significant decrease in TC to 3.6 ± 0.7 mmol/l (by 43%, $p < 0.05$); LDL to 2.1 (1.8, 2.8) mmol/l (50%, $p < 0.05$);
In the comparison group, the baseline lipid profile values were: TC 5.6 (5.05, 6.40) mmol/l; LDL - 3.9 (3.3, 4.5) mmol/l; HDL -1,1 (0,9, 1,4) mmol/l; TG -1.3 (0.8, 1.7) mmol/l. At the end of therapy, there was a significant decrease in TC to 4.1 (3.7, 4.9) mmol/l (by 28%, $p < 0.05$); LDL to 2.6 (2.2, 3.2) mmol/l (by 24.5%, $p < 0.05$). The values of HDL and TG in both groups have not changed significantly.
Initially, the CIMT value in the first group was 739.9 ± 154.2 μm, in the second group - 711.1 ± 141.7 μm. After 48 weeks of therapy, there was a significant decrease of CIMT to 639 (541, 743) μm (by 14%, $p < 0.05$) only in patients receiving high doses of atorvastatin.
Conclusion: atorvastatin therapy 80 mg per day reduces the total cholesterol and low-density lipoprotein more effectively in patients with STEMI. In addition, this approach allows to improve the condition of carotid arteries significantly reducing the intima-media thickness according to the radio-frequency analysis of the ultrasonic signal.

P1196

Left ventricular diastolic function changes in patients with chronic stable angina pectoris in using ranolazine

A Alexey Kuchmin[1]; YV Epelshtein[1]; DY Epelshtein[1]; AA Shevelev[1]; SN Shulenin[1]
[1]*The Kirov Military Academy, St-Petersburg, Russian Federation*

Background: Elevated intracellular Na+ levels and Ca2+ overload result in diastolic dysfunction and microvascular compression that can worsen LV function in patients with chronic stable angina pectoris.
Purpose: The purpose of this study was to investigate whether inhibiting late Na+ current by using ranolazine improved diastolic function in patients with stable ischemic heart disease.
Methods: 21 patients with stable ischemic heart disease were examined using complex of cardiac assessments, including 2D and 3D echocardiography. All of them treated with 1 or 2 antianginal medications were assigned to ranolazine extended-release 1000 mg BID for 4 weeks. Echocardiograms were performed at baseline and after treatment with ranolazine for 4 weeks. Two patients failed to complete the trial.
Results: American and European guidelines recommend the use of ranolazine in the setting of chronic stable angina pectoris (CSAP) in patients who have not derived sufficient benefit from first-line agents chronic stable angina pectoris. There is data than ranolazine may improve diastolic function in some groups of patients. All patients that we enrolled in our study had signs of diastolic dysfunction. After 4 weeks of therapy with ranolazine there were a significant increase in E/A ratio (0.71 ± 0.22 and 0.85 ± 0.18, $P < 0,05$) and reduction in DT (261.6 ± 51.3 ms and 235 ± 47.3 ms, $P < 0,05$) and IVRT (114.3 ± 11.9 ms and 105.4 ± 9.8 ms, $P < 0,05$) values. Ema (TDI-derived lateral mitral annular E wave) was also decreased after treatment with ranolazine (9.11 ± 1.64 cm/s and 7.96 ± 1.89 cm/s). There was a statistically significant decrease in angina frequency ($P < 0.01$), and in doses of weekly sublingual nitroglycerin use ($P < 0.01$) in patients treated with ranolazine.
Conclusions-Results of this study revealed that ranolazine improved relaxation parameters of left ventricle in patients with chronic stable angina pectoris and diastolic dysfunction. It can be explained that impairment of diastolic function in this category of patients may be caused by ischemia of myocardium and is reversible.

P1197

Non-ST-segment elevation of acute coronary syndrome. The factors that influence the revascularization strategy.

SV Malchikova[1]; AN Kolupaev[1]
[1]*Federal State Budgetary Educational Institution of Higher Education "Kirov State Medical University", Internal medicine department, Kirov, Russian Federation*

Introduction: Non-ST-segment elevation of acute coronary syndrome (NSTE-ACS) is the most common form of acute coronary syndrome. Patients with NSTE-ACS with proximal left anterior descending (LAD) coronary artery disease (isolated and multi-vessels diseases) are the most complicated for choice of method of revascularization. There are no clear algorithm of optimal invasive strategy for this category of patients currently.

Purpose: to evaluate factors influencing the strategy of myocardial revascularization in patients with NSTE-ACS with proximal LAD coronary artery disease
Materials and methods.
103 patients with NSTE-ACS with proximal LAD coronary artery disease (hemodynamically significant stenosis) were included in the study on a prospective basis. They were divided into two groups: coronary artery bypass grafting (CABG) group - 63 patients (61.2%) and percutaneous coronary intervention (PCI) group - 40 patients (38.8%). Intervention therapy was performed in Kirov Regional Teaching Hospital, The city of Kirov.
The estimation of clinical features of the disease, the structure of comorbidity, estimation of indexes of scales: EuroScore II, SYNTAX, estimation of indexes of echocardiography were performed.
Results: There were no differences by sex and age between the groups. Statistically significant differences were observed in the structure of comorbidity: presence of hemodynamically significant atherosclerosis of peripheral arteries (4.8% and 17.5% for CABG and PCI group's, respectively, ? < 0.05). Index of Euroscore 2 scale was 1.25 ± 0.58% on average, the mortality rate was 1,6% in reality in the CABG group. The periods of operative treatment were 18.0 ± 7.8 days and 7,2 ± 7,9 days for CABG and PCI group's, respectively, ? < 0.01. Special attention was paid to the scale of angiography status. SYNTAX scores were 18.6 ± 7.0 and 9.9 ± 3.9 for CABG and PCI group's, respectively, ? < 0.05. CABG was perfomed in patients with ostial lesion of LAD, hemodynamically significant multivessels defeat, stenosis of trunk of left coronary artery more than 50%, extended stenosis of LAD (? < 0.01). There have been powerful flows between the left and right coronary artery systems in the CABG group, in comparison with the PCI group. (p < 0.01). Preference is given to PCI with technical feasibility in patients with isolated proximal LAD stenosis from 50% to 80%. The clinical status of the patient played a key role in PCI ad hoc the LAD (isolated proximal stenosis 90% or more): recurrent angina (repeated recurrence of the pain syndrome), refractory to adequate drug treatment, unstable hemodynamic parameters.
Conclusion: Thus, the choice of an optimal strategy for invasive treatment in this category of patients should be guided by the following factors: stratification of patients with NSTE-ACS risk based on the presence of clinical risk factors, evaluation of SYNTAX scale, EuroScore II scale, discussion of the findings by a heart team.

P1198
In-hospital prognostic value of plasma brain natriuretic peptide (BNP) after acute myocardial infarction

R Raymond[1]; T Zaki[1]; I Nour Eldeen[1]
[1]*Ain Shams University, cairo, Egypt*

Background: Acute myocardial infarction is a major mortality cause and in spite of diagnostic and therapeutic improvements, mortality and morbidity rate of this condition remained high. B-type natriuretic peptide (BNP) has been recognized as a useful marker for predicting acute and chronic left ventricular dysfunction. Although BNP plasma level is measured routinely in many centers in acute myocardial infarction, but it is not full determined how it is useful for estimation of left ventricular ejection fraction (LVEF) and other acute complications.
Objective: To investigate the prognostic value of B type natriuretic peptide (BNP) in acute myocardial infarction (AMI) and its correlation with in-hospital left ventricular systolic function and post-myocardial infarction complications.
Methods & Results: We enrolled 90 consecutive patients admitted to coronary care units of Ain Shams University hospitals with acute ST segment elevation myocardial infarction who were successfully reperfused by primary PCI [57 patients (63.3 %)] or thrombolysis [33 patients (36.7%)] in the period from September 2014 to April 2015. Seventy five patients (83.3%) were male, mean age 55.58 ± 8.73 years. Sixty three patients (70.0%) were smoker, 48 (53.3%) diabetic, 41 (45.6%) hypertensive and 45 (50 %) dyslipidemic. Sixty two patients (68.9%) presented with anterior MI & 28 (31.1%) with inferior MI. BNP was immediately assessed after successful reperfusion.Trans-thoracic echocardiography was done on third day of admission. ECG , cardiac enzymes & in hospital clinical follow up were done on daily basis.There was no statistically significant correlation between BNP levels and site of infarction (P-value = 0.141) , timing of symptoms onset (p- value = 0.431), nor type of reperfusion therapy (P-value = 0.744). However, a significant negative correlation was found between BNP levels and ejection fraction (P-value = 0.033) with a cut off value of BNP <1170 pg/ml. Patients with BNP level (= 1238.7 pg/ml) were significantly more likely to experience new or worsening clinical heart failure during their hospital stay (P-value = 0.035).Also, a statistically significant positive correlation was found between BNP levels and mechanical complications in the form of acute mitral regurgitation (P-value = 0.050) with a cut off value of BNP >1116 pg/ml as well as arrhythmias (ventricular tachycardia, complete heart block and atrial fibrillation) (P-value = 0.002) with cut off value of BNP >1418 pg/ml.
Conclusion: Baseline BNP level measured on admission in acute ST segment elevation myocardial infarction could be used as a predictor for the development of acute mitral regurgitation, arrhythmias, impairement of LV systolic function and new or worsening of clinical heart failure.

Valvular Heart Disease - Epidemiology, Prognosis, Outcome

P1199
Functional, haemodynamic and prognostic impact of mitral regurgitation in patients with heart failure and preserved ejection fraction

S Stefan Aschauer[1]; B Oetztuerk[1]; C Zotter-Tufaro[1]; A Kammerlander[1]; J Mascherbauer[1]; P Bartko[1]; F Duca[1]; C Binder[1]; D Bonderman[1]
[1]*Medical University of Vienna, Department of Internal Medicine II, Division of Cardiology, Vienna, Austria*

Background: Functional mitral regurgitation (FMR) is a common finding in various heart failure entities. In patients with heart failure and reduced ejection fraction

P1198 Table 1. Baseline characteristics of HFpEF patients, stratified by mitral regurgitation severity

	Mild MR [n = 132]		Moderate MR [n= 107]	Significant MR [n= 18]			P-value			
Age, years	69.4	±	9.3	73.6	±	7.1	72.2	±	8.5	<0.001
Female, [%]	87.0		[66.5]	78.0		[72.9]	9.0		[52.9]	0.936
History of atrial fibrillation, [%]	63.0		[48.5]	72.0		[67.9]	12.0		[75]	0.004
NYHA										0.717
II, [%]	49.0		[40.15]	31.0		[32.04]	4.0		[25.0]	
III, [%]	71.0		[52.27]	69.0		[62.14]	11.0		[68.8]	
IV, [%]	10.0		[7.58]	6.0		[5.83]	1.0		[6.3]	
6-min walk distance, meters	331.0	±	118.5	308.5	±	116.3	354.8	±	112.0	0.249
NT-pro BNP, pg/mL	1477.7	±	2204.5	1882.7	±	2886.0	3253.4	±	2951.0	0.024
PAP systolic, mm Hg	52.9	±	19.0	53.3	±	16.2	56.1	±	18.6	0.840
PAWP, mm Hg	18.7	±	3.8	20.7	±	5.5	22.1	±	6.0	0.020
RV end-diastolic diameter, mm	40.0	±	7.3	**40.7**	±	6.3	45.6	±	12.6	**0.114**
RVEF, [%]	52.1	±	11.2	**53.1**	±	10.8	39.4	±	10.6	**0.005**

MR indicates mitral regurgitation; NYHA, New York Heart Association functional class; PAP, pulmonary artery pressure; PAWP, pulmonary artery wedge pressure; RV, right ventricular; RVEF, right ventricular ejection fraction

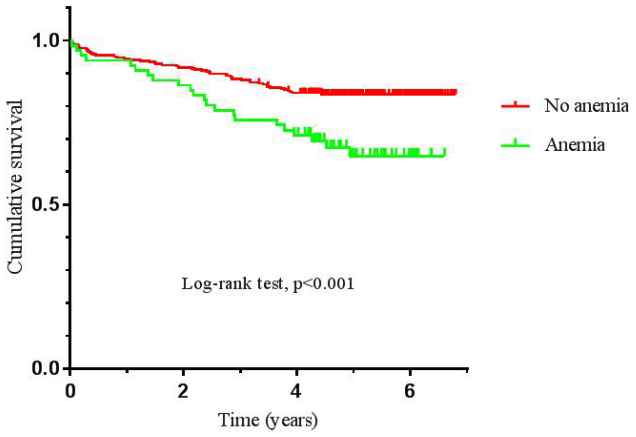
(HFrEF), mitra-clip has emerged as therapeutic opportunity and has been shown to improve functional status. By contrast, the role of secondary MR in HFpEF is fairly unknown. The aim of the present study was to determine the impact of FMR on functional status, haemodynamics and prognosis in HFpEF.
Methods and Results: 261 consecutive patients with HFpEF were screened for the presence of a FMR and were classified into 3 groups: no or mild, moderate and greater than moderate FMR. Patients were followed for a mean of 24 ± 17 months. Between groups, patient with increasing FMR severity were older, had higher rates of atrial fibrillation, higher filling pressures and worse right ventricular function (Table1). Besides, significant FMR was associated with increased mortality risk.
Conclusions: This is the first study that evaluated the role of FMR in a pure HFpEF population. FMR had a negative impact on ventricular filling pressures, right ventricular function and survival. In this light we conclude that further studies are needed to confirm current results and to evaluate interventional therapies that target FMR.

P1200
Prevalence and prognostic implication of iron deficiency in patients with severe aortic stenosis

A B Kvaslerud[1]; A Auensen[1]; A Hussain[1]; T Ueland[2]; K I Pettersen[3]; L Morkrid[4]; L Gullestad[1]; K Broch[3]
[1]Oslo University Hospital, Department of Cardiology, Rikshospitalet and Faculty of Medicine, University of Oslo, Oslo, Norway; *[2]Oslo University Hospital, Research Institute of Internal Medicine and Institute for Clinical Medicine, University of Oslo, Oslo, Norway*; *[3]Oslo University Hospital, Department of Cardiology, Oslo, Norway*; *[4]Oslo University Hospital, Department of Medical Biochemistry and Institute for Clinical Medicine, University of Oslo, Oslo, Norway*

Objectives: The clinical importance of iron deficiency (ID) in patients with heart failure (HF) is well established, but the prognostic implications of ID in patients with other chronic cardiovascular diseases are less studied. By employing the definition of ID frequently used in patients with HF (ferritin < 100 μg/L or ferritin 100-299 μg/L with a transferrin saturation < 20%), this study investigates the prevalence, predictors and prognostic value of ID in patients with severe aortic stenosis (AS).
Methods: In a prospective study of 464 patients (age 75 ± 11 years, 56% men) with severe AS who were evaluated for aortic valve replacement (AVR), iron stores were assessed at presentation.
Results: ID was detected in 246 patients (53%). 94 patients (20%) had anemia (Hgb < 13.0 g/dL for men, < 12.0 g/dL for women). Anemic patients were more often iron deficient than non-anemic patients (63% vs 51%, p = 0.03). Other independent predictors of ID were female sex, use of antacids/proton-pump inhibitors and smaller aortic valve area (all p < 0.05). 373 patients (80%) were offered surgical (337) or transcatheter (36) AVR and 91 (20%) received conservative, medical treatment (MT). During follow-up (median 4.7 years, IQR 3.8-5.5 years), 129 patients (28%) died, of whom 57 (63%) was in the MT group and 72 (19%) in the AVR group. 69 died of cardiac causes. There was no significant difference in all-cause or cardiac mortality between patients with and without ID in neither the AVR nor the MT group. Anemia, on the other hand, was associated with increased all-cause (p < 0.001) (Figure 1), but not cardiac, mortality in patients referred to AVR. Neither anemia nor ID were independent predictors of all-cause or cardiac mortality in multiple analyses adjusted for predetermined clinical, biochemical and echocardiographic predictors in either the AVR or MT groups. The composite of major adverse cardiovascular events (MACE), defined as all-cause death, myocardial infarction, stroke or transient ischemic attack, occurred in 73 of 464 patients (16%) within the first year after inclusion (21 (23%) in the MT group and 52 (14%) in the AVR group). There was no significant difference in the event rate between patients with and without ID or anemia in the MT or the AVR group. Neither anemia nor ID were independent predictors of MACE.
Conclusions: Our results indicate that ID is common in patients with severe AS. Neither anemia nor ID provided independent prognostic information on top of conventional risk factors. More studies are required to evaluate whether the definition of ID used in patients with HF is useful in other chronic cardiac diseases, such as aortic stenosis.

Figure 1. Survival analysis. Kaplan-Meyer curve reflecting overall survival in patients with severe aortic stenosis referred to operation with and without anemia



P1201
Clinical outcomes of Transcatheter Aortic Valve Implantion in patients with degenerated bioprosthetic surgical valves versus aortic stenosis

E Munoz-Garcia[1]; M Munoz-Garcia[1]; A J Antonio Jesus Munoz Garcia[1]; F Carrasco-Chinchilla[1]; AJ Dominguez-Franco[1]; JH Alonso-Briales[1]; JM Hernandez-Garcia[1]; MF Jimenez-Navarro[1]; E De Teresa Galvan[1]
[1]University Hospital Virgen de la Victoria, Department of Cardiology, Malaga, Spain

Most surgical heart valves currently implanted are bioprosthetic tissue valves but such valves deteriorate with time and re-operation carries significant risk. Implantation of a transcatheter valve inside a failed surgical valve (valve-in-valve) has recently emerged as an alternative, less-invasive option. The aim this study was to evaluate the clinical results of this technique using autoexpandible prosthesis in patients with degenerated bioprosthesis surgical valves and comparing them with patients with aortic stenosis.
Methods: The CoreValve prosthesis (Medtronic, Minneapolis, MN, USA) was implanted in 19 patients with symptomatic degenerated surgical aortic valves (SAV) and in 596 patients with aortic stenosis (AS).
Results: The mean age was lower in SAV compared with AS 74.2 vs. 79.6 ± 6.3 years, p = 0.001 and logistic EuroSCORE was higher by SAV 27.6 ± 16% vs. 17 ± 11, p= 0.001. TAVI procedure was successful in all patients with degenerated bioprosthesis. In two patients required to implant a second valve prosthesis and there were not complications after procedure including mortality at 30 days. After procedure and 1-year, the mean gradient was higher in patients with SAV than AS, 19.7 ± 13 mmHg vs. 8.8 ± 3 mmHg, and 15.1 ± 9 vs. 9 ± 4 mmHg, p < 0.001, respectively. The aortic regurgitation grade post-procedure in patients with SAV compared wit AS were: none (63.2% vs 40.1%); mild (26.3% vs. 33.8%), moderate (10.5% vs. 23.5%) and severe (0% vs. 0.9%), p= 0.045. There were more moderate and severe prosthesis-patient mismatch when compare with the rest of patients treated (75% vs. 36%, p = 0.09 and 43.8% vs. 8.2%, p = 0.001, respectively). There were tend to lower requiring pacemaker after procedure (12.5% vs. 26.1%, p = 0.175). In the follow-up, after 41.4 ± 27 months, the total mortality was similar in both groups, 42.1% vs. 34.9%, p = 0.238 and 80 % of patients was at an Association functional class I-II.
Conclusions: The valve-in-valve procedure is clinically effective in patients with degenerated bioprosthesis aortic valves. The procedure and outcomes are similar in some aspects to TAVI in the setting of native aortic valve stenosis

P1202

Mitral Valve Prolapse - a single-centre study of outcomes

R Rita Carvalheira Dos Santos[1]; A Marques[2]; S Alegria[2]; AR Pereira[2]; D Sebaiti[2]; I Cruz[2]; AR Almeida[2]; P Fazendas[2]; I Joao[2]; H Pereira[2]
[1]Hospital de Vila Franca de Xira, Vila Franca de Xira, Portugal; *[2]Hospital Garcia de Orta, Almada, Portugal*

Backgound: Mitral Valve Prolapse (MVP) is a common condition, with a wide clinical range.
Objective: Description of a MVP population and analysis of the clinical and echocardiographic relevant prognostic parameters.
Methods: Retrospective unicentric study based on electronic patient records and echocardiogram review, between 01/2012 and 12/2016. Occurrence predictors of ventricular tachycardia (VT), stroke, acute myocardial infarction (AMI), infective endocarditis (IE) and overall mortality (OM) were considered.
Results: 106 patients were included: 55.7% male with mean age of diagnosis 60 ± 14 years. In initial evaluation 36.8% of patients were asymptomatic; among the symptomatic patients, 34.9% presented NYHA class = II. Most of them had moderate mitral regurgitation (MR), 23.6% severe MR; 69,8% with posterior leaflet prolapse and 19.8% with involvement of both leaflets; mean telediastolic e telesystolic volumes of 110.6 ± 38mL and 42 ± 20mL respectively, mean left ventricle ejection fraction (LVEF) of 62 ± 7%. With a 39.4 months median follow up, the overall incidence of events was 38.7%. The stroke incidence was 8.5%, mainly in males (p = 0.036), asymptomatic (p = 0.006) or with palpitations (p = 0.007); 12.3% of patients had AMI, most diabetics (p = 0.023) with anterior leaflet prolapse (p = 0.038). The incidence of VT and IE was 5.7%, with no significant impact factors identified. The OM was 8.5%, all male, mostly symptomatic (p = 0.005). The mean age of deceased patients was significantly higher (mean 70 ± 8.6 vs 59.6 ± 14 years, p = 0.006). As expected, patients with severe MR were more submitted to surgery (p < 0.001), although they didn't have a significantly higher OM (16 vs 5.1%, p = 0.077). Of the remaining echocardiographic parameters analyzed, none showed statistically significant association with the events, even though a greater tendency for the occurrence of VT with a lower mean ejection fraction (56.7% ± 3 vs 62.8% ± 7, p = 0.058) and a greater OM with a higher LV telesystolic volume mean (51 ± 23 vs 39 ± 19mL, p = 0.068) was verified.
Conclusion: The overall incidence of events, in this population, was 38.7%, being sex, age and symptoms the main factor for their occurrence. The echocardiographic parameters analyzed may provide information regarding the severity of these patients, particularly LVEF and VTSVE.

P1203

Predictors of embolism in Infective Endocarditis

AC Ana Catarina Gomes[1]; I Cruz[1]; AI Marques[1]; S Alegria[1]; AR Pereira[1]; D Sebaiti[1]; I Rangel[1]; I Joao[1]; H Pereira[1]
[1]Hospital Garcia de Orta, Cardiology, Almada, Portugal

Background: Infective endocarditis (IE) still represents a major cause of morbimortality in patients with valvular heart disease. Among the morbidity causes, embolism burden is responsible for major disability in this patients.
Methods: We studied the endocarditis population in our hospital, from 2006-2016. The clinical and imaging data were collected as well as the complication rates, particularly the embolic-related data.
Purpose: To determine the predictors of embolism in IE.
Results: 148 patients, 75% males, 61.5 ± 15.9 years. 51.4% with hypertension (HTN), 18.9% with diabetes mellitus. Comorbidities: heart failure (HF) in 27% (6.8% with HF device), pulmonary disease (PD) in 14%, chronic renal disease (CRD) in 14.9%, 3.4% on hemodialysis (HD), chronic hepatic disease (CHD) in 22.3%.
Signs at presentation: fever 67.1%, murmur 53.3%, anemia 39.5%. Native valve disease in 72.3%.
Echocardiographic identified lesions: vegetation in 80.4%, abscess in 13.5%, pseudoaneurysm in 4.7%, valve obstruction in 6.1%, aneurysm in 3.4% and fistula in 4.1%. Global embolism occurred in 33.6% of our patients, being in 19.1% to the cerebral territory.
Embolism was directly associated IV drug use (r = 0.241, p = 0.003), septic shock (r = 0.275, p = 0.001) and lack of favorable operative condition (r = 0.286, p = 0.004). Although, it is inversely associated with Streptococcus IE (r=-0.17, p = 0.039), local complications (r=-0.268, p = 0.001), presence of abcess (r=-0.185, p = 0.032), age (r=-0.194, p = 0.018), HTN (r=-0.202, p = 0.014), HF (r=-0.20, p = 0.015) and CRD (-0.175, p = 0.034).
Conclusion: Embolism was associated with IV drug use, septic shock and non-surgical approach. It was inversely associated with Streptococcal IE, HF and local complications, including abscess.

P1204

Predictors of relapse in Infective Endocarditis

AC Ana Catarina Gomes[1]; I Cruz[1]; AI Marques[1]; S Alegria[1]; AR Pereira[1]; D Sebaiti[1]; I Rangel[1]; I Joao[1]; H Pereira[1]
[1]Hospital Garcia de Orta, Cardiology, Almada, Portugal

Background: Infective endocarditis (IE) still represents a major cause of morbimortality in patients with valvular heart disease. Apart from causes of morbimortality related to the index episode, recurrence/relapse is one of the long-term complications, particularly related to non-effective clearance of microorganisms from tissues.
Methods: We studied the endocarditis population in our hospital in the last 10 years. The clinical and imaging data was collected as well as the complication rates and rate of relapse.
Purpose: To establish the predictors of relapse in IE, particularly related to IE risk factors and associated complications.
Results: 148 patients, 75% males, 61.5 ± 15.9 years. 51.4% with hypertension, 18.9% with diabetes. Comorbidities: heart failure (HF) in 27% (6.8% with HF device), pulmonary disease (PD) in 14%, chronic renal disease (CRD) in 14.9%, 3.4% on haemodyalisis (HD), chronic hepatic disease (CHD) in 22.3%, HIV seropositive 13.5%, cancer in 9.5%, 98.6% on imunossupression (medical cause or drug-related).
Echocardiographic lesions: vegetation in 80.4%, abscess in 13.5%, pseudoaneurysm in 4.7%, valve obstruction in 6.1%, aneurysm in 3.4% and fistula in 4.1%.
Rate of relapse: 2.6%
Relapse was associated with local complications (100% vs 43.6%, p = 0.040) and local destructive lesions (75.0 vs 22.1, p = 0.043). It was not associated with specific microorganisms, type of valve and patient comorbidities.
Conclusion: Relapse was associated with endocarditis-related local complications, although not related to specific etiology, microorganisms or comorbidities.

Valvular Heart Disease - Treatment

P1205

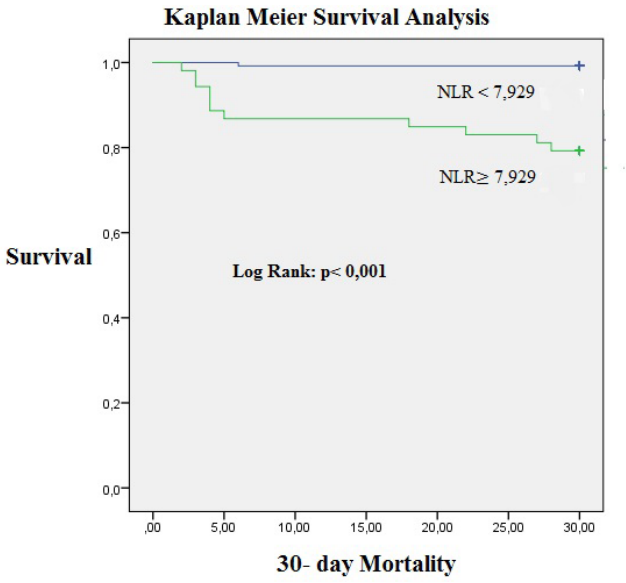
Retrospective evaluation of the predictive value of neutrophil lymphocyte ratio (NLR) on 30-day mortality after transcatheter aortic valve implantation (TAVI)

E Emre Yilmaz[1]; S Turen[2]; B Uygur[2]; A R Demir[2]; C Z C Gevher[1]; S T Karakurt[1]
[1]Kanuni Sultan Süleyman Education and Research Hospital , Cardiology, Istanbul, Turkey; *[2]Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Training and Research Hospital, Cardiology, Istanbul, Turkey*

Introduction: Neutrophil lymphocyte ratio (NLR) has been found to be an independent predictor of prognosis in coronary artery disease and valvular diseases. Current knowledge about the relation of NLR with prognosis after transcatheter aortic valve implantation (TAVI) is not sufficient.
Purpose: The aim of this study is to investigate if neutrophil lymphocyte ratio (NLR) is an independent predictor of 30-day mortality after TAVI.
Methods: A total of 196 patients who underwent TAVI between October 2010 and December 2016 were screened and 184 patients were included in the study. The cut off value for NLR was determined by ROC analysis. The cut off value for postoperative 3rd day NLR (NLR3) was defined as 7.93. The study population was divided into two groups: those who have higher and lower than this cut off value as "high NLR" and "low NLR" respectively. Baseline, peroperative, and postoperative clinical features, echocardiographic and laboratory findings of high and low NLR groups were analyzed by univariable and multivariable analyses.
Results: One hundred thirteen (61.4%) of the patients were female and mean age was 79,41 ± 7,88. Sixteen patients died within 30 days follow up after the TAVI. Three patients died within 24-72 hours. Mortality was found to be significantly higher in the high NLR group [12 (22.2%) versus 1 (0.8%), p <0.001]. In Kaplan-Meier survival analysis, 30-day survival was lower in the high NLR group (Log-rank, p <0.001). In multivariable Cox regression analyses, NLR3 [Odds Ratio (OR): 30,98, 95% Confidence Interval (GA): 2,4-399,48 p: 0,008], acute renal damage [OR: 6.58, 95% GA: 1,360-31,875 p = 0,019] and preoperative peak gradient [OR: 1,045, 95% GA: 1,008-1,084 p = 0,018] were found to be as independent predictors of 30-day mortality after TAVI.
Conclusion: In this study, NLR3 was found to be an independent predictor of 30-day mortality after TAVI.

P1205 NLR cut off values by ROC analysis

	Cut Off Value	Area Under the Curve (AUC)	%95 CI	Sensitivity, %	Specificity, %	p value
NLR Basal	2,46	0,704± 0,047	0,612- 0,797	87,5	56	0,007
NLR 1	9,74	0,524± 0,062	0,403 - 0,645	75	44	0,753
NLR 3	7,93	0,914± 0,035	0,846 - 0,982	92,3	75	0,000



Kaplan Meier Survival Analysis

P1206

Transcatheter aortic valve implantation without balloon valvuloplasty is not associated with transient left ventricular dysfunction

M Mirna[1]; B Wernly[1]; S Eder[2]; M Lichtenauer[1]; C Jung[3]; C Reiter[4]; A Kypta[4]; UC Hoppe[1]; M Hammerer[1]

[1]Paracelsus Private Medical University, Internal Medicine II, Cardiology, Salzburg, Austria; *[2]Oberndorf Hospital, Department of Internal Medicine, Oberndorf, Austria*; *[3]Medical Faculty, University Duesseldorf, Division of Cardiology, Pulmonology, and Vascular Medicine, Duesseldorf, Germany*; *[4]Kepler University, Department of Cardiology, Linz, Austria*

Background: Transcatheter aortic valve implantation (TAVI) is a therapeutic alternative to conventional heart surgery in patients with high-grade aortic valve stenosis. Balloon aortic valvuloplasty (BAV) under rapid ventricular pacing (RVP) has been a routine part of TAVI. However, it carries substantial risks and therefore an increasing number of interventionists have started to refrain from it. In our study, we investigated if TAVI without prior balloon valvuloplasty ("direct TAVI") was associated with a similar increase in cardiac biomarkers and decrease in ejection fraction as reported previously.
Methods: A total of 164 consecutive patients undergoing "direct-TAVI" were followed up for one year and were retrospectively analyzed regarding mortality, safety and efficacy endpoints as well as common laboratory and echocardiographic values.
Results: According to the VARC2 (Valve Academic Research Consortium) 89.1% of patients remained free of a combined safety endpoint and technical success rate was 96.3%. Mortality rates at 30 days and 1 year were 3.0% (n= 5) and 10.4% (n= 17), respectively.
TAVI without rapid ventricular pacing was highly effective in lowering aortic valve peak velocity from 4.36 ± 0.63 m/s before to 1.7 ± 0.45 m/s post intervention, resulting in a significant decrease of mean aortic valve peak velocity ($p < 0.01$). Left ventricular function remained unaltered (50,64 ± 10% prior to TAVI and 50,86 ± 8,99% post TAVI) after the intervention, whereas high sensitive troponin T, a well-established marker for myocardial injury, increased significantly from 26 ng/L (IQR= 18.00-44.00) to 119 ng/L (IQR= 73.25-166.00, $p < 0.001$) during this time. Myocardial injury (<15 ULN) was associated with mortality at one month (10% vs 2%; $p = 0.04$) and one year (8% vs 23%; HR 4.28; 95%CI 1.63-11.28; $p = 0.003$).
Conclusion: "Direct TAVI" is feasible, safe and effective. Mortality and safety resulted in similar outcomes as the frequently used approach with rapid ventricular pacing and balloon valvuloplasty. In contrast to a cohort of patients who underwent TAVI with BAV and RVP previously published by another center, our cohort did not suffer from transient impairment of left ventricular function. Furthermore, hs-troponin showed a less pronounced increase than reported previously. We therefore conclude that "direct TAVI" is a less invasive option involving less myocardial stress and is therefore be better suited for the elderly and multimorbid.

P1207

Single center initial experience with mitral annuloplasty using Carillon device for patients with significant functional mitral regurgitation and left ventricular disfunction

S Mazzetti[1]; G Singh[1]; J Rossi[1]; R Abete[1]; A De Marchi[1]; G Valenti[1]; CA Santambrogio[1]; G Sorropago[1]; F Scalise[1]; A Andrea Mortara[1]

[1]Dipartment of Cardiology Policlinico di Monza, Monza, Italy

Aims and Objectives: Presence of significative functional mitral regurgitation in patients with left ventricular dysfunction adds to worsening hemodynamics of already decompensating myocardium. Surgical annuloplasty results have shown to reduce regurgitation thus improve functional status, however data is scant to prove a survival benefit after surgical correction in these high-risk patients. Hence, different percutaneous technique have been proposed with promising Results: Aim of the present study was to assess procedural feasibility, safety, efficacy of Carillon device and intermediate term clinical and hemodynamic outcomes both by invasive (catheterization) and non-invasive (Echocardiography) evaluation in patients with secondary mitral regurgitation and left ventricular dysfunction.
Methods and Results: We performed Carillon device implantation in 6 patients from Jun'2016- May'2017. We included patients with left ventricular dysfunction and annular dilatation having moderate-to-severe mitral regurgitation, III NYHA, minimum length > 9cm of coronary sinus. We excluded patients with significant coronary artery disease (SYNTAX > 32), candidates for resynchronization therapy and renal dysfunction. Mean age was 79 ± 4 years, with mean NYHA class 3.16 ± 0.4. Mean annular dimensions (AP) by ECHO were 39.33mm and mean coronary sinus length was 11.5 ± 1.04 and diameter 9.15 ± 2.03mm. Mean device size was 10 ± 1.60 for distal anchor and 18 ± 1.78 for distal anchor with a mean length of 60mm. In one patient left circumflex occlusion was observed after releasing of distal anchor and was redeployed after stenting LCX; however no myocardial infarction was seen in any patient. Mean contrast volume used for procedure was 121.33 ml with implantation time of 35 ± 22.1 minutes. At follow up of 6 months NYHA class changed to a mean of 2.16 ± 0.40, effective orifice area reduced from 0.33 to 0.12(p value- 0.014) Vena contracta from 6.33mm to 2.33 (p value 0.03), annular dimensions from 39.67 mm to 37.50 (p value 0.086) and with MR severity 3.14 to 2 (p-value-NS). There was a reduction in left ventricular volumes as seen by ECHO (end dysatolic volume from 200.50ml to 190.40 ml (p value0.59) and end-systolic volume from 142.83ml to 129ml (p value0.79)). Right catheterization showed reduction, although not significant of PCWP(m) from 28.33(basal) to 19 (3 months) and to 20.40 (6 months) (p value NS). Similarly, RA(m) reduced from 18.67 to 13.40(p-NS), PAP(m) from 54 to 40.60(p value - NS). PVR from 1.92 to 1.68 WU (p value NS). There was no mortality at 6 months, but one patient required re-hospitalization for heart failure and renal failure.
Conclusion: Mitral annuloplasty using Carillon is safe, technically simple and fast in terms of time taken to deploy the device. Echocardiographic as well as hemodynamic data are promising. We expect further improvements in the parameters at 12 months follow-up. However, further large multi-center trials with longer follow up are needed.

P1208

Impact of TAVI referral reasons on morbimortality during hospitalization and follow-up

S Torres[1]; A Nunes[1]; P Araujo[1]; M Braga[1]; R Pinto[1]; J Rodrigues[1]; R Rodrigues[1]; JC Silva[1]; D Magalhaes[1]; M Vasconcelos[1]; PB Almeida[1]; MJ Maciel[1]

[1]Sao Joao Hospital, Porto, Portugal

Introduction: Transcatheter aortic valve implantation (TAVI) has emerged as a safe alternative to surgical aortic valve replacement (SAVR) for prohibitive or high-risk surgical patients (pts) with severe aortic stenosis. There are several reasons for referring patients for TAVI, which are often interconnected and related to the advance aged group of patients in which this valvulopathy is commonly diagnosed.
Purpose: To describe the main reasons for referring a patient for TAVI instead of conventional surgery, and to assess their impact on morbimortality during hospitalization and follow-up.
Methods: We retrospectively evaluated pts who were submitted to TAVI in our tertiary care center between October 2014 and December 2016. Clinical and laboratorial data were evaluated.
Results: A total of 89 pts, of whom 51.7% (n = 46) were female, with a mean age of 80.2 ± 7.1 years were included. All pts had symptomatic severe aortic stenosis prior to TAVI. The median EuroSCORE II was 4,5% (0.8-25.9). The main reasons for referral for TAVI were: porcelain aorta (PA) (n= 47; 52.8%); severe pulmonary disease (PD) (n= 6; 6.7%); frailty (Fr) (n= 5; 5.6%); prior cardiac surgery (CS) (n= 4; 4.5%); high surgical risk based on other major comorbidities (HSR) (n = 27; 30.3%).
During hospitalization, the median stay was similar (PA - 8 days; HSR - 12; PD - 10; Fr - 14; CS - 11; p= 0.60). The incidence of complications was higher in the Fr group (100%), compared to the remain (PA - 63.8%; HSR - 74.1%; PD - 33.3%; CS - 50%), although not significant (p = 0.10). Only one patient had in-hospital mortality (HSR).
Pts were followed up in cardiology appointments during a mean time of 386 ± 93 days. During this period, pts with PD had significantly higher rates of NYHA class = II: 100% (PA - 34.9%; HSR - 40.9%; Fr - 25.0%; CS –25.0%) (p < 0.01).
Hospitalization rates were similar between groups (PA - 23.9%; HSR - 30.8%; PD - 33.3%; Fr - 20%; CS - 75%; p = 0.29). All-cause mortality was higher in the PD (16.7%) and HSR (15.4%) groups (PA - 2.2%; Fr - 0%; CS - 0%), but cardiovascular deaths occurred only in the HSR group (11.5%).
Conclusion: Based on our results, the presence of severe pulmonary disease has a negative impact on patient outcome after TAVI, as seen by the higher rates of NYHA class = II on follow-up and higher all-cause mortality. On the other hand, cardiovascular mortality was verified in pts referred for TAVI due to high surgical risk based on other major comorbidities.

Myocardial Disease - Clinical

P1209
S100A8/S100A9 alarmin as a potential biomarker in patients with active myocarditis

I Mueller[1]; U Kuehl[2]; T Vogl[3]; B Pieske[2]; S Van Linthout[1]; C Tschoepe[2]
[1]Berlin-Brandenburg Center for Regenerative Therapies, Charite - Campus Virchow Klinikum, Berlin, Germany; *[2]Charite - Campus Virchow-Klinikum (CVK), Department of Cardiology and Pulmonology, Berlin, Germany*; *[3]University of Muenster, Department of Immunology, Munster, Germany*

Background: S100A8/S100A9 is a damage-associated molecular pattern molecule and has been shown to be important under inflammatory conditions including arteriosclerosis and coronary heart disease. Clinical evidence highlights that high plasma levels of S100A8/S100A9 are a risk factor for future cardiovascular events.
Purpose: We aimed to evaluate the potential of serum S100A8/S100A9 levels as a prognostic biomarker in patients with endomyocardial biopsy (EMB)-proven active myocarditis (A-MC) vs non-ischemic dilative cardiomyopathy (DCM) and controls.
Methods: S100A8/S100A9, high sensitivity C-reactive protein (hsCRP) and n-terminal (NT) pro-brain natriuretic protein (BNP) levels were analyzed in serum and plasma of A-MC (n = 27; ejection fraction (EF): 38.8% ± 14%) and DCM patients (n = 16; EF: 22.5% ± 4.7%), and controls (n = 51; EF: 60% ± 5%) by specific ELISAs. Patients serum and plasma were collected at time point (T) 1, where also EMBs were collected. EMB S100A8, S100A9, and NLRP3 mRNA levels and the number of invaded inflammatory cells in EMBs were determined by real-time PCR and immunohistology stainings, respectively. Ejection fraction (EF) was determined at T1 and T2 by echocardiography and the improvement/deterioration in EF between T1 and T2 was calculated.
Results: Serum S100A8/S100A9 did not differ between controls and DCM. In contrast, serum S100A8/S100A9 levels were 3.7-fold (p <0.0001) higher in A-MC patients vs controls. Using a cut-off of 570 ng/ml, S100A8/S100A9 levels showed a diagnostic specificity and sensitivity of 77% and 89%, respectively, vs controls. Alarmin levels correlated with hsCRP (r = 0.588, p <0.012), but not with plasma NT pro-BNP levels (r =-0.210, p = 0.3013). The increase of peripheral alarmins correlated strongly with the mRNA expression of S100A8 (r = 0.731, p = 0.0006) and S100A9 (r = 0.702, p = 0.0011) and moderately with lymphocyte function-associated antigen 1 presence (LFA1; r = 0.435, p = 0.0233) in EMBs of A-MC patients. In A-MC patients, EMB mRNA levels of inflammasome 3 (NLPR3), known to belong to the intracellular signaling of alarmins, correlated with EMB S100A8 (r = 0.6, p = 0.024) and S100A9 (r = 0.66, p = 0.012) mRNA expression. Clinically, alarmin serum levels correlated with the EF T1 (r = 0.6032, p = 0.0011) and moderately with the EF improvement/deterioration (EF T2 - EF T1 7.8% ± 6.5%) over time (r = 0.498, p = 0.0415) in A-MC patients. A correlation with the EF over time did not exist for hsCRP (r = 0.363, p = 0.151) or NT pro-BNP (r=-0.180, p = 0.5046) levels.
Conclusions: The S100A8/A9-NPLR3 axis is activated in human A-MC, but not in DCM patients, and reflected by increased serum S1008/S100A9 levels. S1008/S100A9 serum levels are increased under these conditions like some other inflammatory tissue and plasma markers such as hsCRP, but correlated best with the change in LV function. We conclude that the measurement of S100A8/S100A9 serum levels can provide an additional value for the diagnosis and monitoring of A-MC.

P1210
Viral genome changes and the impact of viral genome persistence in myocardium of patients with inflammatory cardiomyopathy

D Dalibor Mlejnek[1]; JK Krejci[1]; PH Hude[1]; LS Spinarova[1]; EO Ozabalova[1]; VZ Zampachova[2]; IS Svobodova[2]; RS Stepanova[3]
[1]St. Anne's University Hospital, First Department of Internal Medicine - Cardioangiology, Brno, Czech Republic; *[2]St. Anne's University Hospital, First Department of Pathological Anatomy, Brno, Czech Republic*; *[3]Masaryk University, Brno, Czech Republic*

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Introduction: Viral infections are considered the most frequent cause of myocarditis and dilated cardiomyopathy (DCM).
Material and Methods: We investigated the changes in viral presence and the impact of viral genome persistence in myocardium on echocardiographic parameters, functional status and some laboratory parameters in a 6-month follow-up. Fifty-four patients with a recent onset DCM, left ventricular ejection fraction < 40% and biopsy-proven myocarditis (<14 mononuclear leukocytes/mm2 and/or >7 T-lymphocytes/mm2) were enrolled. Polymerase chain reaction was performed to detect pathogens in myocardium. Patients were divided according to the administered therapy: standard heart failure medication (46 patients) and immunosuppressive therapy (8 patients).
Results: In the standard heart failure medication group viral clearance was observed in 13 patients and viral persistence in 24 patients in the follow-up period. Comparing both groups, there was no statistically significant difference - LVEF improvement of 12.0 ± 11.4% vs. 18.3 ± 12.6%, decrease in NYHA class of 0.7 ± 0.7 vs. 1.0 ± 0.7, decline in NT-proBNP of 1335 ± 1933ng/l vs. 1942 ± 3242ng/l and decrease in infiltrating leukocytes of 11.1 ± 15.8 vs. 6.7 ± 23.0 cells/mm2 and T-lymphocytes of 5.8 ± 15.1 vs. 1.8 ± 10.9 cells/mm2 (all p = n.s.). A decrease in PCR positive patients from 37 to 29 was observed. The number of PVB19 positive PCR findings decreased from 5 to 4 in patients with immunosuppressive therapy.
Conclusions: A decrease in the number of positive PCR findings in control EMB was observed. Viral genome persistence was not associated with worse outcome in short-term follow-up.

P1211
THE CLINICAL, MORPHOLOGICAL DIAGNOSIS AND PROGNOSTIC VALUE OF THE MYOCARDITIS IN THE LEFT VENTRICULAR NONCOMPATION SYNDROME

O V Olga Blagova[1]; EV Pavlenko[1]; NV Varionchik[1]; AV Nedostup[1]; EA Kogan[1]; AE Donnikov[2]; VV Kadochnikova[2]
[1]I.M.Sechenov I Moscow State Medical University, Moscow, Russian Federation; *[2]DNA technology, Moscow, Russian Federation*

Purpose: to study the prevalence and prognostic value of the myocarditis in the left ventricular noncompation syndrome (LVNC).
Methods: we studied 103 adult patients with LVNS (61 males, 45.6 ± 14.9 years). The average EDD LV was 6.0 ± 0.8 cm, LV EF 38.8 ± 14.5. To diagnose LVNC were performed Echo-CG, CT (n = 81) and MRI (n = 39). DNA-daignostic had included NGS (Ion Torrent) simultaneous sequencing of gene panel (12 genes), followed by Sanger sequencing of detected variants. The pathogenic mutations were detected in 9% of patients in the following genes: MYH7, MyBPC3, LAMP2, DES, DSP, TTN. We also investigated anti-heart antibodies and viruses by PCR. The morphological study was performed in 19 patients (endomyocardial biopsy in 14, intraoperative biopsy in 1, explanted heart study in 1 and autopsy in 3). The mean follow-up was 12 [2; 32] months.
Results: Acute/chronic heart failure was in 79.6% of patients diagnosed. In other cases, the main symptom of LVNC were arrhythmias, ischemia and/or thromboembolism. The average LV diastolic size was 6.0 ± 0.8 cm, LV ejection fraction 38.8 ± 14.5%. The myocarditis was diagnosed in 55 (53.4%) patients with LVNC: in 19 patients by morphological study (active in 10 and borderline in 9 patients) and in 36 patients on the basis of a complex examination (the relationship with a respiratory infection, a 3-4-fold increase in the anti-heart antibodies, the viral genome

in the blood, pericardial effusion, subepicardial LGE). The sarcoidosis was detected in one case by biopsy of lymph nodes. The myocarditis was virus-positive in 17 patients (36.1%). The parvovirus B19, human herpes virus type 6, cytomegalovirus, herpes simplex virus and Epstein-Barr virus were detected in 8 patients in the myocardium (42.1%), and in 14 patients (25.5%) in the blood. The myocarditis was associated with arrhythmic form of LVNC (in 44.4% of this patients), ischemic form (12.5%), dilated pattern (57.5%) and other cardiomyopathies (myopathies, arrhytmogenic right ventricular cardiomyopathy, hypertrophic or restrictive cardiomyopathy, 50.0%). In 10% of all patients with LVNC, acute / subacute myocarditis became the first manifestation of the disease.The association of LVNC with myocarditis led to more severe myocardial dysfunction with a more severe heart failure (NYHA class 2 [1;3] v 1.75 [0;2], $p < 0.01$), lower EF (33.8 ± 13.5 v $44.7 \pm 13.6\%$, $p < 0.001$), higher rate of the nonsustained ventricular tachycardia (67.3% v 29.3%, $p < 0.01$), appropriate defibrillators shocks (38.9% v 0, $p < 0.05$), death (16.4 ? 4.2%, OR 5.75, 95%CI 1.21-27.43, $p < 0.05$), and heart transplantation (7.3% v 2.1%, $p>0.05$). The causes of death were myocardial infarction, arrhythmias, heart failure.

Conclusion: LVNC is a favorable platform for the myocarditis (including viral), which is diagnosed in half of patients. The myocarditis is one of the leading causes of increased heart failure and ventricular arrhythmias, appropriate shocks of defibrillators and lethality in LVNC.

P1212

Cardiac involvement in the full cohort of Romanian Fabry disease patients

S Militaru[1]; R Adam[1]; A Mursa[1]; E Rusu[2]; BA Popescu[1]; C Ginghina[1]; A Saftoiu[3]; R Jurcut[1]

[1]Institute of Cardiovascular Diseases Prof. C.C. Iliescu, Cardiology, Bucharest, Romania; *[2]Fundeni Clinical Institute, Bucharest, Romania*; *[3]Craiova Univeristy of Medicine and Pharmacy, Craiova, Romania*

Background: Fabry disease is a rare X-linked genetic disorder, in which alpha-galasidase deficiency leads to lysosomal accumulation of globotryaosilceramide, affecting most organs and tissues. Cardiac, renal and neurologic involvement influence prognosis. The aim of this study is to describe the particularities of cardiovascular involvement in the full cohort of Romanian Fabry disease patients (pts).

Methods: We evaluated cardiovascular parameters in all consecutive pts diagnosed with Fabry disease in Romania. Obtained data included clinical, biologic (cardiac and renal markers), ECG, ECG holter and echocardiographic (conventional measurements and myocardial Doppler velocities and Speckle tracking based deformation study). Patient files included complete data on renal and neurologic involvement.

Results: The database included 39 pts consecutively diagnosed with Fabry disease, with an average age of 47 ± 15 years, 22 women (56.4%). Women were older than men (52 ± 15 vs 40 ± 12.5 years, $p < 0.05$). More than half had been diagnosed through family screening and 8 pts were first diagnosed because of cardiovascular symptoms or signs. Patient symptomatology included: dyspnea in 19 pts, angina, palpitations and syncope. Permanent pacemakers were present in 7 pts, of which 5 were women. Lab work-up showed high levels of BNP (211 ± 378pg/ml), Troponin I (0.034 ± 0.05 ng/ml) at baseline. ECG analysis showed 16 pts with LVH criteria, while short PR interval (< 120 ms) was present in 11 pts. Holter ECG study showed supraventricular arrhythmias in 2 pts and nonsustained ventricular tachycardia in 2 pts. Cardiac ultrasonography findings included: normal global systolic LV function (LVEF: $63.3 \pm 6.5\%$), but abnormal LV longitudinal function (mean GLS $-15.6 \pm 4.4\%$); LV hypertrophy (LVH) was present in 24 pts, of which 21 pts also had RV hypertrophy and 12 pts had papillary muscle hypertrophy. Analysis showed a correlation between age and cardiac dysfunction parameters (mainly in the absence of treatment), with more severe disease in men at similar ages. Initiation of enzyme replacement therapy at an early age (< 25 yo) led to absence of significant cardiovascular changes.

Conclusions: Fabry disease pts in Romania have important cardiovascular involvement, this being the diagnostic modality in 20.5% of cases. Most frequent cardiovascular abnormalities were LVH, LV longitudinal dysfunction with normal LVEF, indication for pacemaker implant. This data reflects the importance of expert centers for the diagnosis, cardiac evaluation and family screening.

P1213

Long-term follow-up after reconstructive surgery of hypertrophic cardiomyopathy with multi-level obstruction.

YF Yulia Frolova[1]

[1]Petrovsky National Russian Research Center of Surgery, Cardio Surgery of Heart Failure, Moscow, Russian Federation

Aim: To study morphofunctional changes of the heart, genetic testing, the indications and long-term results of surgical treatment of patients with hypertrophic cardiomyopathy (HCM) with multilevel obstruction.

Material and methods: : From 2009 to 2017 a total of 124 patients (pts) with HCM (63 women, 61 men) were analyzed. The mean age was $53 \pm 2,8$ years. 79 (64%) pts had III - IV FC NYHA (functional class, New York Heart Association). According to ECHO, there was found a significant increase of the thickness of interventricular septum (IVS) ($2,24 \pm 0,03$ sm,$p < 0.05$), increase of the gradient at left ventricle (LV) outflow tract (OP) ($71,5 \pm 6.9$ mm hg,$p < 0.05$) and unreliable decrease in end-systolic volume (ESVLV) ($31,3 \pm 2.6$ ml). According to MRI/MCT of the heart in 77pts there was registered increased volume of the anterior and posterior papillary muscles, to their dystopia with reduction of ESVLV and significantly increased myocardial mass of LV in diastole (311 ± 45gr;$p < 0.05$), which we determined as a diffuse-generalized form of HCM; in 22 pts - asymmetric form of HCM. 63 pts with the obstructive form of HCM underwent operation of the extended myectomy with parietal resection of the papillary muscles in conditions of open heart surgery (included 42 pts with replacement of the mitral valve), 5 - endovascular ablation of septal perforator, 27 - implantation of cardioverter defibrillator (ICD), 39 - conservative therapy.

Results: In pts after open heart surgery found a significant improvement in a 1, 3, 5 and 7 years after surgery: I FC (NYHA) - 34 (57%) patients, of FC II (NYHA) - in 25 (53%) patients. Triggering ICD was observed in 5 (19%) pts in the postoperative period. 4 patients (6,3%) died due to life-threatening arrhythmias. ECHO revealed a significant decrease in thickness of IVS (from 2.27 ± 0.02 to 1.5 ± 0.02 cm, $p < 0.05$) and the gradient at OPLV ($71,38 \pm 6.7$ to $4,75 \pm 1.3$ mm hg, $p < 0.05$), the false increase of ESVLV ($28,31 \pm 2.8$ ml to $34.4 \pm 2,9$ml $p>0.05$). Classic "sarcomeric" genetic mutations were surprisingly only found in 14% pts, in86% pts were found other genetic disorders.

Conclusion: Reconstructive extended myectomy with the parietal resection of papillary muscle and mitral valve replacement with chordal preservation provides several long-term benefits in pts with HCM. Many questions remain unanswered about the phenotype-genotype correlations and the prognostic value of particular mutations in different genes.

P1214

Cardiac amyloidosis: a five-year series

A Vigario[1]; M Cravo[1]; I Marques[1]; C Gomes[2]; C Mendonca[1]

[1]Hospital Center of Porto, Internal Medicine, Porto, Portugal; *[2]Hospital Center of Porto, Cardiology, Porto, Portugal*

On behalf of: GEstIC

Background: Amyloidosis is a group of systemic diseases of protein-folding disorders. Prognosis is determined both by type of amyloid and involved organs, in which the cardiac involvement carries the worst one. Achieving an early diagnosis is essential for a better outcome.

Purpose: This study aims to characterize a group of patients with diagnosed cardiac amyloidosis in a tertiary university hospital, to identify the timing of diagnosis and its impact on survival.

Methods: Retrospective observational study recruiting patients from January 2013 to December 2017. All patients with cardiac amyloidosis from our heart failure clinic were enrolled and also those admitted in the Cardiology, Internal Medicine or other wards with diagnosis of amyloidosis and heart failure (HF) stated in discharge summaries. Electronic medical records, procedures and other exams were reviewed. From a total of 29 patients, 10 were excluded because they didn't have imagiological or histological evidence of infiltrative myocardial disease.

Results: These 19 patients with diagnosed cardiac amyloidosis had moderate to severe left ventricular hypertrophy associated with: 1) cardiac Magnetic Resonance Imaging (MRI) reporting typical features of amyloidosis, 9 patients; 2) histologic evidence of amyloid deposition in noncardiac tissue, 12 patients; 3) 99mTc-DPD radionuclide cardiac uptake suggesting TTR amyloid deposition, 3 patients; and/or TTR genetic mutation, 1 patient. One patient refused MRI and tissue biopsy but had plasma cell dyscrasia with free light chain and serum monoclonal gammopathy IgG lambda.

The median age of patients at diagnosis was 71 years, with a ratio of male to female of 12:7. The median time from HF symptoms to diagnosis was 10 months. At diagnosis, New York Heart Association functional class II was the most common (n = 14; 73.7%), followed by class III (n = 3; 15.8%); median NT-ProBNP was 7115 pg/mL; and high sensitive troponin T was elevated in 14 (73.7%) patients. The median ventricular septum thickness was 18.5 mm.

Immunological studies showed plasma cell dyscrasia in 13 (68.4%) patients; tissue biopsy was performed in 15 (78.9%) patients, revealing amyloid deposition in 12 (63.2%), all AL amyloid type. Seven AL amyloid patients received treatment for their haematological disease. The global mortality rate was 68.4%; the AL amyloid patients' mortality was 75%. The median time from HF symptoms to death was 16 months and from diagnosis of cardiac amyloidosis to death was 5 months.

Conclusions: This five-year series reports 19 patients with cardiac amyloidosis, a single centre population with a rare and deadly disease, as described in the literature. Although it was not possible to obtain a histological diagnosis in all the cases, the clinical scenario and imaging results ensured the diagnosis. Establishing this

diagnosis can be challenging but awareness of the early manifestations is crucial to anticipate treatment and modify prognosis.

P1215

The hypertrophic cardiomyopathy - a particular cause of the heart failure with preserved ejection fraction

A Alicja Nowak[1]; Z Oko-Sarnowska[1]; M Kaluzna-Oleksy[1]; M Lesiak[1]
[1]*Poznan University of Medical Sciences, 1st Department of Cardiology, Poznan, Poland*

Introduction: Hypertrophic cardiomyopathy is a recognized, although a particular cause of the chronic heart failure with preserved ejection fraction. Elevated BNP level, as well as diastolic dysfunction occur in both: HFpEF and HCM, however most of the HCM-patients remain asymptomatic. The specific pattern of heart failure in this group require further studies.
Purpose: the aim of the study was to determine the relationships between BNP level and diastolic dysfunction in patients with HCM, according to NYHA functional classification degree.
Material and Methods: We evaluated 145 patients (49% men) diagnosed with HCM aged 19-82 years (mean 49,6 ± 15,9 years) with preserved ejection fraction (EF = 50%). 96 (67,6%) of patient were NYHA class I, 41 (28,3%) NYHA class II and 6 (4,1%) class III. Every patient underwent echocardiographic examination (2 D as well as TDI) with evaluation of left ventricular diastolic function (E/E'av). Additionally, plasma BNP levels were measured. We classified patients into two group according to the occurred HF symptoms (NYHA I vs NYHA II/III).
Results: The significant differences between two groups of patients in BNP levels (249,2 in NYHA II/III vs 151,0 in NYHA I, p = 0,004) were proved. However, 121 patients (83,4%) had BNP level = 35 pg/ml (including 78 (79,8%) of asymptomatic patients). Patients in NYHA II/III class had higher E/E'av ratio when compared to patients in NYHA I class (13,9 vs 9,8; p = 0,00008). Moreover, the correlation between BNP level and E/E'av ratio was proved ($p < 0,05$, r = 0,54) and was higher in NYHA II/III patients (r = 0,63 vs r = 0,44). The predictors of symptomatic HF in ROC curves analysis were: BNP = 245 pg/ml (45% sensibility, 85% specificity, AUC 0,66; p = 0,002) and E/E'av = 16,4 (34% sensibility, 93% specificity, AUC 0,68; p = 0,0006).
Conclusions: Patients with HCM characterize with high BNP levels and impaired diastolic function depending on heart failure functional degree (NYHA class). There are the correlations between BNP level and E/E'av ratio in patients with HCM (more significant in symptomatic patients).

P1216

Results and clinical consequences of endomyocardial biopsy diagnostics over 12 years in a tertiary center

M Noutsias[1]; SE Ludwig[2]; G Mall[3]; K Haentze[2]
[1]*University Clinic Halle (Saale), Mid-German Heart Center, Department of Internal Medicine III (KIM-III), Division of Cardiology, Halle, Germany*; [2]*University Hospital of Jena, Jena, Germany*; [3]*Darmstadt Clinic , Pathology, Darmstadt, Germany*

Background: Diagnostics of endomyocardial biopsies (EMB) is an important cornerstone for the management of cardiomyopathy patients. However, the value of EMB diagnostics in routine settings outside of clinical trials is not well defined.
Purpose: Analysis of consecutive EMB-diagnostics in adult cardiomyopathy patients and the clinical consequences over 12 years.
Results: Between 2004 and 2016, EMB procedures were performed in n = 463 cardiomyopathy patients (mean age: 49.3+13.2 years; males: 72%; LVEF: 33.3+14%) presenting with either dilated cardiomyopathy, clinically suspected myocarditis with left ventricular dilatation, or clinically myocardial storage disease at our tertiary center. Based on the Dallas criteria, myocarditis was confirmed by histology in n = 24 (5.2%) of the patients, whereas the positivity rate of immunohistological confirmation of inflammatory cardiomyopathy (DCMi) was significantly ($p < 0.01$) higher (n = 79/16.7%). All investigated infiltrate phenotypes (lymphocytes: CD3, CD4, CD8; Kp1 macrophages; HLA class II) were significantly associated with the immunohistological diagnosis of DCMi, and were statistically interrelated ($p < 0.01$). Viral genomes were detected by polymerase chain reaction (PCR) in 40% of the EMB, with parvovirus B19 (B19V) being the leading viral genome (89%). There was no statistical significance in the comparison of PCR proof of viral genomes and the histological or immunohistological proof of intramyocardial inflammation. A cardiac amyloidosis was confirmed by histological means in 4.4% of the EMB, and a Fabry's disease was diagnosed in one male patient. These histological diagnoses led to specific treatment strategies. However, no specific therapeutic consequences were drawn by the histological proof of myocarditis, the immunohistological proof of DCMi, and the PCR proof of viral genomes.
Conclusions: Our EMB data on 463 consecutive cardiomyopathy patients with impaired LVEF confirmed the higher sensitivity of immunohistological versus histological EMB diagnostics for the detection of intramyocardial inflammation, which however are both not statistically associated with the PCR proof of viral genomes. Specific therapeutic consequences of EMB diagnostics were, however, drawn from rare histological diagnoses (cardiac amyloidosis and Fabry's disease). Immunomodulatory treatment in DCMi with or without proof of viral genomes in the clinical routine setting needs still to be established.

P1217

The dilated phenotype in left ventricular non-compactation cardiomyopathy

N Craveiro[1]; H Antunes[2]; N Marques[3]; L Reis[4]; R Santos[5]; AR Almeida[6]; O Azevedo[7]
[1]*Hospital of Santarem, Cardiology, Santarem, Portugal*; [2]*Hospital Sao Teotonio, Viseu, Portugal*; [3]*Algarve Biomedical Center, Centro hospitalar do Algarve, Department of Cardiology, Faro, Portugal*; [4]*University Hospitals of Coimbra, Coimbra, Portugal*; [5]*Hospital Espirito Santo de Evora, Evora, Portugal*; [6]*Hospital Centre do Tamega e Sousa, Penafiel, Portugal*; [7]*Hospital Guimaraes, Department of Cardiology, Guimaraes, Portugal*

On behalf of: Sunshine

Introduction: Patients with left ventricular non-compaction cardiomyopathy (LVNC) have a higher prevalence of heart failure, ventricular arrhythmias and thromboembolic events leading to increased mortality and morbidity. The clinical presentation varies widely and it's often difficult to differentiate LVNC from other severe forms of hypertrophic or dilated cardiomyopathy.
Aim: To evaluate and characterize a population of patients with LVNC comparing the dilated phenotype with the non dilated.
Methods: Multicenter retrospective study involving 12 hospital centers including 119 patients diagnosed with LVNC. Two groups were formed: Group DL (n = 66; 55,5%) with a left ventricle end-diastolic diameter (LVED) >58mm (men) or >52mm (women), and a group NDL (n = 53; 44,5%) with LVED in the normal range. We evaluated demographic, clinical, electrocardiographic, echocardiographic, cardiac magnetic resonance imaging, and follow-up data.
Results: The patients of DL group were predominantly of the male gender (74,2%, $p < 0,001$) with less family history of LVNC (p = 0,013) and presented with more symptomatic (NYHA class III/IV p = 0,005) heart failure symptoms ($p < 0,001$), mainly dyspnea ($p < 0,04$). The echocardiogram showed depressed left ventricular function as assessed by ejection fraction (EF) ($p < 0,001$) and mitral S wave velocity (septal p = 0,005; lateral $p < 0,001$) as well as more diffuse wall motion abnormalities ($p < 0,003$) and more diastolic dysfunction (Diastolic E wave velocity (p = 0,017) with elevated left atrial volume (p = 0,07)). In this population cardiac MRI was consistent with a bigger (Mass p = 0,04) LV with reduced EF ($p < 0,001$) and with the presence of late gadolinium enhancement at the LV apex (p = 0,033) when compared with the NDL group. LBBB was more frequent as assessed by ECG (p = 0,01) as well as non-sustained ventricular tachycardia assessed by Holter (p = 0,05). There were no differences related to thromboembolic events or prognostic variables between groups.
Conclusion: LVNC patients with the dilated phenotype are a particular population: more symptomatic and with worst LV function, however, prognosis seems not be different when compared to LVNC patients with non-dilated left ventricle as assessed by LVED. More studies are needed for better stratification of LVNC patients.

P1218

The role of Left Bundle Branch in patients with dilated cardiomyopathy and mildly to moderately reduced Left Ventricular Function

P Gentile[1]; A Paldino[1]; A Cannata'[1]; G Barbati[1]; F Ramani[1]; E Fabris[1]; A Aleskova[1]; D Stolfo[1]; M Zecchin[1]; M Merlo[1]; G Sinagra[1]
[1]*University Hospital Riuniti, Cardiovascular Department, Trieste, Italy*

Background: Left bundle branch block (LBBB) is a known prognostic feature in heart failure (HF) patients with a reduced ejection fraction (EF). Little is known about the prognostic role of LBBB in the setting of dilated cardiomyopathy (DCM) presenting a mildly to moderate reduced EF under optimal medical treatment.
Purpose: To assess the prognostic role of LBBB in patients with DCM without severely reduced EF after adequate period of optimal medical treatment.
Methods: We analyzed all patients with DCM consecutively enrolled in the Trieste Heart Muscle Disease Registry with available 6 (3 to 9) months follow-up evaluation under optimal medical treatment. The primary study end-point was a composite of death/heart transplantation (D/HT). CRT implantation or EF worsening below 36% during follow-up was considered as secondary end-point.
Results: The study population included 348 DCM patients (46% of initially enrolled patients) that showed mild to moderate reduced EF (35% to 49%) after 6 months

of optimal medical therapy. LBBB was present in 75 (22%) of them and it did not significantly correlate with worse long-term D/HT rates. During a mean follow-up of 177 months, 52 out of 75 (72%) patients experienced CRT implantation or LVEF worsening. At multivariate analysis moderate-severe mitral regurgitation (MR) [hazard ratio (HR) 1.228; 95% confidence interval (CI) 1.038-1.454, p= 0.017] and indexed left atrium atrial [HR 3.117; 95% CI 1.097-8.859, p= 0.01] emerged as independent predictors of secondary end-point.
Conclusions: LBBB did not emerge as a prognostic predictor in DCM patients with no-severely reduced EF after an adequate period of optimal medical therapy. However CRT could be considered in this setting of patients in case of persistence of moderate-severe MR and dilated left atrium.

P1219
Anemia and gender characteristics of DCM patients with decompensated CHF

I A Igor Tsoy[1]; TA Abdullaev[1]
[1]Specialized Cardiology Center of the Republic of Uzbekistan, heart failure , Tashkent, Uzbekistan

The aim: To detect the incidence of anemia in pts with decompensated CHF due to DCM, depending on gender characteristics
Material and Methods: We performed the analysis of 300 pts data with DCM (42.1 ± 18,6 years), admitted to the hospital due to decompensation of HF. DCM pts with different degrees of anemia (with a hemoglobin level below 13 g / dL for men and < 12 g / dL for women) were evaluated for clinical data, 6MWT, and EchoCG. The arithmetic mean and standard deviation (M ± d) were calculated. In order to identify the relationship between different indicators, the method of linear regression and correlation was used.
Results: The analysis showed that among pts with DCM, anemia of varying degrees was detected in 15.3% of pts (28 women and 18 men), with an average Hb level of 11.15 ± 1.6 g / dl. The correlation analysis revealed a reliable inverse relationship between the level of Hb and 6MWT, which was 205 ± 48.4 m (r = -0.3438; p = 0.05). The study of cardiac function showed that the mean LVEF of pts with anemia was 34.97 ± 12.7% also had an indirect correlation with the severity of anemia (r = -0.37, p = 0.03). The mean values of EDD and ESD without having a reliable association with the level of hemoglobin (r = -0.1443, p = 0.4), respectively, were 71.2 ± 15mm and 58.5 ± 11mm.The study of gender characteristics showed that anemia in women with DCM was more pronounced (hemoglobin deficiency was 15%), compared to men (11% deficiency). However representatives of the male were characterized by lower values of LVEF (30.65 ± 12.2 vs. 40.4 ± 8.9, p = 0.04), with prevalence of EDD values (77.4 ± 2.5 versus 64.53 ± 4.3, p = 0.04) and ESD (61.5 ± 13 versus 51.33 ± 7.26, p = 0.05).
Thus, anemia of varying severity was found in almost 1/5 of DCM pts. It is noted that anemia is more common in female pts, however, in men such association is accompanied by a greater LV dilatation and worse contractility

P1220
Aetiology-driven diagnoses based on endomyocardial-biopsy results in a large cohort of 3072 consecutive patients with unexplained heart failure

F Felicitas Escher[1]; DL Lassner[2]; UK Kuehl[1]; BP Pieske[1]; HP Schultheiss[2]
[1]Charite - Campus Virchow-Klinikum (CVK), Berlin, Germany; *[2]Institute of Cardiac Diagnostics and Therapy (IKDT), Berlin, Germany*

Background: The diagnosis of unexplained heart failure is challenging. The current expert consensus statement of the European Society of Cardiology (ESC) maintains that endomyocardial biopsies (EMBs) remain the gold standard for definitive diagnosis of unexplained heart muscle diseases. However, EMB is used infrequently, although histology, immunohistochemical, and molecularbiological analysis of EMB is a prerequisite to make an etiology-driven diagnosis with the aim to identify those patients in whom specific therapy would be appropriate.
Methods and results: We enrolled n = 3072 consecutive patients with unexplained heart failure (2034 men/ 788 women, mean age 51.44 ± 16.04 years) from January 2014 to March 2017, who underwent EMB. The suspected diagnosis had been made by clinicians. EMBs were send to a FDA-proved laboratory (Institute for Cardiac Diagnostic and Therapy Berlin, Germany). Analysis included histology, immunohistochemistry, molecular virology, and gene profiling.
In n = 810 patients the suspected diagnosis was acute myocarditis, in 1772 patients myocarditis or inflammatory/dilated cardiomyopathy was suspected. In n = 240 patients a storage disorder was suspected.
Based on EMB-results in 58.9% (n = 1664 patients) a specific heart muscle disease could be diagnosed.
In particular, Coxsackie-Adenovirus genomes were present in n = 44, Ebstein-Barr-Virus in n = 77, Human-herpesvirus 6 (HHV6) in n = 426 (including 21 patients with chromosomal integrated (ci) HHV6), and erythrovirus with active viral replication (positive mRNA) in n = 649 patients.
Virus-negative intramyocardial inflammation was present in n = 810 patients, including a histologically-proven active myocarditis in n = 64. Histological proof of giant cells was present in n = 20 patients. However, in n = 133 patients idiopathic giant cell myocarditis or eosinophilic myocarditis was diagnosed by analysis of myocardial gene expression profile. 116 patients showed evidence of cardiac storage disease.
Conclusions: Based on EMB-results in 58.9% of this large cohort of patients a specific heart muscle disease could be diagnosed. These aetiology-driven diagnoses implicate a specific, causal therapy.
Our data clearly show the necessity of an EMB-based diagnosis, which has a direct clinical consequence regarding a specific therapy in a notable high percentage of patients with unexplained heart failure.

P1221
The effectiveness of bromocriptine in the therapy of patients with chronic heart failure (CHF) due to peripartal cardiomyopathy

ST Mirzarakhimova[1]; TA Abdullaev[1]; I A Igor Tsoy[1]; RSH Bekbulatova[1]
[1]Specialized Cardiology Center of the Republic of Uzbekistan, heart failure , Tashkent, Uzbekistan

Aim: To study the effectiveness of additive therapy with bromocriptine on the clinical and functional indices of pts with peripartal dilated cardiomyopathy (PDCM) against the background of basic treatment following the results of 1 month observation.
Materials and methods. Included 60 pts aged from 20 to 41 (an average 28,2 ± 0,8 years). The pts was divided into grs: I included pts with clinical symptomatology of CHF, who were on therapy (n = 31). In addition to standard therapy, II gr received bromocriptine (n = 29). Clinical and functional status was assessed using ECG, Echo-CG, a 6-minute walk test (6MWT). The duration of the observation was 1 month. Initially and after 1 month of observation, the concentration of prolactin and testosterone in the blood was determined.
Results: All grs were equivalent: 6MWT-155.56 ± 62.61 and 147.12 ± 82.5 m, EDD-7.12 ± 0.1 and 6.9 ± 2.3 cm, LA -3.95 ± 3.1 and 40.1 ± 2.6 cm, EF-32 ± 9.1 and 34.9 ± 12.3, the RV - 3.82 ± 4.6 cm and 3.62 ± 5.78, prolactin concentration158.4 ± 7.4 mkg / ml and 160.4 ± 4.4 mkg / ml and testosterone 7.7 ± 1.05mIU / l and 7 , 4 ± 2.05mIU / l in the I and II grs, respectively.
During the observation period, a decrease in the level of prolactin and testosterone in the bromocriptine application gr was observed up to 76.4 ± 7.4 mkg / ml and prolactin-up to 3.7 ± 2.05 mIU / l, p < 0.05. In gr 1, the decrease in both indicators was unreliable. The functional status in the dynamics has significantly improved, however, without significant differences between the grs: CAS - 2,3 ± 1,1 and 2,4 ± 1,6 points. SMWT-247.3 ± 79.1 and 241.3 ± 83.4 meters (p> 0.05).
The parameters of intracardiac hemodynamics endured the following changes: mean LV ejection fraction (EF) increased significantly in grs 1 ± 2 and 2 grs 38 ± 6.1% and 39 ± 9.6% (? < 0.05), which was accompanied by a decrease in cardiac dilatation , moreover, more pronounced in gr 2; a decrease in the CBD to 6.9.12 ± 5.1 and 6.3 ± 5.3 cm, respectively (p < 0.05). On the right ventricle side, there was also a greater regression in gr 2, up to 3.2 ± 4.1 cm, (in gr 1, 3.4 ± 6.6, respectively (p> 0.05)).
Conclusion: The addition of bromocriptine in women with PDCM to the standard therapy of CHF, improves the clinical status and stabilizes hemodynamic parameters.

P1222
Clinical forms of arrhythmogenic right ventricular dysplasia/cardiomyopathy with high risk of sudden cardiac death and chronic heart failure: factors of progression and prognosis.

Y A Yulia Alexandrovna Lutokhina[1]; O V Blagova[1]; A V Nedostup[1]; S A Alexandrova[2]; E A Mershina[3]; A G Shestak[4]; E V Zaklyazminskaya[4]
[1]I.M. Sechenov First Moscow State Medical University, Moscow, Russian Federation; *[2]Bakoulev Center for Cardiovascular Surgery RAMS, Moscow, Russian Federation*; *[3]Roszdrav Medical Rehabilitation Center, Moscow, Russian Federation*; *[4]Russian Research Center of Surgery, Petrovsky, Moscow, Russian Federation*

Purpose: to distinguish the clinical forms of ARVD with a high risk of sudden cardiac death/ chronic heart failure (CHF) and to identify the predictors of adverse events (AE).
Methods: 50 patients (38.1 ± 14.6 y; 20 males) with ARVD according to Revised Task Force Criteria 2010 were evaluated (26 patients with definite, 13 - with borderline, 11 with possible diagnosis). Follow-up period: 13.5 [4; 34] months. All patients underwent ECG, 24h-Holter monitoring, echocardiography, blood tests for detection of anti-heart antibodies and DNA of viruses. Also were performed DNA-diagnostic

(n = 46, detected mutations were reaffirmed by Sanger sequencing), cardiac MRI (n = 44), signal-averaged ECG (n = 16), morphological study of the myocardium (endomyocardial biopsy - 2; autopsy - 2).
Results: According to the features of clinical course of ARVD, we identified 4 clinical forms of the disease. I. Latent arrhythmic form (n = 25) - frequent premature ventricular contractions and/or nonsustained ventricular tachycardia (VT) in the absence of sustained VT (SVT) and syncope. II. Manifested arrhythmic form (n = 10) - SVT /ventricular fibrillation (VF). III. ARVD with progressive chronic heart failure (CHF) as the main manifestation of the disease (n = 8). IV. Combination of ARVD with left ventricular (LV) noncompaction (n = 7). Mutations were identified in 13 patients in the following genes: PKP2, DSG2, DSP, DES, TMEM43, FLNC, SCN5A, MYH7, MYBPC3. Associated myocarditis was diagnosed in 35 (70%) patients (viral in 7). The presence of mutations and myocarditis did not significantly affected outcomes. AE (death, syncope, appropriate ICD therapy, SVT, VF) occurred in 16.7%, 100%, 62.5% and 57.1% of patients in the I, II, III and IV forms, respectively. Determinants of AE were ?HF (odds ratio (OR) 4,3 [1.3-14.8], p = 0.014), atrial fibrillation (AF, OR 11.7 [1.3-104.3], p = 0.01), tricuspid regurgitation (TR, OR 6.3 [1.6-24.4], p = 0.01), mid right ventricle diameter (RVD2) = 2.3 cm (OR 23.8 [2.7-210], p <0.001). Cardiac death was associated with LVEF <35% (OR 623 [10.7-36658.2], p <0.001), CHF, NYHA class = 3 (OR 623 [10.7-36658.2], p = 0.001), severe TR (OR 67.7 [3-1536.7], p = 0.002), complete right bundle branch block (RBBB, OR 26.7 [1.8-387.2], p = 0.028). Appropriate ICD therapy was predicted by syncope (OR 45 [1.5-1364], p = 0.01), male sex (OR 24.2 [0.93-632], p = 0.027), low QRS voltage (OR 24.2 [0.93-632], p = 0.027), CHF (OR 21 [0.8-566.4], p = 0.045), TR (OR 21 [0.8-566.4], p = 0.045), RVD2 = 2.85 cm (OR 33 [1.06-1028.1], p = 0.024). Development of CHF was associated with low QRS voltage (OR 6.5 [1.6-27], p = 0.009), AF (OR 16.9 [1.9-153.3], p = 0.004), 1-st degree AV block (OR 7.8 [1.3-48.5], p = 0.027) and disease duration = 5,5 years (OR 10.6 [2.6-43.7], p = 0.001).
Conclusions: the highest risk of AE was observed in patients with manifested arrhythmic form and with progressive CHF. AE in ARVD patients were associated with RV enlargement, the development of CHF, complete RBBB block, AF and low QRS voltage.

P1223
Clinical profile and prognosis of senile cardiac amyloidosis

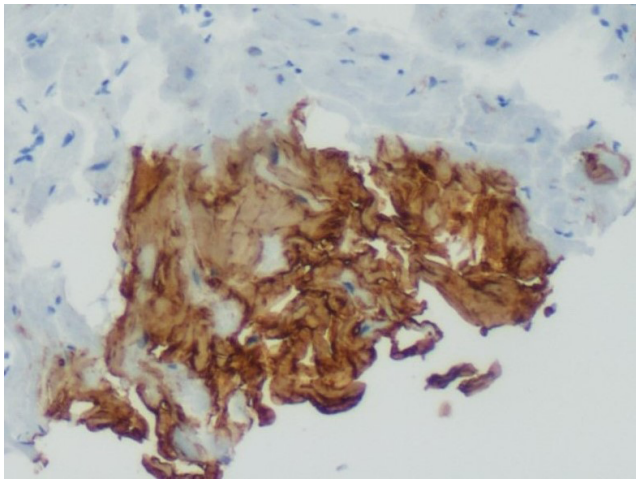
M Margarida Oliveira[1]; O Azevedo[1]; B Faria[1]; P Von Hafe[1]; G Dias[1]; M Lourenco[1]; A Lourenco[1]
[1]*Alto Ave Hospital Center, Guimaraes, Portugal*

Introduction: Cardiac amyloidosis has different clinical profile, evolution and prognosis depending on the type of amyloidosis. Senile amyloidosis is frequently underdiagnosed mainly because it affects people in advanced age and it has limited systemic involvement. The development of new therapeutic option for amyloidosis patients with wild type transtirretin deposition makes it very important to improve our knowledge about the natural history of this disease.
Aim: Describe clinical profile and prognosis of patients with senile cardiac amyloidosis.
Methods: We included all patients with clinical diagnosis of senile cardiac amyloidosis and performed a retrospective analysis of clinical, scintigraphy, electro and echocardiographic variables.
Results: We included 23 patients (18 men and 5 women). Age at diagnosis was 83 years old (SD = 3,93). 53% of patients were referred from general doctors because of left ventricular hypertrophy finding in transthoracic eco and the rest of the patients were referred after being admitted at cardiology award for decompensated heart failure (21,7%), rapid atrial fibrillation (21,7%) and complete atrioventricular block (4,3%). At the time of diagnosis, 17,4% of patients were asymptomatic, and in the symptomatic group, 73,9% of patients complain about effort dyspnoea. 26,1% have atrial fibrillation at diagnosis and 34,8% had previous diagnosis of tunnel carpal syndrome. 48,8% of patients had depressed left ventricular ejection fraction, from mild to severely depressed. Every patient had some grade of diastolic dysfunction, mostly (56%) grade II. Left ventricular mass was 314,49g (SD = 69,43) e de 178,60g/m2 (SD = 41,88). We performed cardiac scintigraphy Tc99m-DPD suggesting transthyretin amyloidosis in every patient.
Mean follow-up was 34,5 months (SD = 32,95). Incidence of complication in follow-up period was 74%: 21,7% developed atrial fibrillation, 65,2% heart failure, 21,7% needed a pacemaker implantation and 4,3% had a stroke. Number of admissions because of decompensated heart failure was 1,26 (DP = 2,00) with an annual rate of 0,8 admissions/year (DP= 1,35). Mortality was 34,8% with an annual rate of 11,9% mainly due to infection (85.7%) and occurred about 14 months (DP = 9,99) after diagnosis.
Conclusion: Cardiac amyloidosis has high mortality and complication rate. In senile amyloidosis, due to advanced age and lack of therapeutic options, mortality is reported between 70% in older studies and 40% in more recent ones. In our study mortality was a little lower - 35%. It should also be noticed that the most frequent cause of dead was infection, which was expected regarding age, comorbidity and fragility of this patients.

P1224
TTR-amyloidosis. Not so rare as we thought?

R Renata Aiglova[1]; M Taborsky[1]; M Lazarova[1]; L Pavlu[1]; P Flodrova[2]; P Flodr[2]
[1]*University Hospital Olomouc, Department of Internal Medicine I - Cardiology, Olomouc, Czech Republic*; [2]*Palacky University, Faculty of Medicine and Dentistry, Department of Clinical and Molecular Pathology, Olomouc, Czech Republic*

Introduction: Amyloidosis is a rare systemic disease caused by build-up of amyloid deposits within the tissues. For TTR amyloidosis are typical deposits of wild-type transthyretin. This disease is described in people aged over 70 years, more often in men. Restrictive cardiomyopathy and carpal tunnel syndrome are included to the clinical picture of TTR-amyloidosis.
Purpose: To improve, that cardiac TTR-amyloidosis is in our population more common, than we thought. To assess the significance of endomyocardial biopsy in differential diagnosis of amyloidosis.



TTR-amyloidosis
Methods: Patients with recently diagnosed restrictive filling failure, who were examined in years 2016-2017 in our University Hospital. Within the differential diagnosis endomyocardial biopsy and cardiac MRI are usually performed. All patients with confirmed diagnosis of TTR-amyloidosis are referred to haematologist.
Results: For suspicion of TTR-amyloidosis were in years 2016-2017 in our University Hospital examined 10 patients. All patients underwent endomyocardial biopsy. Cardiac MRI couldn't be performed by 1 patient with MRI-incompatible pacemaker. TTR-amyloidosis (Fig. 1) was immunohistochemically confirmed in 5 patients - 3 men, 2 women. Mean age of our patients was 79,6 years. AL-amyloidosis was immunohistochemically confirmed in 2 patients, both were men, mean age 55,4 years.
Conclusion: TTR-amyloidosis is described as rare disease. It is a relatively common, but very poorly diagnosed disease. Golden standard in differential diagnosis is endomyocardial biopsy with following immunohistochemically examination. In these patients is very important to provide multidisciplinary care with cooperation of cardiologist and haematologist.

P1225
Added value of genetics on top of clinics in predicting treatability of dilated cardiomyopathy patients

J A J Job Antonius Jozef Verdonschot[1]; MR Hazebroek[1]; S Sanders - Van Wijk[1]; JJ Merken[1]; YA Adriaansen[2]; A Van Den Wijngaard[2]; IPC Krapels[2]; HP Brunner-La Rocca[1]; HG Brunner-La Rocca[2]; SRB Heymans[1]
[1]*Cardiovascular Research Institute Maastricht (CARIM), Cardiology, Maastricht, Netherlands*; [2]*Maastricht University Medical Centre (MUMC), Clinical Genetics, Maastricht, Netherlands*

Background/Introduction: Predicting improvement of left ventricular (LV) function (reverse remodeling (LVRR)) in patients with dilated cardiomyopathy (DCM) remains

difficult. The added value of gene mutations on top of clinical parameters for predicting LVRR remains largely unknown.
Purpose: To determine if adding mutation status to clinical parameters improves prediction of LVRR in DCM patients.
Methods. DCM patients (n = 346; mean ejection fraction (LVEF) 30%) underwent genotyping for 47 DCM-associated genes on top of extensive phenotyping. LVRR was defined as improvement of LVEF >50% or = 10% increase, with cardiac dimensions (LV end-diastolic diameter) £33mm/m2 or = 10% decrease. After testing the predictive value of clinical variables for LVRR in univariable and multivariable logistic regression, the added value of gene mutations was tested for discrimination, calibration, and reclassification.
Results: LVRR occurred in 180 (52%) patients after a median follow-up of 12 months upon conventional treatment. LVEF, familial DCM, female gender, AV-block and treatment with beta-blockers or ACE-I/ARB, were independent clinical predictors of LVRR. Genetic mutations –with exclusion of TTN mutation- were strongly associated with a lower rate of LVRR (OR: 0.22 [0.10 to 0.47]; p < 0.001). Addition of specific gene mutations such as TTN and miscellaneous gene mutations (eg. PLN, RBM20) to the clinical prediction model was significantly associated to LVRR (OR: 3.06 [1.27-6.62]; p = 0.01 and OR: 0.1 [0.01-0.85]; p = 0.04 respectively). Adding mutation status significantly improved calibration and reclassification of the clinical model predicting LVRR (IDI 8.2% and NRI 48%, both p < 0.001), with a trend for improved discrimination (C-statistic: 0.69 versus 0.75, p = 0.059).
Conclusions: Addition of mutation status to clinical parameters in DCM improves patient stratification in terms of LVRR.

Pulmonary Circulation, Pulmonary Embolism, Right Heart Failure - Clinical

P1227
Functional class and prognosis in advanced pulmonary arterial hypertension

A Lescano[1]; A Ferro[1]; E Barimboim[1]; ML Coronel[1]; D Garcia Brasca[1]; C Huerta[1]; C Stepffer[1]; G Svetliza[1]; L Lobo Marquez[1]; C Manfredi[1]; M Villar[1]; N Naval[1]; M Diez[1]; D Echazarreta[1]; ER Perna[1]
[1]Finochietto Clinic, Buenos Aires, Argentina

Introduction: Pulmonary arterial hypertension (PAH) is a multifactorial disease associated with high morbidity and mortality. However, the diagnosis and therapeutics strategies used in most of the Argentinean regions are poorly known. The advanced functional class (FC) is an indicator of poor prognosis and one of the therapeutic goals.
Aims: 1-To determine the impact of advanced FC in patients with PAH on established markers of poor
prognosis, such as clinical, biomarker, hemodynamic, and echocardiographic parameter 2-To compare treatment strategies between an advanced and non advanced FC
Method: Between July 2014 and May 2015, 322 patients with confirmed PAH were prospectively included in a multicenter, collaborative, observational registry by 62 investigators from 22 provinces in Argentina. Inclusion criteria were as follows: 1-patients over three months of age; 2- mean pulmonary arterial pressure (mPAP) at rest = 25 mmHg by right heart catheterization (RHC) and 3-clinical stability in the absence of hospitalization in last month. WHO FC III or IV at diagnosis was defined as advanced (AFC) whereas WHO FC I or II were considered as non advanced (NAFC)
Results: Mean age was 47 years (SD 17) and 77% were female. According with the Nice classification, the distribution was: idiopathic 51.6%, inherited 1,6%, drugs 2.4%, connective tissue disease 15.3%, portal hypertension 1.6% and congenital heart disease 27.4%. WHO FC at initial diagnosis was: I: 3%; II: 27%; III: 43% and IV: 22% and during followup was: I: 19%, II 54%, III 22% and IV 6% (p < 0.001). AFC at initial diagnosis was 65% and during follow up 28% (p < 0.001). Clinical manifestations in AFC compared with NAFC was: syncope 11 vs 13% (NS); heart failure 55 vs 38% (p < 0.001); BNP 552 vs 158 pg/ml (0.02), NtproBNP 1918 vs 668 pg/ml (0.01), TAPSE 17 vs 18.8 mm (0.01), pericardial effusion 18 vs 10% (p = 0.020); 6MWT 367 vs 373 (NS); CI 2.6 vs 2.9 (0.03); RAP 11 vs 12 mm Hg (NS);. PAH targeted drugs in AFC was = None in 11%, monotherapy in 29.7% and combined therapy in 67%.
Conclusion: In our registry of PAH, we observed a high percentage of patients with AFC (65 %) at initial diagnosis and a significant decrease during followup (28%). Advanced FC at initial diagnosis was significantly associated with other variables of poor prognosis and combined therapy in 67%. These findings emphasize the need for strategies for early detection and therapy.

P1228
The prognostic role of right ventricular dysfunction decreases with an increase in pulmonary hypertension

J Julija Bugaite[1]; D Gabartaite[1]; E Paleviciute[2]; K Cerlinskaite[2]; R Norvilaite[3]; D Verikas[3]; G Ziubryte[3]; G Balciunaite[2]; A Krivickiene[3]; J Motiejunaite[3]; D Zaliaduonyte-Peksiene[3]; D Zakarkaite[2]; A Mebazaa[4]; A Kavoliuniene[3]; J Celutkiene[2]
[1]Vilnius University, Vilnius, Lithuania; *[2]Vilnius University, Clinic of Cardiac and Vascular diseases, Center of Cardiology and Angiology, Vilnius, Lithuania*; *[3]Lithuanian University of Health Sciences, Kaunas, Lithuania*; *[4]University Paris Diderot , U942 Inserm, Hospital Lariboisiére, Paris, France*

On behalf of: GREAT network
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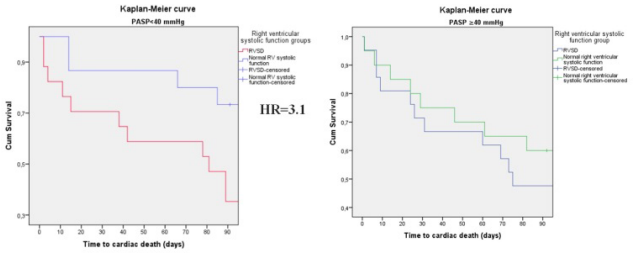
Introduction: Right ventricular dysfunction (RVD) alone or together with pulmonary hypertension (PH) is associated with severity of symptoms and poor prognosis.
Objective: To evaluate the prognostic significance of right ventricular function assessed by echocardiography at follow up of 3 months and 1 year for rehospitalizations (RH) and mortality in patients with acute dyspnea depending on the level of PH.
Design and Methods: 1482 acutely dyspneic patients were prospectively enrolled in the observational cohort study in two university hospitals. Echocardiography was performed during the first 48 hours after admission. The RVD was defined by reduced FAC < 35%, TAPSE < 1.7 cm and RV S' < 9.5 cm/s. Patients were distributed in 2 groups - PASP < 40 (no and mild PH) and = 40 mmHg (moderate and severe PH). Hazard ratio was adjusted to gender, age and left ventricular ejection fraction.
Results: Of 482 (32.5%) examined patients (mean age 68.6 ± 12.9 years) 193 (40.0%) were female. Mean PASP was 46.54 ± 16.19 mmHg. Right ventricular

P1228 Table.1

	PASP <40mmHg	PASP≥40mmHg		
Outcomes	Hazard ratio	Confidence interval	Hazard ratio	Confidence interval
Cardiac deaths in 3-months	3.19*	1.01;10.04	1.41	0.57;3.5
Cardiac deaths in 3 months (adjusted)	4.1*	1.02;16.45	1.14	0.42;3.12
Deaths due to all causes in 3-months	1.4	0.62;3.2	1.51	0.72;3.21
Cardiac RH in 3-months	1.15	0.63;2.09	1.32	0.63;2.77
RH due to all causes in 3-months	1.35	0.76;2.41	1.05	0.58;1.9
RH due to all causes in 1-year	1.94*	1.1;3.41	1.45	0.79;2.65
RH due to all causes in 1-year (adjusted)	1.97*	1.03;3.78	1.47	0.77;2.81
Cardiac deaths in 1-year	1.91	0.88;4.33	1.07	0.55;2.01
Deaths due to all causes in 1-year	1.26	0.68;2.34	1.14	0.66;1.99
Deaths and RH due to all causes in 3-months	1.13	0.73;1.74	1.1	0.72;1.18
Deaths and RH due to cardiac causes in 3-months	1.09	0.66;1.81	1.02	0.65;1.67
Deaths and RH due to all causes in 1-year (adjusted)	1.51*	1.02;2.25	1.01	0.68;1.49
Deaths and RH due to cardiac causes in 1-year	0.96	0.64;1.45	1.07	0.71;1.61

*p value < 0.05

dysfunction was found in 188 (39%) patients, almost two thirds of them (n = 106, 60.6%) had PASP = 40 mmHg. RVD prognostic value was significant only in no or mild PH group (Table 1).
Conclusion: Right ventricular dysfunction is significantly associated with short- and long-term outcomes in acute dyspnea patients with no or mild pulmonary hypertension, however, loses its prognostic role in case of moderate or severe pulmonary hypertension.



Kaplan-Meier survival curves

P1229

Severe pulmonary hypertension during pregnancy: a specialist center experience

E Karelkina[1]; O Irtyuga[1]; Y Kokonina[2]; O Li[2]; A Yakubov[3]; V Mazurok[3]; I Zazerskaya[2]; A Bautin[3]; O Moiseeva[1]
[1]Almazov National Medical Research Centre, Department of Noncoronary Diseases, Saint Petersburg, Russian Federation; *[2]Almazov National Medical Research Centre, Perinatal Centre, Saint Petersburg, Russian Federation*; *[3]Almazov National Medical Research Centre, Department of Anesthesiology, Saint Petersburg, Russian Federation*

Background: Pulmonary hypertension (PH) in pregnancy is associated with a high mortality rates (30-50%) with most of the deaths occurring in the 3rd trimester and within the first 10 postdelivery days. Despite risks, patients may actively plan pregnancy. Patients may also present whilst pregnant with previously undiagnosed PH.
Methods: We report the outcomes of 18 pregnancy in women with PH associated with congenital heart disease at a specialist center between 2010 and 2017. The criteria for inclusion were the presence of CHD and pulmonary artery systolic pressure more than 60 mm Hg. Two women were after cardiac surgery. In 12 of 18 cases (66,7%) patients developed Eisenmenger syndrome.
Results: 18 pregnancies in 18 women resulted in 16 live births, 1 miscarriages and 1 terminations (range 90 - 134 days gestation). All patients were supervised by a multi-professional team. Sixteen deliveries were by Caesarean section with 1 vaginal delivery and planned between 28 to 34 weeks. Patients underwent epidural or combined spinal/epidural regional anaesthesia and were monitored peri-delivery in an intensive care environment with arterial and central venous access. In all patients after delivery had decompensation of the state with the increase of pulmonary hypertension, progression of right ventricular failure, an increase in shunting from right to left. In 4 cases, a transfer to mechanical ventilation was required, intensive therapy included a combined use of vasodilators, the use of inotropes, the prevention of thromboembolic complications. Of 18 pregnancies, 3 women died within 6 months of delivery (9, 14 and 15 days post-delivery) and none during pregnancy (16,7%). Mortality in the subgroup of Eisenmenger syndrome was 25% (3/12). 15 (83,3%) children were discharged from the hospital in a satisfactory condition.
Conclusion: Mortality of PH in pregnancy in a setting of experienced and coordinated care is less than historical series but remains significant. Counselling women with PH of these risks remains an essential part of disease management. In the event of pregnancy, patients should be managed by a multiprofessional team.

P1230

Potential role of Interleukin-18 in Pulmonary Arterial Hypertension in Systemic Sclerosis Patients

Y Yoshiyuki Orihara[1]; M Asakura[1]; A Eguchi[1]; T Ando[1]; Y Okuhara[1]; M Ishihara[1]; T Masuyama[1]
[1]Hyogo College of Medicine, Cardiovascular Division, Nishinomiya, Japan

Background: Systemic sclerosis (SSc) is a clinically heterogeneous disorder affecting the connective tissue of the skin, the wall of blood vessels, and internal organs such as the gastrointestinal tract, lungs, heart, and kidneys. SSc can develop pulmonary arterial hypertension (PAH) caused by fibrosis of pulmonary arteries. Three-year survival for SSc patients with PAH has been estimated to be 56% compared with 94% in those without PAH. Early detection of PAH in SSc patients is important for improvement in prognosis. However, there exists no useful biomarker for detecting PAH in SSc patients. Previous study reported the association of endothelin-1 (ET-1) with the development of PAH. Moreover, we revealed that the disruption of murine interleukin-18 (IL-18) gene suppressed PAH induced by hypoxia. These results suggest that ET-1 and IL-18 are potential biomarkers for early detection of PAH in SSc patients.
Purpose: The purpose of this study was to examine roles of IL-18 and ET-1 for PAH in SSc patients.
Methods: Twenty SSc patients who visited our hospital between January 2014 and June 2016 and presented tricuspid regurgitation jet velocity = 2.5 m/s were enrolled in this single-center retrospective observational study. We performed right heart catheterizations (RHC) and measured the serum levels of IL-18 and ET-1 as well as periostin as a marker of fibrosis. One patient who had WHO-FC IV and one patient with >20 mmHg of pulmonary artery wedge pressure were excluded. Finally 18 patients were assessed in this study.
Results: Mean age was 65.1 years old and 16 patients were female. Echocardiographical data showed that mean left ventricular ejection fraction was 69.9 % and mean tricupcid regurgitation (TR) velocity was 2.81 m/s. RHC showed average mean pulmonary artery pressure (PAP) and pulmonary vascular resistance index (PVRI) were 24.0 mmHg and 4.6 wood, respectively. Mean serum levels of IL-18, ET-1 and periostin were 288.4 pg/ml, 2.27 pg/ml, and 864 pg/ml, respectively. TR velocity was correlated with neither PAP nor PVRI (mPAP; R = 0.343, p = 0.178, PVRI; R = 0.327, p = 0.200). Whereas, both of IL-18 and ET-1 levels showed significant correlations with PVRI (IL-18; R = 0.674, p = 0.002, ET-1; R = 0.639, p = 0.004). ROC analysis to predict PVRI = 3 wood units showed that area under the curve (AUC) of IL-18 was higher than AUC of ET-1. (IL-18; 0.802, ET-1; 0.778). Moreover, we found a significant association between IL-18 and periostin (R = 0.498, p = 0.042). It is a possible mechanism that the elevation of IL-18 may induce expression of periostin resulting in the fibrosis of pulmonary arteries in SSc patients.
Conclusion: We revealed that both serum levels of IL-18 and ET-1 were significantly associated with the elevation of PVRI in SSc patients. IL-18 and ET-1 are potential biomarkers for early detection of PAH in SSc patients.

P1231

First collaborative registry of pulmonary hypertension in argentina (RECOPILAR). Epidemiology, clinical profile and management of pulmonary arterial hypertension

ML Maria Lorena Coronel[1]; ER Perna[1]; D Echazarreta[2]; G Tuhay[3]; ML Talavera[4]; J Caneva[3]; L Lema[5]; JP Cimbaro Canella[1]; V Saurit[5]; F Daghero[6]; S Deleo[7]; G Cursack[8]; A Echazarreta[2]; G Bargazzi[9]; J Bono[6]
[1]J.F. Cabral Cardiology Institute, Corrientes, Argentina; *[2]Hospital San Juan de Dios, La Plata, Argentina*; *[3]Favaloro Foundation University Hospital, Buenos Aires, Argentina*; *[4]Cardiovascular Institute of Buenos Aires (ICBA), Buenos Aires, Argentina*; *[5]Model Institute of Cardiology, Cordoba, Argentina*; *[6]Sanatorium Allende, Cordoba, Argentina*; *[7]Hospital Interzonal General de Agudos, La Plata, Argentina*; *[8]Sanatorio Esperanza, Esperanza, Argentina*; *[9]Spanish Hospital of Mendoza, Mendoza, Argentina*

On behalf of: RECOPILAR

Pulmonary arterial hypertension (PAH) has been poorly characterized in Latin America. The aim of this report was to describe the clinical-epidemiological profile and management of PAH in Argentina.
Method: From Jul-14 to Oct-16, 399 incident and prevalent patients with PAH were prospectively included by 62 investigators from 22 provinces of Argentina in a collaborative registry involving 5 societies of different specialties: cardiologist, rheumatologist, pulmonologist and pediatricians. Patients must fullfill all the following inclusion criteria: 1-Age over three months; 2 - mean pulmonary arterial pressure (mPAP) at rest = 25 mmHg by right heart catheterization (RHC) and 3 - clinical stability in the absence of hospitalization in last month.
Results: Mean age was 47 ± 18 years and 79% were women. They were classified as idiopathic 160 (40.1%), heritable 5 (1,3%), drugs 2 (0.5%), connective tissue disease 95 (23.8%); portal hypertension 16 (4%); HIV 20 (5%) and congenital heart disease 101 (25.3%) and 49.4% were incident cases. RHC showed systolic/diastolic/mean PAP: 82 ± 25/36 ± 15/52 ± 17 mmHg; with pulmonary vascular resistance 9.9 ± 6.1 WU, right atrial pressure 12 ± 11 mmHg and cardiac index 2.8 ± 1 l/min/m2. Pulmonary vasorreactivity test was performed in 305 patients (76.4%) and was positive in 12.7%. 21). Baseline WHO functional class was I: 4.3%; II: 30.7%; III: 48.4% and IV: 16.5%; 27% have been previously hospitalized, half of them due to heart failure. Non specific treatment included diuretics 47%; aldosterone antagonists 43%; digoxin 18%; anticoagulants 37%, calcium channel blockers 11%; and specific therapy included prostanoids 14.3% , half of them subcutaneous; phosphodiesterase-5 inhibitors 70.7%, endothelin receptor antagonists 54.4%. Prescription of none, one

o combined specific drugs was used in 19.5, 30.1 and 50.4%. The follow up was obtained in 65% of cases, and the survival at 1, 2 and 3 years was 92, 82 and 74%.
Conclusion: The contemporary population with PAH in Argentina is comparable to other series: late diagnosis and severe profile. There was a high use of specific drugs, with combined therapy in two thirds, according with recommendation of guidelines. These results demonstrated the crucial role of specialist in the management of PAH in developing countries.

P1232
In patients with Pulmonary Hypertension, does the podometria provide anything?

V Gregorietti[1]; MF Acosta[1]; R Coronel[1]; M Muzzio[1]; PA Fernnadez[2]
[1]Sanatorio Sagrado Corazon, Cardiologia, Buenos Aires, Argentina; *[2]Hospital El Cruce, Trasplante Cardiaco, Hipertension Pulmonar, Florencio Varela, Buenos Aires, Argentina*

Objective: To assess the relationship of the steps taken during the 6-minute walk test with other parameters obtained from it and clinical parameters of prognosis and evolution.
Material and Methods: We prospectively analyzed 318 walk test studies of 6 minutes, which were performed consecutively to 318 patients
carriers of pulmonary hypertension of various etiologies according to the NICE 2013 classification.
From March / 2016 to December / 2017.
They were used:
• Pulse Saturometer, for oximetry and heart rate control,
• Sphygmomanometer for baseline blood pressure control and at the end of the study.
• Digital pedometer
• Borg scale.
• Clinical history of the patient
• Routine Laboratory, with dosing of ProBNP.
The statistical analysis was carried out through the Epi.info program
Results: Data were obtained from 318 studies in 318 patients with pulmonary hypertension, 56% of the population corresponds to the female sex.
The average age of the population is 51 ± 17 years.
The average distance traveled was 340 meters (range = 510-40), the number of steps was 526 (range = 1150-47)
The mean BNP pro levels were 270 pg / ml (14-1110).
The proBNP correlation was analyzed with the number of steps and the distance traveled, Functional Class at the time of the study, and statistical significance was observed between the proBNP levels and the number of steps walked (p: 0.001) and the functional Class at the time of the study (p: 0.003).
Conclusions: The number of steps taken in the 6-minute walk test is correlated with clinical and laboratory parameters, which make the prognosis of patients with pulmonary hypertension.
The control of the number of steps with a simple pedometer during the performance of the walk test of 6 minutes adds a useful data for the evaluation and monitoring of patients with pulmonary hypertension.

Cardiovascular Surgery - Other

P1233
Idarucizumab for urgent dabigatran reversal at the heart transplantation surgery. Multicenter experience from Spain

M G Maria G Crespo-Leiro[1]; F Carrasco-Avalos[2]; S Mirabet-Perez[3]; T Blasco-Peiro[4]; D Rangel-Sousa[5]; F Gonzalez-Vilchez[6]; E Barge-Caballero[1]; A Lopez-Granados[2]; E Roig[3]; A Portoles-Ocampo[4]; A Grande-Trillo[5]; JA Vazquez-De-Prada[6]; V Brossa[3]; JM Arizon-Del-Prado[2]
[1]Hospital Universitario A Coruña, La Coruña, Spain; *[2]University Hospital Reina Sofia, Cordoba, Spain*; *[3]Hospital de la Santa Creu i Sant Pau, Barcelona, Spain*; *[4]University Hospital Miguel Servet, Zaragoza, Spain*; *[5]University Hospital of Virgen del Rocio, Seville, Spain*; *[6]University Hospital Marques de Valdecilla, Santander, Spain*

Anticoagulation in heart transplant (HT) recipients increases the risk of serious hemorrhagic complications during the perioperative period therefore urgent anticoagulation reversion is a challenge. Dabigatran is a direct thrombin inhibitor incresingly used for anticoagulation in patients with heart failure and atrial fibrilation. Idarucizumab is the first targeted reversal agent available and is specific for dabigatran. In emergency situations like threatening bleeding or urgent surgery, idarucizumab promptly, durably, and safely reversed the anticoagulant effect of dabigatran. The usefulness of idarucizumab for dabigatran reversal at the HT surgery is not well known.
Aim: To present preliminary experience of idarucizumab use for dabigatran reveral in patients undergoing HT.
Methods: Observational multicenter study of using idarucizumab for urgent dabigatran reversal at the HT surgery in 6 HT Spanish centres from August 2016 to November 2017. The following variables were collected to assess effectiveness and safety: recipient's characteristics, Idarucizumab dose, need for redo in the immediate postoperative period to control bleeding, blood products transfusions, intensive care unit (ICU) and total hospitalization stay and survival.
Results: 11 patients from 6 centers, mean age 54.6 years, 7 males (63.6%) were treated with idarucizumab for dabigatran reversal at HT surgery. Etiology of heart disease: 7 non-ischemic dilated cardiomyopathy (63.6%), 3 hypertrophic cardiomyopathy (27.2%) and 1 other (9.1%). None of the cases had a prior sternotomy. Idarucizumab dose was 5 mg (2,5 mg x 2) in all cases and none of the patients needed rescue doses for bleeding control. Redo for bleeding control was needed in 3 (27.2%) patients. 7 (63.6%) patients required blood products transfusions: plasma 4 patients (mean 1312,5 cc), packed red blood cells 6 patients (mean 4.5 units) and platelets 4 patients (mean 2.25 platelets pools. Mean ICU stay was 10.5 days and mean hospital stay was 33.9 days. There was only one intrahospital death at 47th day after HT due to multiorgan failure and infectious complications but not considered related to bleeding.
Conclusions: This preliminary experience with the use of idarucizumab (5 mg) for urgent reversion of dabigatran at HT surgery is encouraging. Although one third of patients required early redo due to bleeding complications and 2/3 transfusions, no perioperative early mortality was appreciated. These results may support the use of dabigatran as an alternative to vitamin K antagonists in HT candidates that require anticoagulation. More studies are needed to corroborate these observations.

P1234
The influence of LVAD on mitral regurgitation and pulmonary system

M Cottini[1]; AC Aldo Cannata[1]; DB Dario Brenna[1]; AC Alessandro Costetti[1]; ML Marco Lanfranconi[1]; MPG Maria Pia Gagliardone[1]; MF Maria Frigerio[1]; CFR Claudio Francesco Russo[1]
[1]Niguarda Ca' Granda Hospital, Cardiovascular Department, Milan, Italy

Purpose: The Left Ventricle Assist Devices (LVADs) become more and more standard therapeutic choice for patients with advance heart failure. Most of the LVAD patients have mitral regurgitation (MR) due to functional mechanism: the tethering of mitral valve leaflets secondary to left ventricle (LV) dilatation and geometry/shape LV modifications. We investigated the perioperative and postoperative hemodynamic and echocardiographic parameters of LVAD patients to monitor the MR, pulmonary system parameters and the device function.
Methods: We retrospectively reviewed 85 patients undergoing continuous-flow LVAD implantation between 2007 and 2017, 62% Thoratec HMII (n = 54) and 38% Heartware (n = 31). 50.5% of them were affected by ischemic cardiomyopathy (ICM) and 49.5% by idiopathic dilated cardiomyopathy (IDCM). All included patients had done preoperative transthoracic echo (TTE), were undergone only to LVAD surgery. Study follow-up ended at 1 year after implantation.
Results: MR was at least moderate to severe in 54.1% of patients before LVAD implantation, 54.7% in ICM patients and 53.5% in IDCM patients. The statistical analysis revealed the IDCM patients had significantly preoperative larger LVEDD (74.3 ± 9.2 mm vs 66.4 ± 8.6 mm, p 0.0001) and lower sPAP (49.115.6 vs 61.6 ± 17.5 mmHg, p 0.002) as compared to ICM patients. After LVAD implantation, the prevalence of MR was 8.3% at 1 year (significantly lower than preoperative general value, 54.1%, p 0.0001). Among the ICM patients the MR and LVEDD decreased more than among IDCM patients (MR prevalence 4.7% vs 11.9%, p 0.19; LVEDD 61 vs 70.6 mm, p 0.18). In both groups the sPAP and the mean PAP decreased postoperatively (p 0.0001). The sPAP were lower in HMII than in HW patients (mean sPAP 31.0 vs 38.2 mmHg respectively, p 0.01). Postoperatively the devices performed well without significant complications during the first year.
Conclusion: According to our experience, the patient with moderate to severe MR after the only LVAD implantation had a significant reduction of MR (prevalence from 54.1 to 8.3% at 1 year, p 0.0001) with an improvement of hemodynamic and great pulmonary parameters due to a mechanism of ventricular reverse remodeling supported by unloading of LV due to LVAD. The decrease of MR degree was greater in ICM than ICDM group.

P1235
Reversal of anticoagulation with idarucizumab. Initial experience in heart and heart-and-lung transplantation

R Lopez Vilella[1]; J Sanz Sanchez[1]; I Sanchez Lazaro[1]; E Marques-Sule[2]; J Rueda Soriano[3]; L Almenar Bonet[1]
[1]Hospital Universitario y Politécnico La Fe, Heart Failure and Transplant Unit. Cardiology Department, Valencia, Spain; *[2]University of Valencia, Physiotherapy Department. , Valencia, Spain*; *[3]Hospital Universitario y Politécnico La Fe, Adult Congenital Heart Disease Unit. Cardiology Department, Valencia, Spain*

P1235	Case 1	Case 2	Case 3	Case 4
Gender	Male	Male	Male	Male
Age (years)	33	51	49	51
Basal cardiopathy	ccTGA + IVC (Eisenmenger syndrome)	HCM in dilated-phase	IDC	Laminopathy
Combined transplantation	Yes, heart and lung transplantation	No	No	No
Dabigatran dose	75 mg/12 hours (low weight)	150 mg/12 hours	150 mg/12 hours	150 mg/12 hours
VHA2DS2VASc-Score	1	2	4	2
HASBLED-Score	2	2	3	2

ccTGA: Congenitally corrected transposition of great arteries; HCM: Hypertrophic cardiomyopathy; IDC: Idiopathic dilated cardiomyopathy; IVC: intraventricular communication; CHA2DS2-VASc Score for Atrial Fibrillation Stroke RisK: congestive heart failure, hypertension, age, diabetes, stroke, vascular disease history and sex; HASBLED Score for Major Bleeding Risk: hypertension uncontrolled, renal disease, liver disease, stroke history, prior major bleeding or predisposition to bleeding, labile INR, age, medication usage predisposing to bleeding, alcohol use.

Introduction and purpose: Idarucizumab is a recently approved drug to reverse the anticoagulant effect of dabigatran, although the clinical experience in heart transplantation (HT) is scarce. We present a series of cases of patients undergoing HT and heart and lung transplantation (HLT) in whom anticoagulation with idarucizumab was reversed.
Methods: All patients undergoing HT or HLT and anticoagulated with dabigatran, in which anticoagulation with idarucizumab was reversed for the transplant, were selected from January 2016 to December 2017.
Results : 4 patients underwent elective HT (table 1). Anticoagulation was indicated because of atrial fibrillation or atrial flutter. Idarucizumab was administered in a dose of 5 mg, in two doses of 2.5 mg each. The drug was administered when the donor was confirmed to be valid, just before going to the operating room. No intraoperative or postoperative hemorrhagic complications were reported.
Conclusions: : This is the largest series of cases in Spain about reversal of anticoagulation with idarucizumab in HT. Our series of cases demonstrates a rapid and safe reversal of the anticoagulant effect in situations requiring a rapid reversal of the effect of dabigatran.

P1236
Preoperative levosimendan improves outcomes of coronary artery bypass grafting in patients with poor left ventricular function: cardiologist's opinion

E Vlasova[1]; V Gazizova[1]; E Dzybinskaya[1]; G Kheymets[1]; R Akchurin[1]
[1]National medical research center of cardiology of the Ministry of healthcare of the Russian Federati, Cardiac surgery, Moscow, Russian Federation

Background: We suggested that in patients with coronary heart disease (CHD) and low left ventricle ejection fraction (LVEF) scheduled for coronary artery bypass grafting (CABG), levosimendan (L) when administered preoperatively would effect the outcomes of operation and early postoperative period.
Purpose: to determine the benefit of preoperative levosimendan administration in patients with low LVEF underwent CABG.
Methods: The design of investigation was non-randomised study with retrospective control; 46 patients with multivessel coronary disease and LVEF = 35%, subjected to on-pump CABG in 2014-2017 were included. All pts received standart therapy for congestive heart failure (ACE-inhibitor, ß-blocker, spironolactone, diuretic, statin, aspirin) and were not taken to surgery until maximal possible compensation. 17 pts (mean age 64 ± 5 years, 82.7% male), received L, administered by a cardiologist, as infusion of 12.5mg for 24 h, without a bolus, 2 days before surgery (group L). 29 pts (mean age 60 ± 6 years, 82.3% male) made up the retrospective control group (group C).
Results: One patient in the group C but none in the group L died within 30 days of surgery. Need for inotropic support in preperfusion period was 12% in group L and 48% in group C, p = 0,023. Failure to wean developed in 12% vs 48% in groups L and C resp., p = 0,023. In group L the incidence of preperfusion atrial fibrillation and re-cardiopulmonary bypass (CPB) were lower. Doses of dopmin, epinephrine and norepinephrine at the end of the operation were lower in group L. CPB duration, tracheal intubation time, length of inotropic support, length of Intensive Care Unit stay and postoperative length of stay were shorter in group L. Those differences did not reach statistical significance probably due to the small number of pts in the group L.
Conclusion: In CHD-patients with low LVEF a preoperative levosimendan definitely shows cardioprotective effects that could provide better results of CABG and benefits in the postoperative period.

P1237
concurrent implantation of intra-aortic balloon pumping with extracorporeal membrane oxygenation improved survival of patients with postcardiotomy cardiogenic shock

K Kai Chen[1]; HW Tang[1]; JF Hou[1]; SS Hu[1]
[1]Fuwai Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, department of cardiac surgeon, Beijing, China People's Republic of

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Background: Extra-corporeal membranous oxygenation (ECMO) and intra-aortic balloon pumping (IABP) are widely used in patients with severe circulatory failure. The decision to initiate ECMO and IABP on optimal occasion in postcardiotomy cardiogenic shock (PCS) remains controversial in the absence of guidelines.
Objectives: The aim of this study is to report the combining application of ECMO with IABP in PCS in Fuwai Hospital.
Methods: A total of 60 consecutive patients who received both ECMO (<24 hours) and IABP for PCS between February 2006 to March 2017 in Fuwai Hospital were included in our study. Clinical characteristics of the patients were collected retrospectively and compared between survivors and non-survivors. Logistic regression analysis was used for predictors for survival of discharge.
Results: The study cohort had mean age of 51.4 ± 12.7 years in which 75% were males. ECMO was implanted intraoperatively in 38 (63%) patients and post-operatively in 22 (37%) patients. IABP was implanted concurrently with ECMO in 38 (63%) patients. Heart transplantation (38%) and coronary artery bypass graft (33%) was the main surgical procedure. ECMO was weaned successfully in 48% patients, and the survival to discharge was 43%. Survivors showed a lower rate of bedside ECMO implantation (12% vs. 41%, P = 0.012) and higher rate of concurrent implantation of IABP with ECMO (81% vs. 50%, P = 0.014). Concurrent implantation of IABP with ECMO (OR = 0.013, P = 0.017, 95% CI: 0-0.457) was an independent predictor for survival to discharge. As for complications, the rate of renal failure (59% vs. 15%, P = 0.001) and multiple organ dysfunction syndrome (29% vs. 0, P = 0.003) was higher in patients who failed to survive to discharge.
Conclusions: Although remaining unresolved problems, combined use of ECMO with IABP is recommendable as the short-term circulatory assistfor rescuing the patient with PCS. Concurrent implantation of IABP with ECMO provides better outcome for PCS.

Hypertension - Other

P1238
Subendocardial systolic dysfunction in hypertensive patients with strain st-t changes on electrocardiogram by 2-d speckle tracking

G Gerges Thabet[1]; MA Soliman[1]; MB Mena[1]
[1]Faculty of Medicine, Menoufia University , Department of cardiovascular diseases, Shebin El Kom,Menoufia, Egypt

Background: Hypertension can cause ST-T changes on ECG which may predict sub clinical left ventricular systolic dysfunction detected by 2D speckle tracking. Objective: the aim of this study was to evaluate left ventricular longitudinal strain by speckle tracking in hypertensive patients with strain ST-T on ECG.
Patients and Methods: left ventricular longitudinal strain analysis in 61 hypertensive patients with Echocardiographic evidence of left ventricular hypertrophy divided into two subgroups the 1st include 30 hypertensive patients with strain ST-T changes on ECG (G1) and 2nd include 31 hypertensive patients without changes on ECG (G2) and control group include 21 hypertensive patients without Echocardiographic evidence of left ventricular hypertrophy (G3).

P1238 Speckle tracking data

Speckle tracking data Mean ±SD	G1 (N = 30) Mean ±SD	G2 (N = 31) Mean ±SD	G3 (N = 21)	F Test	P value	Post hoc test
Average global longitudinal strain	-14.24±1.71	-18.05±1.99	-19.21±1.39	59.27	<0.001*	1 vs. 2 <0.001* 1vs.3 <0.001* 2vs.3 = 0.022*
Apical 4 longitudinal strain	-14.22±2.40	-18.43±2.16	-19.02±1.69	41.17	<0.001*	1 vs. 2 <0.001* 1vs.3 <0.001* 2vs.3 = 0.339
Apical 3 longitudinal strain	-13.90±2.13	-17.52±3.75	-18.72±2.68	19.14	<0.001*	1 vs. 2 <0.001* 1vs.3 <0.001* 2vs.3 = 0.155
Apical 2 longitudinal strain	-14.20±3.20	-18.17±2.83	-19.46±1.88	26.19	<0.001*	1 vs. 2 <0.001* 1vs.3 <0.001* 2vs.3 = 0.103

Table (1): Speckle tracking data of the studied groups:

Results: A high significant difference was detected in relation to Hypertension duration which divided into two categories (>10yrs and = 10yrs) which is the median of patients duration of hypertension (P-value <0.001). A high significant increase was present as regard to conventional echocardiography data on Left ventricular mass (P-value <0.001), Left ventricular mass index (P-value <0.001), Inter ventricular septum Diameter (P-value <0.001), Posterior wall Diameter (P-value <0.001), Left Atrium Diameter (P-value <0.001), Aortic root Diameter (P-value 0.002) and Relative wall thickness (P-value <0.001) between G1 compared to G2 and between G1& G2 compared to G3.also significant decrease was found on Doppler data as regard to E/A ratio between G1 compared to G2 and G1&G2 compared to G3. There was a high significant reduction between G1 compared to G2 and G1&G2 compared to G3 as regard mean value of longitudinal systolic strain of walls in apical 2 view, apical 3 view, apical 4 view and global left ventricular strain (P-value <0.001).
Conclusions: Subtle left ventricular systolic dysfunction evident by speckle tracking (systolic longitudinal strain) was present in hypertensive patient with ST-T changes on ECG and patients with uncontrolled BP (>140\90) independent on Left ventricular ejection fraction.

P1239

Arterial stiffening is associated with adverse cardiovascular outcome in patients without high blood pressure

S Satoru Sakuragi[1]; M Nakashima[1]
[1]Iwakuni Clinical Center, Department of cardiology, Iwakuni, Japan

Objective: Although blood pressure (BP) is a major determinant of arterial stiffness, whether high pulse wave velocity (PWV) adversely influences cardiac parameters and cardiovascular (CV) outcome in patients without high BP remains unclear.
Methods: Outpatients without high BP (n = 320), defined as systolic BP = 140 mm Hg, were enrolled in this retrospective study. At baseline, all patients underwent echocardiography and multidetector CT to determine the coronary artery calcification (CAC) score. Arterial stiffness was assessed based on brachial-ankle PWV (baPWV), from which patients were classified into two groups: those with high (= 18 m/s, n = 89) and low baPWV (< 18 m/s, n = 231). Cardiac parameters and CV event incidence during the follow-up period were compared between these groups.
Results: In multivariable linear regression analysis, baPWV was significantly associated with CAC score and serum N-terminal pro-brain natriuretic peptide hormone level, after adjustment for confounding factors. In multivariable logistic regression analysis, baPWV = 18 m/s was significantly associated with CAC score = 400 (OR 2.466, 95% CI 1.012 to 6.009, p = 0.0471). Kaplan-Meier analysis showed that the high-baPWV group experienced more CV events during the 575 days of follow-up (20% vs 6%, p = 0.0003).
Conclusions: High baPWV was associated with greater CAC and a high risk of a future CV event, especially coronary artery disease, even in patients without high BP.

P1240

NT-proBNP and metabolic risk factors in two ethnic groups - The SABPA cohort study

A Amra Jujic[1]; O Melander[1]; PM Nilsson[1]; L Malan[2]; A Fedorowski[1]; M Magnusson[3]
[1]Lund University, Malmo University Hospital, Department of Clinical Sciences, Lund, Sweden; *[2]North-West University, Hypertension in Africa Research Team (HART), Potchefstroom, South Africa*; *[3]Malmo University Hospital, Department of Cardiology, Malmo, Sweden*

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Background: Natriuretic peptides are vasoactive peptides with several metabolic actions.
Purpose: We aimed to explore associations of N-terminal pro-brain natriuretic peptide (NT-proBNP) with metabolic traits in a mixed ethnic African-Caucasian cohort.
Methods: Within the Sympathetic activity and Ambulatory Blood Pressure in African Prospective cohort study (SABPA), baseline examination was performed between 2008 and 2009, and re-examination after a 3-year follow-up in 397 South African teachers (African n = 194; Caucasian n = 203).
Results: In cross-sectional linear regression analyses, each 1SD increment of age and sex adjusted NT-proBNP was inversely associated with body weight (ß = -2.23; p = 0.042), body mass index (ß = -1.01; p = 0.007), waist circumference (ß = -1.82; p = 0.033), HbA1c (ß = -0.14 %; p = 0.009), insulin (ß = -1.66; p = 0.002), homeostatic model assessment of insulin resistance (ß = -0.47; p = 0.006) and triglyceride levels (ß = -0.04; p = 0.002). Intra-ethnic differences were observed, where lower NT-proBNP levels affected glucometabolic status stronger among Africans. Each 1SD increment of age, sex, waist circumference and follow-up time adjusted NT-proBNP was associated with reduced odds of incident diabetes, and subjects within the highest quartile of NT-proBNP were at lowest risk compared with the lowest quartile (OR 0.24; CI95% 0.06-0.96; p = 0.041).
Conclusions: In a cohort consisting of two ethnic groups, NT-proBNP in the high normal range is associated with lower prevalence of metabolic risk factors such as high BMI, increased waist circumference, impaired glucose tolerance, high insulin levels and hypertriglyceridemia, with strongest associations for Africans. Inspite of similar NT-proBNP concentrations, BNP may affect the propensity for metabolic disturbances differently in Africans and Caucasians.

P1241

On-treatment decreases in aortic pulse pressure induced by antihypertensive therapy are accounted by reductions in backward wave in mild hypertensive patients

EN Libhaber[1]; GR Norton[2]; G Tade[2]; I Ballim[2]; CD Libhaber[2]; P Sareli[2]; AJ Woodiwiss[2]
[1]University of the Witwatersrand, School of Clinical Medicine, , Johannesburg, South Africa; *[2]University of the Witwatersrand, Cardiovascular Pathophysiology and Genomics Research Unit, School of Physiology, Johannesburg, South Africa*

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Background: Aortic haemodinamics are predictors of heart failure. Brachial pulse pressure may not accurately reflect aortic pulse pressure measurements. Numerous factors contribute towards central pulse pressure and these may influence aortic pulse pressure by modifying either aortic backward (reflected) or forward wave pressures. Several studies suggest a more important role of the backward wave than the forward wave in contributing to variations in central pulse pressure, cardiovascular end-organ measures and outcomes than forward wave pressures at mediating cardiovascular damage. Prior studies reporting on antihypertensive drug effects on aortic blood pressure have not compared the contribution of forward and reflected wave pressures to decreases in central pulse pressure.
Purpose: We aimed to determine the relative contribution of decreases in forward vs backward wave pressures to antihypertensive treatment-induced decreases in aortic pulse pressure.
Methods: We randomized 54 mild hypertensives of black African ancestry to receive indapamide (2.5mg) (n = 27) or amlodipine (CCB) (10mg) (n = 27) daily for a month and then to receive the angiotensin-converting enzyme inhibitor, perindopril (4mg) as add-on therapy if target office pressures were not achieved, for a further 5 months. Aortic haemodynamics were determined using applanation tonometry, ShygmoCor software and echocardiography.
Results: Mean age in both groups was similar (60 ± 14 and 57 ± 14 years), the majority were females (79-85%) and obese (BMI ˜32 kg/m^2) and 19-33% had left ventricular hypertrophy. Backward and forward wave pressures were reduced to a similar degree in both the CCB (-3.6 ± 1.2 and -3.3 ± 8.9 mmHg, p < 0.01) and indapamide (-4.8 ± 1.0 and -4.6 ± 1.2 mmHg, p < 0.01) treated groups. However, in both treatment groups, with backward and forward waves in the same multivariate model

the slope of the relationship between decreases in aortic pulse pressure and backward wave pressure (indapamide: ß-coefficients: 0-1 month = 1.145 ± 0.085, 0-6 months = 1.183 ± 0.131,p < 0.0001; CCB: ß-coefficients 0-1 month = 1.192 ± 0.105, 0-6 months = 1.493 ± 0.160, p < 0.0001) was much higher than between aortic pulse pressure and forward wave (indapamide: ß-coefficients: 0-1 month = 0.611 ± 0.075, 0-6 months: 0.513 ± 0.118, p < 0.0001: CCB: ß-coefficients: 0-1 month = 0.516 ± 0.086, 0-6 months= 0.243 ± 0.148, p < 0.0001).
Conclusions: The benefit of reductions in pulse pressure mediated by major classes of antihypertensive agents are accounted more by decreases in backward than forward wave pressures .

Diabetes and the Heart

P1242
Skin autofluorescence as a measure of advanced glycation end product levels is associated with plaque burden in subjects free from diabetes

A Amra Jujic[1]; G Ostling[1]; M Persson[1]; G Engstrom[1]; PM Nilsson[1]; O Melander[1]; M Magnusson[2]
[1]Lund University, Malmo University Hospital, Department of Clinical Sciences, Lund, Sweden; *[2]Malmo University Hospital, Department of Cardiology, Malmo, Sweden*

Funding Acknowledgements: Swedish Medical Research Council. the Swedish Heart and Lung Foundation, the Medical Faculty of Lund University, Skane University Hospital

Background: Advanced glycation end products (AGEs) is an established risk factor in diabetic vascular disease, but possible associations between atherosclerosis and AGE in a population free from diabetes are yet to be investigated. Skin autofluorescence is a novel marker of AGE-levels in long-lived tissue.
Purpose: We studied the degree of atherosclerosis in an elderly population free from diabetes and its association with skin autofluorescence.
Methods: Carotid ultrasound and skin autofluorescence measurements was performed in a subpopulation within "Malmö Diet and Cancer Cardiovascular Cohort" (n = 523). Total plaque area including all prevalent plaques in the right carotid artery, was calculated. Subjects with diabetes were excluded. Complete data on all variables was available for 375 subjects.
Each 1 standard deviation (SD) increment of skin autofluorescence was associated with increased total plaque area in the right carotid artery (ß = 2.88, p = 0.018) independently of metabolic and cardiovascular risk factors. Similarly, each 1 SD increase of skin autofluorescence was associated with an approximately 1.4-fold increased risk of large total plaque area (= 34mm2) (OR 1.39; 95% CI 1.07 - 1.80; p = 0.015). The top versus bottom quartile of the skin autofluorescence was associated with an approximately 2.5-fold increased risk of total plaque area = 34mm2 (OR 2.56; 95% CI 1.22 - 5.39; p = 0.010) in fully adjusted analysis.
Conclusions: In a population free from diabetes, skin autofluorescence was independently associated with increasing degree of atherosclerosis measured as total plaque area, implicating a role of advanced glycation end products in the development of atherosclerosis even in a non-diabetic population.

P1243
The significance of diabetes mellitus on left ventricular function, heart rate variability and frequency of supraventricular arrhythmias in patients after myocardial infarction

V Stoickov[1]; M Deljanin Ilic[1]; M Stoickov[2]; S Saric[2]; S Andonov[2]; D Marinkovic[2]; I Tasic[1]; D Simonovic[2]; S Mitic[2]
[1]University of Nis, Medical Faculty, Institute of Cardiology Niska Banja, Nis, Serbia; *[2]Institute of Cardiology, Niska Banja, Serbia*

Background/Introduction: Coronary patients with diabetes are at high risk of cardiovascular events. Coronary disease in diabetic patients has speed up, progressive course because of the synergic work of hyperglycemia and other risk factors of the coronary disease, as well as dyslipidemia, hypertension, obesity and smoking too.
Purpose: The aim of this study was to establish the significance of diabetes mellitus on left ventricular function, heart rate variability and freqency of supraventricular arrhythmias in patients after myocardial infarction (MI).
Methods: We studied 337 patients after MI, in the sinus rhythm without AV blocks or branch blocks. 112 patients were with diabetes mellitus, and 225 were without diabetes. Patients were of similar age, site of infarction and baseline stress test duration. In all subjects 24-hour ECG recording and echocardiographic examination were performed. From the holter record, the analysis of the heart rate variability was performed by software. Four parameters of the time domain heart rate variability were assessed: SDNN, SDANN, RMS-SD and NN>50 ms.
Results: Patients with diabetes had a higher percentage of frequent (<10 supraventricular premature complexes / hour) and complex supraventricular arrhythmias (38.5 vs 19.2%, p < 0.001) and supraventricular tachycardias (28.8 vs 6.1%, p < 0.001) than in those without diabetes. Patients with diabetes also had significantly lower values of followed parameters of the heart rate variability (78.6 ± 20.1 vs 102.1 ± 28.7 ms, p < 0.001 for SDNN; 66.9 ± 18.7 vs 85.6 ± 29.7 ms, p < 0.001 for SDANN; 24.7 ± 10.6 vs 35.4 ± 14.9 ms, p < 0.001 for RMS-SD and 5.8 ± 5.6 vs 12.2 ± 10.3, p < 0.001 for NN>50ms) in comparison to those without diabetes. Patients with diabetes also had significantly lower values of left ventricular ejection fraction (45.0 ± 9.6 vs 54.3 ± 13.8 %, p < 0.001) and significantly higher values of left ventricular end-systolic diameter (39.5 ± 5.6 vs 35.6 ± 6.8 mm, p < 0.001), left ventricular end-diastolic diameter (55.8 ± 5.4 vs 53.1 ± 5.6 mm, p < 0.001) and left atrium (43.2 ± 5.6 vs 39.2 ± 4.7 mm, p < 0.001), in comparison to those without diabetes.
Conclusions: The study showed that in patients after MI, diabetes mellitus have a significant impact on left ventricular function, heart rate variability and supraventricular arrhythmias. The reason for that is more severe degree of the left ventricle dysfunction, diabetic neuropathy and greater inhomogeneous repolarization of myocardium.

P1244
Beneficial effect of short-term dapagliflozin therapy on arterial stiffness assessed by cardio-ankle vascular index in type 2 diabetic patients

K Takagi[1]; N Sato[1]; S Ishihara[1]; W Shimizu[2]
[1]Nippon Medical School Musashi-Kosugi Hospital, Department of Cardiology and Intensive Care Unit, Kanagawa, Japan; *[2]Nippon Medical School, Department of Internal Medicine and Cardiology, Tokyo, Japan*

Background: In type 2 diabetes mellitus (T2DM), arterial stiffness is related to the progression of complications. However, previous studies showed no relationship between glycemic control and changes in arterial stiffness. We evaluated whether or not dapagliflozin, a SGLT2 inhibitor, therapy can improve arterial stiffness using cardio-ankle vascular index (CAVI) and HbA1c after a short-term period in T2DM patients.
Methods: Sixteen T2DM patients were treated dapagliflozin 5-10mg/day for 6 months. HbA1c and CAVI were measured before and after treatments.
Results: Significant decreases in HbA1c (7.43 ± 0.60 to 6.68 ± 0.55%, P = 0.0003) and CAVI (figure) were observed after treatment.
Conclusion: In T2DM patients, dapagliflozin had beneficial effects on arterial stiffness in addition to lowering HbA1c after a short-term period, suggesting that dapagliflozin might be useful for prevention of DM-related complications.

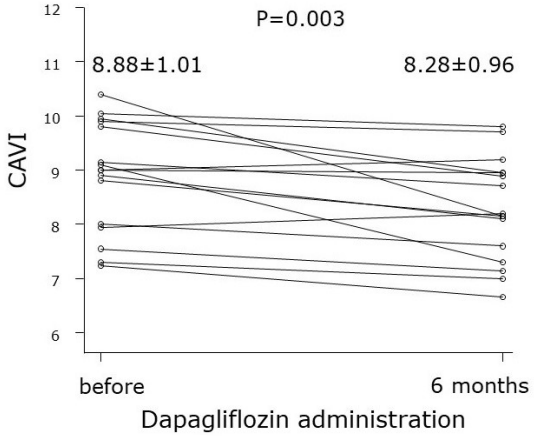


Figure. Change in CAVI after Dapagliflozin treatment for 6 months. Data are presented as mean ± SD, paired t-test.

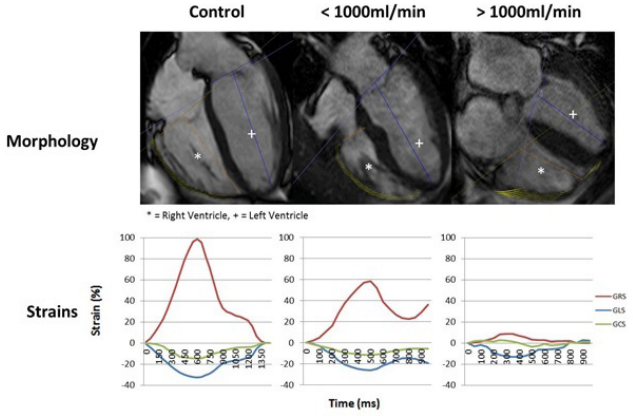
Renal Failure and Cardiovascular Disease

P1245

Effects of the high flow arterio-venous fistula on right ventricular contractility in hemodialysis patients

S C Bhagirath[1]; A De Vette[1]; G Karas[2]; H Suliman[2]; AWM Van Der Graaf[3]; MJW Gotte[4]; MC Weijmer[1]; P Bhagirath[1]
[1]Hospital Onze Lieve Vrouwe Gasthuis, Internal Medicine, Amsterdam, Netherlands; [2]Hospital Onze Lieve Vrouwe Gasthuis, Radiology, Amsterdam, Netherlands; [3]Sint Franciscus Gasthuis, Cardiology, Rotterdam, Netherlands; [4]VU University Medical Center, Cardiology, Amsterdam, Netherlands

Background: The presence of an arterio-venous fistula (AVF) in hemodialysis patients is a source of constant volume overload. The inability of the right ventricle (RV) to adapt to these conditions leaves it more susceptible to dysfunction as compared to the left ventricle (LV). Early recognition of RV failure in this population, especially in relation to the AVF flow, could contribute towards improved and personalized therapeutic strategies.
Purpose: In this study we utilize tissue-tracking cardiac magnetic resonance to describe the relation between AVF flow and RV contractility. It is hypothesized that the RV contractility will be decreased in patients with a high flow AVF due to volume overload related RV dysfunction.
Methods: Hemodialysis patients (n = 11) and age-matched controls (n = 5) underwent CMR. Acquisitions were obtained prior to and after dialysis to distinguish between the effects of AVF flow and volume status (fluid overload). The patients were divided in Group 1 (low flow, < 1000ml/min) and Group 2 (high flow, >1000ml/min) based on the AVF flow measured using ultrasonography. Global longitudinal (GLS), global circumferential (GCS) and global radial strain (GRS) of the RV were calculated with the tissue-tracking module of Circle Cardiovascular Imaging using short- and long-axis cine images.
Results: The contractility parameters between the groups were similar prior to dialysis. After dialysis, there were no significant changes observed between Group 1 (n = 5) and the control group (n = 5). In comparison to the control group, patients in group 2 (n = 6) had a significantly lower GLS (-16.5 ± 3.0% vs. -28.1 ± 4.4%, P < 0.05) and GRS (31.0 ± 8.5% vs. 71.7 ± 23.7%, P < 0.05) after the dialysis session. No significant change was observed for the GCS between the control group and group 2 (-3.6 ± 10.6% vs. -15.6 ± 3.5%, P = 0.06).
Conclusion: These findings suggest that patients with high AVF flow have significantly lower contractile parameters and thereby have at an increased risk for developing right ventricular failure. Tissue-tracking analysis offers the possibility to detect subtle early changes in right ventricular contractility and could have significant therapeutic consequences in this patient group.



RV Strain

P1246

Role of natriuretic peptides in renal outcomes after revascularization in patients with significant atherosclerotic renal artery stenosis

DO Geavlete[1]; C Beladan[1]; D Deleanu[1]; MR Zaharia[2]; O Tautu[3]; BA Popescu[1]; C Ginghina[1]; O Chioncel[1]
[1]Institute of Cardiovascular Diseases Prof. C.C. Iliescu, Cardiology, Bucharest, Romania; [2]Emergency Clinical Hospital St John, Internal Medicine, Bucharest, Romania; [3]Emergency Clinical Hospital Floreasca, Cardiology, Bucharest, Romania

Introduction: Cardiac failure with preserved ejection fraction and flash pulmonary edema are cardinal manifestations of significant bilateral renal artery stenosis (RAS) and RAS in solitary kidney patients. Brain natriuretic peptide (BNP) might be a valuable predictor of clinical outcomes after renal revascularization in terms of renal function preservation.
Purpose: The present study was aimed to compare the BNP levels at admission and 12 months' after renal angioplasty with stent and to identify its' predictive value for renal outcomes (renal function and major renal events) in patients with significant RAS.
Methods: 78 hypertensive patients referred to renal angiography for suspected RAS and diagnosed with significant uni- and bilateral stenosis (<70%) were prospectively enrolled, resulting in 3 groups (34-unilateral, 28-bilateral RAS and 16-RAS in a solitary kidney). Cardiac and renal history, duration of hypertension, cardiovascular risk factors, biological profile (including BNP), extra-cardiac vascular diseases and related comorbidities were assessed. A complete echocardiography was performed in all patients. Renal function was estimated based on the serum creatinine level and glomerular filtration rate (eGFRCKD-EPI). The mean extended follow-up period was 24.27 ± 12.16 months, during which major renal events were observed (acute renal insufficiency and need for dialysis). Statistical analysis correlation followed by logistic regression analysis (stepwise Likelihood ratio method) was used.
Results: Similar baseline characteristics were found for the 3 study groups regarding age, gender, stenosis' severity, comorbidities, blood pressure values and echocardiographic parameters (p?0.05 for all). Although baseline renal dysfunction was significantly higher in patients with RAS in a solitary kidney compared to bilateral and subsequently to unilateral RAS (p = 0.001), BNP and LnBNP levels were similar between groups. The BNP and LnBNP variation percent analysis before and after revascularization showed a significant reduction in LnBNP in all patients after renal stenting (p = 0.002), with significant differences between groups (unilateral - p?0.05, bilateral - p = 0.031 and solitary kidney RAS - p = 0.007). Multivariate logistic regression analysis confirmed baseline LnBNP as an unique independent predictor for major renal events (p = 0.002). The accuracy of the emerged predictive model as quantified by the area under the receiver-operating characteristics curve was 0.95 (95% CI, 0.83-1.01, p = 0.002).
Conclusions: The study demonstrated a strong relationship between elevated BNP and major renal events after renal stenting in high-risk RAS patients, although baseline BNP levels were not predictive for renal function improvement. The present findings strengthen the current indications for renal stenting in bilateral RAS and solitary kidney RAS, groups in which BNP significantly decreased after revascularization when compared to unilateral significant RAS.

P1249

Clinical characteristics and comorbidities in very elderly patients with heart failure admitted as an emergency

A Alice Balaceanu[1]; R Staiculescu[2]; M Fronea[2]; G Dediu[2]; C Voiculet[1]; C Diaconu[3]; G Aron[1]; I Dina[1]
[1]UMF Carol Davila, Emergency Clinical Hospital Sf. Ioan, Internal Medicine Clinic, Bucharest, Romania; [2]Emergency Clinical Hospital Sf. Ioan, Bucharest, Internal Medicine Clinic, Bucharest, Romania; [3]UMF Carol Davila, Emergency Clinical Hospital Floreasca, Internal Medicine Clinic, Bucharest, Romania

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Background: It is hard to estimate the cardiovascular risk in very elderly patients.
Purpose: The aim of the study was to assess the clinical characteristics and cardiovascular risk in very elderly patients with heart failure admitted as an emergency.
Methods: The retrospective study included 84 patients with age more than 90 years old admitted to Clinical Emergency Hospital between January 2014 - May 2017. Of these patients 76.19% (64 patients) had heart failure as a diagnosis.
Results: The average age was 91 years. The maximum age was 97 for women and 98 for men. Gender distribution: 64.06% women and 35.94% men. The following NYHA class distribution in patients with heart failure was observed: class II 42.19%, class III 43.75%, class IV 14.06%.
The most common comorbidity was chronic kidney disease, encountered in 93.75% of cases. The following KDIGO staging was present: G1 3.12%, G2 23.44%, G3a 37.5%, G3b 28.12%, G4 7.82% and G5 0% (evaluated by MDRD equation). The average level of creatinine at admission was 1.46 and at discharge was 1.34. Worsening of renal function was noticed in 9.6% of patients.
Other comorbidities were: hypertension (67.18%), anemia (65.62%), respiratory insufficiency (40.62%), atrial fibrillation (32.81%), mixed dementia (31.25%), Alzheimer disease (28.12%), sequelae of stroke (23.43%), right bundle branch block (14.06%), left bundle branch block (12.50%), depression (15.62%), cancer (14.06%), cachexia (23.43%).
Urinary tract infection has been proven in 26.92% of cases. Identified germs were E. Coli in 71.42% cases of infections, Enterococcus, Klebsiella, Proteus and Pseudomonas.
The principal diagnosis on admission was acute decompensation of heart failure in 29.68%, infection in 25% and acute respiratory insufficiency in 15.62% of cases.

Conclusions: Chronic kidney disease and hypertension are the most common cardiovascular risk factors in the very elderly patients with heart failure. Anemia is an important factor in the management of heart disease in this category of patients. Nonvalvular atrial fibrillation is the most common arrhythmia in very elderly patients.

P1250

Cardiac serum biomarkers in haemodialysis patients: significance of NT-proBNP and troponin in heart failure

B Leskovar[1]; T Furlan[1]; K Vrbinc Vrtek[1]; S Poznic[1]; D Kosuta[1]; A Adamlje[2]
[1]*Trbovlje General Hospital, Department of Internal Medicine, Trbovlje, Slovenia*; [2]*Trbovlje General Hospital, Department of Hemodialyisis, Trbovlje, Slovenia*

Background/Introduction: Plasma NT-proBNP concentrations are elevated in chronic kidney disease (CKD) patients with or without clinically evident heart failure. Cardiac troponins are the preferred biomarkers for the diagnosis of myocardial injury, but stably elevated troponin concentrations are commonly observed in CKD patients in the absence of clinically evident acute myocardial damage.
Purpose: We wanted to evaluate correlations between NT-proBNP plasma levels and echocardiographic parameters that suggest heart failure. Additionally, we wanted to assess whether the plasma level of troponin in CKD patients influences the correlation of NT-proBNP with clinically significant heart failure and whether the level of troponin influences on survival of CKD patients.
Methods: We retrospectively included all CKD patients on chronic haemodialysis in our centre after January 2008. We were regularly assessing the value of troponin T and NT-proBNP every four months and we performed echocardiography in all of our patients. We calculated the average NT-proBNP and average troponin since the start of haemodialysis and divided our patients in three groups based on troponin level (group 1: TnT < 0,01, group 2: TnT 0,01-0,1, group 3: TnT>0,1 (cut-off value 0,1 ng/ml). We compared the correlation of NT-proBNP with heart failure echocardiographic parameters (LVEF, LVOT VTI, E/Em) between groups 1-3 (MANCOVA analysis). We also evaluated survival (overall survival, time to acute cardiac event and time to first heart failure hospitalization) after the start of haemodialysis (Kaplan-Meier analysis).
Results: We included 120 chronic haemodialysis patients (54% male, mean age 71 ± 12 years, mean TnT 0,2 ± 0,3 ng/ml, mean NT-proBNP 2026 ± 1364 pmol/l). None of them had negative level of troponin (TnT < 0,01), 56 were in group 2 and 46 in group 3. NT-proBNP significantly correlated with LVEF, LVOT VTI and E/Em (p = 0,001, p = 0,023 and p = 0,032, respectively), but there was no significant change between selected troponin based groups. We also assessed predicted survival between groups 2 and 3. There was no difference in estimated survival between groups (111 ± 13 vs. 93 ± 16 months, p = 0,112), no difference between predicted time to first heart failure decompensation after the start of haemodialysis (182 ± 14 vs. 191 ± 23, p = 0,43), but the group with higher troponin had shorter predicted time to acute cardiac event after the start of haemodialysis (195 ± 18 vs. 166 ± 23, p = 0,004).
Conclusion(s): Our results confirm a stably elevated troponin level and higher mean NT-proBNP in CKD patients. Nevertheless, our results indicate a positive correlation between NT-proBNP and echocardiographic markers of heart failure even in this population. We did not perform 6MWT because our study was retrospective, but this functional test should be done to confirm our findings. Also, despite persistently elevated troponin, higher troponin showed to correlate with earlier acute cardiac event.

Autoimmune/Chronic Inflammatory Disorders and Heart Disease

P1251

Inflammatory markers TNF, Il6 as predictor of outcome for Peripartum cardiomyopathy

SRS Sai Ravi Shanker[1]
[1]*CONTINENTAL HOSPITALS, CARDIOLOGY, HYDERABAD, India*

On behalf of: DR RAVI SHANKER

Aim/objective: The study aimed at correlating plasma levels of C-reactive protein TNF a and IL6 as prognostic value for major clinical in-hospital events and 6 month follow up in patients with PPCM
Material and methods: A total 86 subjects were enrolled [(patients (n-46) and controls (n-40)]. After checking for the inclusion and exclusion criteria, clinical assessment, echocardiography, and blood analysis were done at baseline and after 6 months of standard therapy. All patients received treatment Inflammatory markers (C-reactive protein, TNF a and IL 6) were measured at baseline and at 6 months.
Results: C-reactive protein (22mg/dl vs 08mg/dl) TNF alpha (9.6 vs 3.2 pg/dl, p < 001) and IL6 were (73.19 vs 8.83pg/dl, p < 0.005) which were significantly abnormal compared with study population ,and these patients showed a significant higher LV dimensions LV EDD (61.6 vs 46 p < 0.004) LV ESD (53.1 VS 32,p < 0.005) and significant lower LVEF (25.9 vs 55 P < 0.001) and well correlate with NYHA FC and death. Left ventricular ejection fraction (LVEF) improved from 25.9 to 42.9% at 6 months (P < 0.0001). Patients who completed 6 months of standard care showed a significant reduction of , LV dimensions, and NYHA FC (P < 0.001).
Conclusion: Plasma markers of inflammation were significantly elevated in PPCM patients and correlated with the pathogenesis of PPCM and its complications and predictors of mortality.

Characteristics of deceased vs.surviving

	Deceased	Survivors	P-value
Age (years)	22±1.2	28±6	0.24
No. of children (n), median (range)	2(1-4)	3(1-7)	0.14
Onset of symptoms after delivery (months), median (range)	1(1-5)	2(1-5)	0.6
NYHA FC	3.2±0.8	2.0±0.6	0.04
EDD (mm)	64±5	60±6	0.03
ESD (mm)	57.6±7	53.2±8	0.03
Echo EF (%)	20±4	26±8	0.04
C-reactive protein (mg/L), median (range)	26	22	0.10
TNF (pg/mL)	9.6	24	<0.001
IL-6(pg/ml)	34	72	<0.001

P1252

Chronic inflammation after splenectomy is a risk factor for increased thrombotic cardiovascular events

M Mario Gerges[1]; C Gerges[1]; M Publig[1]; N Skoro-Sajer[1]; J Bergler-Klein[1]; D Bonderman[1]; M Frey[1]; I Schwarzinger[2]; MP Winter[1]; M Humenberger[3]; J Jakowitsch[1]; V Seidl[1]; B Eichelberger[4]; S Panzer[4]; IM Lang[1]
[1]*Medical University of Vienna, Department of Internal Medicine II, Division of Cardiology, Vienna, Austria*; [2]*Medical University of Vienna, Department of Laboratory Medicine, Vienna, Austria*; [3]*Medical University of Vienna, Department of Trauma-Surgery, Vienna, Austria*; [4]*Medical University of Vienna, Department of Blood Group Serology and Transfusion Medicine, Vienna, Austria*

Purpose: Patients after splenectomy are prone to complicated thrombosis and atherosclerosis. Preclinical studies suggest that this observation may be linked to a chronic inflammatory state characterized by lymphocyte dysregulation. We tested the hypothesis that sustained inflammation and abnormal platelet function in splenectomized patients contribute to atherosclerosis and thrombosis.
Methods: In this prospective case control study, we evaluated 298 outpatients after previous splenectomy referred from 1100 primary care practitioners. 177 (89.4%) splenectomies were due to trauma. Functional asplenia was assessed by the presence of Howell-Jolly bodies (HJB) on Wright-blood smears. Platelet function was measured in a subset of 36 splenectomized patients in whom splenectomy occurred after trauma, and in 7 matched non-splenectomized controls by multiple electrode impedance aggregometry (Multiplate) and flow cytometry.
Results: Despite similar age functional asplenic patients (HJB+) were more likely to have diabetes mellitus (27.3%, p = 0.037) and stable ischemic heart disease (27.3%, p = 0.047) compared to controls (3.7%, 0%) respectively. In addition stable ischemic heart disease was more common in HJB+ patients (27.3%, p = 0.047) compared to HJB- patients (5.6%). HJB+ patients had a significantly higher number of cumulative thrombotic events (n = 70) compared to HJB- patients (n = 11, p = 0.001) and controls (n = 2, p < 0.001). Time to first thrombotic event was shorter in HJB+ patients (median, 25th and 75th percentiles: 316 months, 165-514 months) compared to HJB- patients (478 months, 466-483 months; p = 0.01) and controls (542 months, 502-581 months; p = 0.003. T cells (CD4+ and CD8+), NK cells and B cells were higher in HJB+ (1298.5 ± 532.4, 844.9 ± 638.3, 523.7 ± 395.2, 447.7 ± 328.9) than in HJB- (1138.8 ± 354.9, p = 0.299; 713.4 ± 285.0, p = 0.452; 304.2 ± 201.2, p = 0.016; 320.3 ± 114.6, p = 0.026) patients and controls (944.6 ± 328.7, 436.4 ± 189.8, 244.4 ± 132.5, 245.0 ± 86.4; all p < 0.01) respectively. Multiplate and flow cytometry analyses revealed increased platelet activatability HJB+ patients compared with HJB- patients and controls. Kaplan-Meier survival curve illustrates time to first thrombotic event or "thrombotic" death.
Event-free survival was significantly (p < 0.001) shorter in splenectomized patients compared with the general Austrian population.

Conclusions: Patients after splenectomy show sustained inflammation with higher numbers of pro-inflammatory cells and increased platelet activation. This observation may underlie the increased risk for thrombotic cardiovascular events.

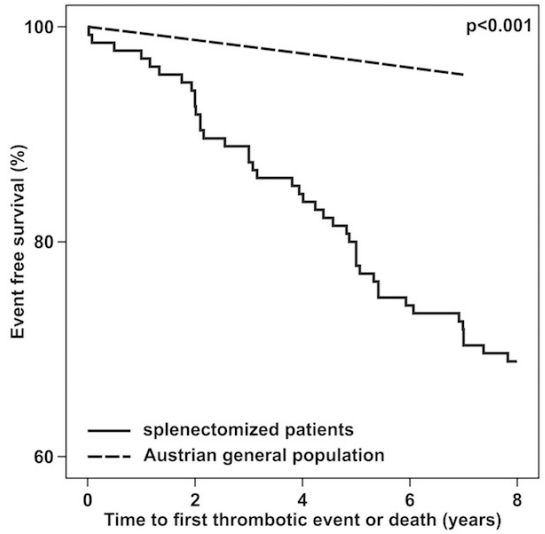


Figure 1

Cardiovascular Nursing - Other

P1253

The long road to a care pathway

C J Caroline Wulffraat[1]
[1]*ijsselland ziekenhuis, capelle aan den ijssel, Netherlands*

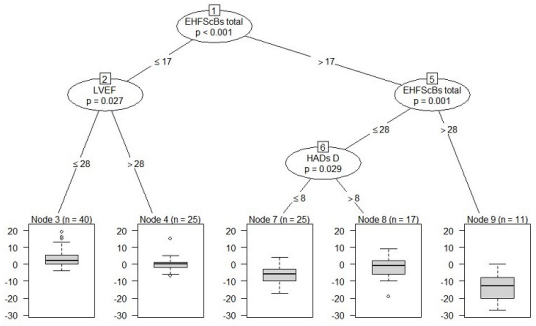
Context: Older patients have a difficult choice to make when they are confronted with a cardiac diagnosis which can be treated best with active cardiac intervention. It can technically be done in fragile, older patients, but it is difficult for the individual patient to weigh the risks and benefits. Patients are dependent on advice from their doctors at the time of decision-making. There is growing group of elderly patients with cardiac diseases who will not undergo active intervention. There is a need for a palliative care pathway that supports these patients with the adaptation to a life limiting disease from the moment of diagnosis.
Method: This study used a modified action research approach. Eleven patients, and one relative, with this specific cardiac condition were interviewed (semi structured). Two multidisciplinary heart teams gave input through patient assessments. Focus groups with local cardiologists, NP's, GP's and homecare nurses provided a multi-faceted view on the concept of the care pathway. For data analysis the approach of manifest content analysis was used.
Findings: At the time of shared decision-making patients rate honesty and expertise the highest. They expect the doctor to know best. The cardiologists used a paternalistic approach and used hard data for decision-making, however, the widely used EuroSCORE does not cover this patient category. Patients who chose for themselves not to be operated seemed to have better self-control and better adaptation to the disease. However, at discharge there was often poor communication between care professionals, particularly about symptom recognition and relief. All patients in this study used >6 medications and nearly all were dependent on homecare. They reported symptoms such as tiredness, fluid retention and weakness. They had a fear of acute, severe symptoms, such as dyspnoea, chest pain and the feeling of suffocating/ dying recurring in the night. They needed palliative care as described by WHO, but prior to this study did not receive it.
Conclusions: Inclusion of frailty scores such as ISAR, KATZ ADL and TUG can provide a better patient assessment. The cardiologists and NP demonstrated a paternalistic approach to decision-making, however, this suited the expectations of the patients in this study as "the doctor knows best". Patients who had made their own decision had more self-control and were coping better. Poor communication at discharge led to inadequate symptom recognition and relief. The unpredictability and fear of returning symptoms should be addressed by a palliative approach. There is an unclear operation of the definition of palliative care.
Recommendations Specific risk cores for frailty need to be included in risk stratification for a better patient assessment for cardiac surgery. Education for NP and homecare nurses is needed to provide palliative care for patients with cardiac diseases, which includes expert symptom recognition and relief.

P1254

Patient profile predisposing the highest potential to change self-care behaviour: data of the IN TOUCH study

E Edita Lycholip[1]; IM Aamodt[2]; I Lie[2]; T Simbelyte[3]; R Puronaite[1]; H Hillege[4]; A De Vries[4]; I Kraai[5]; A Stromberg[6]; T Jaarsma[6]; J Celutkiene[1]
[1]*Vilnius University, Clinic of Cardiac and Vascular diseases, Vilnius, Lithuania*; [2]*University of Oslo, Oslo University Hospital, Department of Cardiothoracic surgery, Oslo, Norway*; [3]*Vilnius University, Faculty of Medicine, Vilnius, Lithuania*; [4]*University of Groningen, Department of Cardiology, Groningen, Netherlands*; [5]*University of Groningen, PRA Health Sciences - Early Development Services, Groningen, Netherlands*; [6]*Linkoping University, Department of Medical and Health Sciences, Linkoping, Sweden*

Background: Self-care is an essential component of chronic heart failure (HF) management, necessary for improvement of patient's well-being, quality of life and prognosis. However, it is known that self-care is sub-optimal in HF patients worldwide and cannot always be easily improved. In attempts to design more effective interventions to improve HF management it is important to know which factors determine self-care.
Methods: The methods and design of the IN TOUCH study (INnovative ICT-guided-DMS combined with Telemonitoring in OUtpatient clinics for Chronic HF patients) were reported elsewhere. The current analysis included 118 participants (mean age 69 ± 11.5 years; 70% male) who filled PRO instruments. These included the 9 item European Heart Failure Self-care Behaviour scale (EHFScBs, range from 9 to 45 points, higher scores reflect worse self-care), Hospital Anxiety and Depression scale (HADs) and Minnesota Living with HF Questionnaire (MLHFQ). To identify subgroups with the greatest potential to improve self-care, conditional inference trees were constructed. In this case, a regression tree with a continuous target variable of change in self-care and input variables (intervention group, sex, left ventricular ejection fraction (LVEF), smoking, age, MLHFQ total scale/physical subscale/emotional subscale, EHFScBs, HADs Depression subscale, HADs Anxiety subscale, New York Heart Association (NYHA) class, N-terminal pro Brain Natriuretic Peptide [NT-proBNP]), were used. Based on the regression tree distribution, the impact of depression was separately investigated in 3 groups of different initial self-care level by univariable regression analysis.
Results: The subgroups of patients who had an initial EHFScBs total score >28 (consistent with poor self-care), or EHFScBs total score in the range from 17 to 28 (medium level) with concomitant depression subscale (HADc_D) score = 8, demonstrated the greatest potential to improve self-care during the study (see Figure: Regression tree showing variables influencing changes in self-care [decrease in EHFScBs total score means improvement in self-care]).



Regression tree of changes in self-care

Depression was significantly related to HF self-care deterioration not in the whole study group, but in the subgroup with medium range of EHFScBs score (from 17 to 28), increasing the chances of self-care worsening by 10.22 times (95% CI 1.81;57.69).
Conclusion: Depression and initial level of self-care play a major role in the change in self-care behaviour in chronic heart failure patients. Intervention aimed to improve self-care behaviour should be adapted for patients with depressive symptoms.

P1255

Cross-cultural adaptation and psychometric testing of the brazilian version of the caregiver contribution to self-care of heart failure index

C Wahast Avila[1]; D De Souza Bernardes[1]; LC Jacoby Silveira[1]; E R Eneida Rejane Rabelo-Silva[1]
[1]*Federal University of Rio Grande do Sul, Heart Failure Clinic and Transplant Group at Hospital de Clinicas de Program at the Nursing School, , Porto Alegre, Brazil*

Introduction: Caregivers make an important role in self-care of patients with heart failure (HF). Although we have validated scales to evaluate this behavior in HF patients few instruments are available to measure caregiver's contribution.
Purpose: To adapt and test the psychometrics properties of the Caregiver Contribution to Self-Care of Heart Failure Index (CC-SCHFI) into Brazilian Portuguese.
Methods: The CC-SCHFI was derived from the Self-Care of Heart Failure Index version 6.2 (SCHFI v. 6.2) and it has already been validated by Italians researches. CC-SCHFI measures the contribution of caregiver to the self-care maintenance and self-care management, as well as their ability's confidence to contribute to the HF patients' self-care. After the approval of the original author, we conducted a complete cross-cultural adaptation of the scale (translation, synthesis, back translation, synthesis of back translation, expert committee review, and pretesting). The psychometric properties assessed were face and content validity (by expert committee review), confirmatory factor analysis (CFA) and reliability.
Results: We enrolled 100 caregivers of HF patients who completed the CC-SCHFI. Most of caregivers were women (72%) with a mean age of 52 years old. The adapted version was named Brazilian version of CC-SCHFI. Face and content validity were indicative of semantic, idiomatic, experimental, and conceptual equivalence. CFA supported the original three-factor model (SCHFI v. 6.2) as having the best fit. In the present study were obtained lower fit indices compared to Italian study. The reliability of the instrument, expressed by Cronbach's alpha, was 0.78, 0.57 and 0.90 for the self-care maintenance, self-care management, and self-care confidence scales, respectively.
Conclusions: Brazilian version of CC-SCHFI was successfully adapted for its use in Brazil and can be used to measure the contribution of caregivers to self-care of HF patients. Nevertheless, further studies should be carried out to improve its psychometric properties.

P1256
Anticoagulation clinic - nursing intervention

S Susana Quintao[1]; IS Martins Sarmento[1]; JC Moreira Campos[1]; CB Girao Bastos[1]; IA Araujo[1]; FM Marques[1]; CF Fonseca[1]
[1]*Hospital de Sao Francisco Xavier, Day Hospital, Lisbon, Portugal*

Introduction: The consultation of oral anticoagulation (ACO) has undergone significant changes in recent years. This is based on referral protocols that promote accessibility and adherence to the proposed therapeutic regimen.
Objectives: To evaluate the efficiency of the method, namely the teaching performed to the user under antagonist of vitamin K (AVK) and family, through efficacy / safety and its adherence to the therapeutic regimen.
Methodology: Retrospective descriptive study, through the Gota v.8.5.0.5.6 program, of time monitoring in the therapeutic interval (TIT), by the Rosendaal method, as well as clinical events related to ACO with AVK. The consultation performed by the nurse, according to pre-defined protocol under medical supervision. INR is performed by point-of-care and drug dosage according to the INR, instructions to the user / family (feeding, drug interaction, invasive procedures, falls and warning signs), problems are identified and validated learning. Throughout the teaching, the constant availability to clarify doubts in person or via telephone is demonstrated.
Population: Patients under chronic ACO therapy, monitored in this clinic, between 2010 and 2016.
Results: We performed 73386 ACO consultations with AVK on 404 women and 410 men, mostly aged 60-89 years, and 62.8% have atrial fibrillation. We obtained a TIT greater than 60% in 89.76% and greater than 65% in 85.9% of patients. As clinical events we recorded 41 cases of major bleeding, 293 minor bleeding, 20 thromboembolic events and 58 (all causes) deaths.
Conclusion: Excellency of TIT, well above what is usually reported in the literature and the low rate of thrombotic and hemorrhagic events, attest to the efficiency and safety of the method, that includes instruction/teaching to the patient and family, reflected in the excellent adherence to the therapeutic regimen and in the low number of events related to ACO.

P1257
Low perceived social support is associated with a poorer health related quality-of-life in heart failure patients living with an implantable cardioverter defibrillator

H Hanna Allemann[1]; A Stromberg[2]; I Thylen[2]
[1]*Linkoping University, Department of Medical and Health Sciences, Linkoping, Sweden*; [2]*Linkoping University, Department of Cardiology and Department of Medical and Health Sciences, Linkoping, Sweden*

Funding Acknowledgements: Medical Research Council of Southeast Sweden (FORSS)

Introduction: The associations between cardiovascular diseases, social support and health-related quality-of-life (HRQOL) have previously been explored. To our knowledge only two small-scaled studies have focused on social support in persons with heart failure (HF) and implantable cardioverter defibrillators (ICD) with or without resynchronisation therapy (CRT-D). Furthermore, studies investigating the association between social support and self-reported HRQOL in this population are lacking. This information could be of importance when designing interventions aimed at this group.
Purpose: The aim was to study HRQOL in relation to perceived social support status in a large cohort of persons living with HF and ICD/CRT-D.
Methods: Eligible adult ICD-recipients in the Swedish Pacemaker- and ICD registry were invited to participate in a cross-sectional study. For this sub-analysis, only the ICD-recipients diagnosed with HF was included. To assess perceived social support and HRQOL, validated self-reported questionnaires were used (Multidimensional Scale of Perceived Social Support and EuroQol-5D-3L).
Results: In total, 1,515 ICD-recipients with HF (67 ± 10 years, 19% female) had complete data on the outcome variables. About half of the participants had received their ICD (52%) as secondary prevention. Time elapsed since ICD implementation varied between 1-23 years, with 57% having had their ICD < 3 years. Nearly two thirds (65%) reported slight or much discomfort from their HF symptoms. Most persons had one or more co-existing health problem (89%) and most shared a household (79%). In total, 262 (17%) described a low/medium support and 1,253 (83%) experienced a high social support.
When comparing the groups depending on their perceived social support, this indicates that persons with low/medium social support have a poorer HRQOL compared to persons with high social support (index 0.72 vs. 0.80, p<.001). Significant differences in relation to perceived social support were found in three out of five HRQOL dimensions (p<.05). For persons with low/medium social support, 48% experienced problems with mobility, compared to 39% of those with high social support. In the dimension pain/discomfort, 63% with low/medium social support reported problems, whereas 48% with high social support experienced this. Fifty percent of those with low/medium social support had problems concerning anxiety/depression, compared to 29% amongst those with high social support. No differences were found concerning self-care and usual activity in the social support groups (7% vs 4% and 29% vs 25%).
Conclusions: Nearly every fifth person with HF and ICD/CRT-D experience a low/medium social support and their HRQOL is negatively affected. This makes these persons vulnerable. Lack of social support in itself is a risk factor for poor HRQOL why it is important to put focus on patient's supportive network during follow up, and in future interventions for persons with HF and ICD/CRT-D.

Basic Science - Cardiac Biology and Physiology

P1258
SCN5A polymorphisms associated with wolff-parkinson-white syndrome

A Anna Chernova[1]; S YU Nikulina[1]; G V Matushin[1]; I I Lebedeva[1]
[1]*Krasnoyarsk State Medical University named prof. V. F. Voino-Yasenecky, Krasnoyarsk, Russian Federation*

Background: The aim of this study was to investigate whether polymorphisms in SCN5A is associated with family Wolff-Parkinson-White (WPW) syndrome.
Wolff-Parkinson-White (WPW) syndrome is an autosomal-dominant heart disease characterized by an accessory pathway that arises from an aberrant conduction from the atria to the ventricles. Several mutations within the SCN5A gene were shown to be responsible for WPW. The gene SCN5A encodes the main cardiac sodium channel NaV1.5. This channel predominates the cardiac sodium current, INa, which underlies the fast upstroke of the cardiac action potential. As such, it plays a crucial role in cardiac electrophysiology. The protein encoded by this gene is an integral membrane protein and tetrodotoxin-resistant voltage-gated sodium channel subunit. This protein is found primarily in cardiac muscle and is responsible for the initial upstroke of the action potential in an electrocardiogram.
Methods: This first study of WPW in a Russian population comprises the clinical and genetic investigation of 20 Russian families, including 27 affected members. This study consisted of 47 patients with symptomatic WPW syndrome and 50 healthy controls. SCN5A genotypes were determined using real-time polymerase chain reaction assay. Genotype and allele frequencies of SCN5A gene between patients with WPW syndrome and healthy controls were ascertained using chi-square test or Fisher exact test when appropriate.
Results: SCN5A were genotyped in 47 patients (23 men and 24 women; age = 34.4 ± 18.0 years) with WPW syndrome and 50 healthy controls (22 men and 28 women; age = 36.8 ± 4.2 years). There were no significant differences between the two groups in terms of age and sex. The patients with AG and AG+GG genotypes had a significantly increased risk of WPW syndrome compared with those with GG genotype [odds ratio (OR) = 1.99, 95% confidence interval (CI) = 1.01-3.89, p = 0.045; OR = 1.99, 95% CI = 1.04-3.78, p = 0.037, respectively]. The allelic types were not associated with the risk of WPW syndrome. The patients with manifest type with AG and AG+GG genotypes had a significantly increased risk of WPW syndrome compared with those with GG genotype (OR = 2.86, 95% CI = 1.16-7.05,

p = 0.022; OR = 2.84, 95% CI = 1.19-6.80, p = 0.019, respectively). The patients with right-side accessory pathways with AG and AG+GG genotypes had a significantly increased risk of WPW syndrome compared with those with GG genotype (OR = 3.07, 95% CI = 1.25-7.51, p = 0.014; OR = 2.84, 95% CI = 1.19-6.80, p = 0.019, respectively). The allelic types were not associated with the risk of WPW types and locations.
Conclusions: This study shows that SCN5A gene may be associated with family WPW syndrome among a Russian population. Further studies are provided further evidence of the genetic heterogeneity of WPW.

P1259
CNP/NPR-B/NPR-C AND miRNA TRASCRIPTOMIC EVALUATION IN BLOOD SAMPLES OF HEALTHY DONORS BEFORE AND AFTER SANGIOVESE GRAPE JUICE ADMINISTRATION

B Svezia[1]; M Cabiati[2]; C Salvadori[2]; S Masotti[1]; ME Pe'[1]; V Lionetti[3]; C Passino[3]; S Del Ry[4]
[1]Sant'Anna School of Advanced Studies, Institute of Life Science, Pisa, Italy; *[2]Institute of Clinical Physiology of CNR, Pisa, Italy*; *[3]Institute of Life Science, Scuola Superiore Sant'Anna, Fondazione Toscana "G. Monasterio", Pisa, Italy*; *[4]Institute of Clinical Physiology of CNR, Institute of Life Science, Scuola Superiore Sant'Anna , Pisa, Italy*

Funding Acknowledgements: Studio delle proprietá cardiorigenerative dei microRNA contenuti nelle bacche d'uva di sangiovese toscano nella prevenzione dello scompenso cardiaco.

Background: Nutraceutical studies suggest that a regular intake of plant food has a long-term effect in preventing many diseases and in particular the grape is known to have healthy properties. Many studies were focused on the protective effect of grape consumption on cardiovascular diseases but the modulation of natriuretic peptides (NPs) system has not yet been taken into account. Among NPs members the C-type natriuretic peptide (CNP) is one that is principally involved in regulating cardiac hypertrophy and remodeling in patients after myocardial infarction (MI). Moreover, recent studies suggest that plant food are able to provide genetic material (miRNAs) that might influence gene expression in the recipient organism.
Purpose: to evaluate the mRNA expression of CNP and its specific receptors, NPR-B and NPR-C, in whole blood of healthy donors (HD; n = 7; age34 ± 5 years) before and after Sangiovese grape juice (HD+Sgj) (Vitis vinifera L) administration. Moreover, to investigate the possible miRNA modulatory role in human physiology the transcriptomic analysis of specific miRNA was carried out in the plasma of the same subjects. This study is preliminary to the following recruitment of MI patients.
Materials & Methods: Blood samples were collected into PAXgene blood RNA system tubes for RNA expression study and in K3/EDTA tubes for routinely analyses and circulating miRNAs detection. Total RNA and miRNAs were extracted with PAXgene blood RNA kit and miRNeasy Serum/Plasma kit (Qiagen, Italy) respectively. After specific reverse transcription process, the Real-time PCR reactions were performed in duplicate using CFX-96 detection system (Bio-Rad).
Results: Routinely analyses, NT-proBNP (cardiac function) and sST2 (markers of fibrosis) resulted within the limits of normality. CNP mRNA expression resulted increased in HD+Sgj compared to HD (2253 ± 831.7 vs. 4698 ± 2177). NPR-B and NPR-C transcripts resulted counter-regulated respect to CNP. Significant correlations were observed between CNP and NPR-C (p = 0.04) and between NPR-B and NPR-C (p = 0.03). The expression levels of miR-126 and miR-210, respectively associated with coronary heart disease and cellular hypoxia, did not show significant difference after Sgj intake. A slightly decreased in transcriptional levels were observed for miR-221, miR-320 and miR-295, associated with angiogenic and metabolic processes. Interesting, both plant miRNA increased in HD+Sgj(miR-159:0.49 ± 0.13 vs. 1.21 ± 0.80; miR-166:0.11 ± 0.02 vs. 0.54 ± 0.45).
Conclusions: Our data suggest the activation of CNP/NPR-B/NPR-C pathway after grape juice supplementation. The non-invasive induction of CNP expression could be a desirable achievement for MI patients in order to reduce progression to heart failure. Moreover, in these subjects we observed a plant miRNAs absorption that could suggest a possible epigenetic action. The study could represent an important background for the development of functional foods aimed at modulating gene expression.

P1260
Induction therapy in heart transplantation: Italian single-center experience

M Cottini[1]; GP Pedrazzini Giovanna[1]; GM Gabrilella Masciocco[1]; FT Fabio Turazza[1]; BL Botta Luca[1]; SL Silvia Zannoli[1]; FC Francesco Cislaghi[1]; RN Raffaella Nardella[1]; MM Maria Minnini[1]; SGP Sara Giulia Cornero[2]; MPG Maria Pia Gagliardone[1]; MF Maria Frigerio[1]; CR Claudio Russo[1]
[1]Niguarda Ca' Granda Hospital, Cardiovascular Department, Milan, Italy; *[2]University of Milan, Faculty of Medicine, University of Milan, Milan, Italy*

Purpose: The first few days and weeks after cardiac transplantation (CT) have particularly higher risk of allograft rejection. The immunosuppressive regimens for CT recipients are designed to provide additional strenght by administering specialized antibody induction preparations or high-dose intravenous corticosteroids (or a combination of both). We reported our single center experience in the induction therapy of CT patients.
Methods: We retrospectively reviewed 283 consecutive patients undergoing heart transplantation between 2008 and 2018 (61% male, mean age 50.13 ± 18.19 years old, 28,6% Emergency). Patients were divided in two groups according to the first CD4/CD8 ratio obtained after rATG administration (1 mg/Kg in 8 hours, operative room). In addition, our protocol consists in steroid administration (metilprednisolone (MP) 500 mg, operative room) followed by MP 250 mg/three times in ICU, then prednisone 0,8 mg/Kg/die (per os) with tapering to 0,1 mg/Kg/die in the following 2-6 months. Cyclosporine and tacrolimus were usually started on first or second postoperative day, as well as mycophenolate or everolimus. Through the first year, patients were followed closely, and done endomyocardial biopsies periodically. CCA was performed yearly or according clinical/instrumental judgment.
Results: 145 patients had a CD4/CD8 ratio > 1,5 (G1) while 138 patients had ratio < 1,5 (G2). In-hospital mortality was in G1 10,9% and in G2 7,1%. The early rejection requiring iv steroid therapy were 32,5% (G1 39,8% vs G2 22,1%, p < 0,05), the early graft failure was rare (G1 1,37% vs G2 0,72, p = 0,25). In the G1 group, the first documented incidence of acute cellular rejection was at 28 ± 3 days, the G1 possibility of repeated rejection was the 19,7% (vs G2: 5,4%, p < 0,05), and the G1 incidence of short-term infection was 23,1% (vs G2: 15,7%, p < 0,05).
Conclusion: The CD4/CD8 ratio > 1,5 had an increase incidence of in-hospital mortality at 30-days. The early monitoring of Cd4/CD8 addresses us to improve the management of CT recipients with a significant decrease of early graft failure, rejection and infection in the short-term postoperative period.

P1261
LMNA splice variant progerin is upregulated in dilated cardiomyopathy

M Moritz Messner[1]; SK Ghadge[1]; V Goetsch[1]; A Wimmer[1]; J Doerler[1]; G Poelzl[1]; MM Zaruba[1]
[1]Innsbruck Medical University, Cardiology, Innsbruck, Austria

Background: Mutations in the LMNA gene are a known cause of dilated cardiomyopathy (DCM) leading to heart failure, a growing health care problem worldwide. Hutchinson-Gilford syndrome (HGPS) is a premature aging disease also caused by defined mutations in the LMNA gene. The activation of a cryptic splice donor site leads to the transcription of a defective truncated prelamin A protein called progerin. Low levels of progerin are expressed in healthy individuals associated with ageing. The intention of this work is to address the role of progerin in dilated cardiomyopathy.
Methods and Results: mRNA expression levels of progerin were analyzed in heart tissues of DCM (n = 15) and non-failing hearts (NFH) (n = 10) as control and in blood samples from patients with DCM (n = 56) and healthy controls (n = 10). The expression of progerin mRNA in the human heart was confirmed by sequencing. MRNA levels derived from DCM hearts were significantly higher compared to NFH (1.27 ± 0.42 vs. 0.81 ± 0.24; p = 0.005). In contrast, there were no significant differences of progerin mRNA levels in whole blood cells of DCM patients compared to controls. Linear regression analyses showed that progerin mRNA in the heart is significantly negatively correlated to ejection fraction (r=-0.567, p = 0.003) and positively correlated to left ventricular enddiastolic diameter (r = 0.551, p = 0.004). Increased expression of progerin protein in cell nuclei of DCM hearts were also observed in Immunohistochemistry and Immunofluorescence analysis associated with increased TUNEL+ apoptotic cells.
Conclusion: This data suggest an upregulation of progerin in human DCM hearts and a correlation with left ventricular remodeling. Progerin might be involved in progression of heart failure and myocardial aging.

Basic Science - Vascular Diseases

P1262
Potential value of TAM receptors plasma concentrations for early detection of pulmonary vascular involvement in a cohort of systemic sclerosis patients

A Giubertoni[1]; C Piccinino[1]; M Bellan[2]; M Sguazzotti[3]; E Ubertini[1]; A Dimagli[1]; F Grimoldi[3]; J Zanaboni[1]; P Sainaghi[3]; M Pirisi[3]; PN Marino[1]
[1]Hospital Maggiore Della Carita, Cardiology, Novara, Italy; *[2]Sant'Andrea Hospital, Division of Internal Medicine, Vercelli, Italy*; *[3]Hospital Maggiore Della Carita, Division of Internal Medicine, Novara, Italy*

Background: Early identification of Systemic Sclerosis (SSc) patients at hihher risk of developing Pulmonary Arterial Hypertension (PAH) is a mainstay in the management of SSc. However, traditional first-level tests have shown low sensitivity and

right heart catheterization is an invasive procedure reserved for definite diagnosis. Novel biomarkers might improve the specificity of screening algorithms currently available.

Purpose: We aimed to test the potential diagnostic value of two promising biomarkers, the soluble receptors sMER and sAXL for early identification of vascular involvement in SSc.

Methods: We prospectively recruited 80 patients affected by SSc in our PAH outpatient clinic. All patients underwent full clinical, laboratory and echocardiographic evaluation. Right heart catheterization was performed in 12 patients.

Results: According to guidelines definitions, 12/80 patients were diagnosed with PAH. Table 1 show the differences between groups, with respect to echocardiographic, laboratory and clinical data. In particular, patients affected by PAH showed higher sMER and sAXL concentrations (Figure 1, panel A). However, the mean Pulmonary Artery Pressure (PAP), was directly related to sAXL (?= 0.732; p = 0.007), but not to sMER plasma concentration (Figure 1, panel B).

Conclusions: sAXL and sMER plasma concentration are higher in SSc patients developing PAH; sAXL seems to be a promising biomarker for early identification of pulmonary vascular involvement requiring further investigation for timely treatment.

Table 1

	General population (N. = 80)	SSc (N. = 68)	PAH-SSc (N. = 12)	P
Age, years	67 (57 - 74)	65 (55 - 74)	70 (67 - 77)	0.09
Disease duration, years	7 (3 - 12)	7 (3 - 12)	9 (3 - 12)	0.45
CRP, mg/dL	0.20 (0.07 - 0.65)	0.18 (0.85 - 0.46)	0.77 (0.04 - 0.98)	0.34
Uric acid, mg/dL	4.8 (3.7 - 6.0)	4.7 (3.7 - 5.48)	6.2 (4.8 - 7.6)	0.02
BNP, pg/mL	78.1 (36.9 -135.3)	61.4 (34.4 - 113.8)	314.3 (89.6 - 581.7)	0.0001
FEV1/FVC, %	109 (102 - 116)	110 (103 - 117)	102 (99 - 109)	0.05
DLCO-VA, %	89 (72 - 97)	90 (77 - 101)	49 (46 - 70)	0.0002
EF, %	64.0 (59.2 - 67.0)	65.0 (60.0 - 67.7)	63.0 (57.0 - 64.5)	0.13
PAPs, mmHg	29 (25 - 34)	27 (24 - 33)	53 (48 - 73)	< 0.0001
TAPSE, mm	23.0 (20.0 - 24.0)	23.0 (20.0 - 24.5)	20.0 (18.0 - 22.7)	0.02
Right atrium Area, cm^2	14 (11 - 20)	14 (11 - 16)	19 (18 - 26)	0.002
sAXL, ng/mL	15.10 (11.13-19.32)	14.28 (12.48 - 16.41)	18.53 (15.13 - 24.94)	0.02
sMER, ng/mL	7.67 (4.06-15.85)	6.42 (3.87 - 15.27)	11.10 (9.26 - 27.21)	0.01

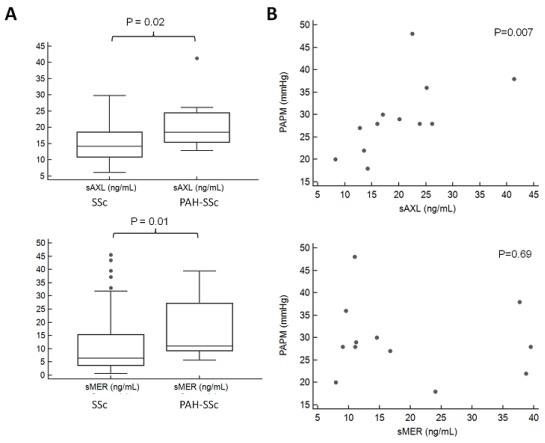


Figure1

Poster Session 2 - Basic Science

Atrial Fibrillation - Pathophysiology and Mechanisms

P1263

Epicardial adipose tissue proteins in heart failure patients: new predictors of long-term atrial fibrillation

RM Agra Bermejo[1]; S Eiras[2]; M Rodriguez Manero[1]; R Fandino[1]; A Fernandez Trasancos[2]; J Sierra[1]; JR Gonzalez Juanatey[1]
[1]*University Hospital of Santiago de Compostela, Santiago de Compostela, Spain*; [2]*Instituto de Investigación Sanitaria de Santiago, Santiago de Compostela, Spain*

Background: Heart failure (HF) is known as an atrial fibrillation (AF) risk factor. Recently, an animal HF model has showed the contribution of epicardial adipose tissue (EAT) to arrhythmogenesis.
Purpose: our main objective was to study if released-proteins by EAT can be predictors of atrial fibrillation in HF patients.
Methods: We obtained EAT from 42 patients undergoing heart surgery with or without HF that survive after 3 years. Patients underwent heart surgery with previous atrial fibrillation were excluded. Released proteins by EAT were collected for 6 hours after being washing overnight. Adiponectin levels in supernatants were analyzed by ELISA. During the follow up (4,74 ± 0,93 years), patients with AF were identified. Differential adiponectin levels between patients with or without HF that developed AF was determined by unpaired t-test analysis. EAT-released proteins between patients whose develop or not AF was analyzed by Liquid Chromatography-Mass Spectrometry (LC-MS/MS).
Results: Our results showed that 22% of HF patients develop AF during follow-up and 13% in those without HF. Released adiponectin levels by EAT were higher in HF with AF during the follow-up than those without AF (14.3 ± 1.5 μg/mL vs. 7.0 ± 5.2 μg/mL; p = 0.03). Moreover, mass spectrometry identified a higher level of EAT-released proteins involved in fibrinolysis pathway (a-2-antiplasmin and plasminogen), leukocytes markers (CD5 antigen-like, leukocyte elastase inhibitor, neutrophil defensin 3) and apoptotic marker (annexin V) in those patients who develop AF.
Conclusions: Epicardial adipose tissue released proteins that could be new predictors of long-term atrial fibrillation in patients with HF and may be possible new therapeutic targets.

P1264

Holter ecg parameters and cardiac fibrosis on mri are stronger predictors of malignant vt and sudden cardiac death than left ventricle ejection fraction among patients with non-ischemic cardiomyopathy

A Azamat Zhambeev[1]; N Shlevkov[1]; O Stukalova[1]; A Gasparyan[1]; KH Tengizov[1]; V Shitov[1]; S Sokolov[1]
[1]*Cardiology Research and Production Center, Department of Arrhythimas, Moscow, Russian Federation*

Background: Risk-stratification of malignant ventricular tachyarrhythmias (VT) and sudden cardiac death (SCD) is one of the unresolved issues in patients with non-ischemic cardiomyopathies (NICMP).
Aim: to identify the most powerful predictors of malignant ventricular tachyarrhythmias and sudden cardiac death in patients with non-ischemic cardiomyopathy.
Methods: Twenty patients (14 males / 6 females, mean age = 55 ± 18 years) with NICMP and LVEF < 35% with recently implanted ICD or CRTD were included into the prospective study. During 19 (18-23) months of follow-up 5(25%) patients exhibit VTs/SCD (group 1), while the remaining 15 patients survived without sustained VTs (group 2). Multiple Holter ECG, echocardiography (ECHO) and contrast magnetic resonance imaging (MRI) parameters were compared between groups.
Results: The ROC-analysis of identified predictors of VTs/SCD in study patients are presented in the table.
Conclusion: The presence of multiple forms of ventricular ectopy on Holter ECG and more substantial cardiac fibrosis by contrast MRI are the most significant predictors of malignant VTs and SCD in patients with NICMP. These parameters are superior to LVEF by ECHO in their diagnostic significance according to ROC-analysis.

Parameters	Group 1 'VT/SCD' (n = 5)	Group 2 'No VT/SCD' (n = 15)
The number of couplet ventricular extrasystoles per day (by Holter ECG) The area under the ROC curve = 0.862	83 (13-124)	2 (0-9)
The total number of ventricular extrasystoles in VTs per day (by Holter ECG) The area under the ROC curve = 0,846	9 (6-11)	0 (0-4)
Total mass of fibrosis, gr (by cardiac MRI) The area under the ROC curve = 0,80	7,3 (6,4-8,1)	4,0 (3,5-5,9)
The LVEF, % (by ECHO) The area under the ROC curve was 0,785	20 (20-23)	30 (25-32)
Determine 2 and more VT (by Holter ECG) The area under the ROC curve = 0,78	80%	20%
Maximum heart rate per day (by Holter ECG) The area under the ROC curve = 0,769	121 (109-130)	100 (97-113)
Number of segments with endomyocardial fibrosis (by cardiac MRI) The area under the ROC curve = 0,746	3 (1-3)	1 (0-2)

Ventricular Arrhythmias and SCD–Treatment

P1265

Increased expression of galectin-3 in the interstitium of left ventricular myocardium of dogs with chronic heart failure

V Singh-Gupta[1]; RC Gupta[1]; HN Hani Sabbah[1]
[1]*Henry Ford Hospital, Detroit, United States of America*

Background: Accumulation of collagen in the cardiac interstitium termed "reactive interstitial fibrosis (RIF)" occurs in heart failure (HF) with reduced ejection fraction (HFrEF) as well as in HF with preserved EF (HFpEF). This maladaptation leads to increased myocardial stiffness that negatively impacts ventricular filling. RIF also results in poor oxygen diffusion between capillaries and cardiomyocytes leading to cardiomyocyte hypoxia that promotes cellular contractile dysfunction and triggers programmed cell death. The protein galectin-3 (GAL-3) is a member of the lectin family. Increased expression of GAL-3 is implicated in the development of fibrosis in multiple organs including the heart. Elevated levels of GAL-3 are significantly associated with higher risk of death in patients with HF. In this study, we examined whether increased expression of GAL-3 occurs in the LV interstitium of dogs with chronic HF that also manifest increased levels of RIF.
Methods: Studies were performed in LV tissue obtained from 7 normal (NL) dogs and 7 dogs with coronary microembolization-induced HF. Frozen LV sections, 6 μm in thickness, were used for fluorescence immunostaining with antibodies against myosin heavy chain and GAL-3. DAPI (4', 6-diamidino-2-phenylindole) was used to stain nuclei. Confocal images of stained sections were obtained with an Olympus Fluoview FV1000 laser scanning biological microscope. From each section, 4-6 fields, each ~10 mm2, were randomly selected for laser scanning and subsequently used to calculate the percent area occupied by GAL-3 (%aGAL-3) from each field. The percent area occupied by RIF (%aRIF) was also calculated using frozen sections stained with fluorescein-labeled peanut agglutinin.
Results: In NL dogs, the %aRIF was 3.70 ± 0.07 and %aGAL-3 was 2.40 ± 0.45. In dogs with HF, the %aRIF increased significantly to 13.5 ± 0.57 ($p < 0.05$) and the %aGAL-3 increased significantly to 12.82 ± 1.15 ($p < 0.05$).

Conclusions: The results indicate that in dogs with HF, increased levels of RIF is associated with increased interstitial levels of GAL-3. The findings support the use of this dog model of HF to evaluate the effects of GAL-3 inhibitors for preventing or attenuating RIF that develop during HF.

Chronic Heart Failure–Pathophysiology and Mechanisms

P1266

Necroptosis in post-ischemic heart failure: causality of cardiac dysfunction and remodeling?

M Martin Lichy[1]; A Szobi[1]; J Hrdlicka[2]; M Kocmalova[3]; T Rajtik[1]; S Franova[3]; J Neckar[2]; F Kolar[2]; A Adameova[1]
[1]Comenius University, Department of Pharmacology and Toxicology, Faculty of Pharmacy, Bratislava, Slovak Republic; *[2]Academy of Sciences of the Czech Republic, Institute of Physiology, Prague, Czech Republic*; *[3]Comenius University, Jessenius Faculty of Medicine in Martin, Bratislava, Slovak Republic*

Funding Acknowledgements: APVV15-607, VEGA 1/0271/16, UK/68/2017

Background: Although failing hearts of ischemic etiology have been associated with progressive cell death, it is still unknown which particular cell death mode is responsible for the phenotypes of this cardiac syndrome. In addition, underlying molecular pathways of this cell death remain to be elucidated.
Purpose: The purpose of this study was to investigate the executive mechanisms of necroptosis in heart failure (HF) involving the canonical necroptotic pathway (RIP1-RIP3-MLKL) and the translocation of the terminal execution protein into the plasma membrane, a cytotoxic event understood to induce cell lysis during necroptosis. By this approach, we intended to determine whether these mechanisms can underlie cardiac dysfunction and remodeling of non-ischemic tissue.
Methods: In male Wistar rats, ligation of the left anterior descending artery was used to induce myocardial infarction progressing to chronic HF of ischemic etiology. 42 days after surgery, echocardiography was performed along with collagen content measurement. Non-ischemic left ventricular tissue was subjected to subcellular fractionation and immunoblotting analysis. To get a more comprehensive view on investigated mechanisms, tissue inflammatory response (cytokines) and oxidative stress (MDA) were assessed.
Results: In post-ischemic failing hearts, which exhibited adverse remodeling and contractile dysfunction as assessed by LVDd, LVDs and a decrease in FS, collagen content and pro-inflammatory cytokine levels were increased. Preliminary analysis showed, that p-MLKL as well as both phosphorylated and nonphosphorylated RIP3 levels were increased in whole cell lysates of HF indicating necroptosis execution. Supportive to these findings, detailed analysis of the membrane fraction of diseased hearts has also revealed the increased expression of pSer232-RIP3. In addition, in this particular fraction, increased extent of oxidative stress was evidenced by higher MDA and NOX2 levels. On the other hand, we were unable to detect any significant apoptosis activation in HF group. Neither active csp-8, a crucial negative regulator of necroptosis and an apoptotic initiator, nor other apoptotic markers such as p17/p19 csp-3, p25 PARP1 and Bcl2/Bax ratio were increased in failing hearts.
Conclusions: This study has indicated that the alterations in pro-necroptotic proteins and their membrane relocalization rather than apoptosis activation, might, at least in part, contribute to decreased adaptation against ischemic injury and thereby promote the phenotypes of HF.

P1267

Genetic diagnosis in transthyretin cardiac amyloidosis - a single Polish centre experience

M Monika Gawor[1]; A Sioma[1]; L Mazurkiewicz[1]; M Franaszczyk[2]; J Szczygiel[1]; M Spiewak[3]; B Milosz-Wieczorek[3]; M Marczak[3]; Z Bilinska[4]; J Grzybowski[1]
[1]Institute of Cardiology, Department of Cardiomyopathies, Warsaw, Poland; *[2]Institute of Cardiology, Department of Medical Biology, Warsaw, Poland*; *[3]Institute of Cardiology, CMR Unit, Warsaw, Poland*; *[4]Institute of Cardiology, Unit for Screening Studies in Inherited Cardiovascular Diseases, Warsaw, Poland*

Background: Transthyretin (TTR) cardiac amyloidosis is an underdiagnosed but increasingly recognized cause of heart failure and may result from the aggregation of mutant or wild-type TTR protein in the heart. More than 100 different disease-causing mutation of the TTR gene have been reported. Countries such as Portugal, Japan and Sweden have certain high frequency mutations. Common mutations in Poland have yet to be identified.
Purpose: This is the first study of the mutational pattern of patients with TTR cardiac amyloidosis in Poland.
Methods: We performed clinical and genetic testing of patients with TTR cardiac amyloidosis, who were hospitalised in our centre in 2014-2017.
Results: Three unrelated male patients have been diagnosed with hereditary TTR cardiac amyloidosis. All of them had the same rare TTR mutation - Phe33Leu. Age of onset differed among the patients. Two patients had first symptoms in their late fifties. One patient had first symptoms in his late forties. Characteristic clinical features included cardiomyopathy with increased left and right ventricular wall thickness, sparkling echoes and decreased function of left ventricle. Cardiac Magnetic Resonance (CMR) scan revealed the presence of late-gadolinium-enhancement (LGE) in subendocardial part of left ventricular segments. The standard 12-lead electrocardiogram demonstrated low QRS voltage in the limb leads and nonspecific ST-T wave changes. One patient had persistent atrial fibrillation. Laboratory examination revealed significantly increased level of troponin T and NT- proBNP. Two patients suffered from painful peripheral polyneuropathy. One patient had carpal tunnel syndrome.
Conclusions: Here we report Polish patients with a rare TTR mutation Phe33Leu. To date, the TTR Phe33Leu mutation has only been reported in two unrelated American families with Polish descent, one Polish-Lithuanian family, one Swedish family and one Taiwanese family. Previous literature data about Polish background in families with Phe33Leu mutation, and our experiences, suggest that this TTR mutation may be frequent in Polish population.

P1268

Differential endomyocardial expression of SGLT1 in idiopathic dilated cardiomyopathy patients with and without diabetes mellitus.

M Marc Vanderheyden[1]; W Heggermont[1]; S Verstreken[1]; R Dierckx[1]; M Goethals[1]; J Bartunek[1]
[1]OLV Hospital Aalst, Cardiovascular Center, Aalst, Belgium

Introduction: Sodium-Glucose cotransporter(SGLT) is thought to be expressed in the heart although more information is required to delineate the exact subtypes expressd in human heart. We herein investigated whether apart from the common glucose transporter 1(Glut1) and 4(Glut4), SGLT1 and 2 are expressed in human heart. In addition to test for differences related to diabetes mellitus we analyzed SGLT mRNA expression in idiopathic dilated cardiomyopathy(CMP) pts with diabetes mellitus (DM+) and without diabetes mellitus(DM-) .
Methods and results : LV endomyocardial biopsies obtained from 76 patients with heart failure due to idiopathic dilated cardiomyopathy (ejection fraction $44 \pm 3\%$; LVEDVI: 115 ± 7 ml/m2 and PCWP 20 ± 1 mm Hg) were analyzed for SGLT1, SGLT2, Glucose transporter 1(Glut1) and glucose transporter 4(Glut4) mRNA gene expression using quantitative RT-PCR.
Results: Baseline hemodynamic characteristics were similar between DM+ and DM- pts(EF: 43 ± 6 vs $43 \pm 3\%$, p = ns; PCWP 20 ± 2 vs 20 ± 1 mm Hg, p = ns). Whereas no difference in Glut1 and Glut4 mRNA gene expression was observed between both groups(p = ns), DM+ pts were characterized by significantly higher SGLT1 expression compared to DM-pts($0{,}2391 \pm 0{,}0280$ vs $0{,}1597 \pm 0{,}0125$ rel units; p = 0.007). In both groups SGLT2 endomyocardial mRNA was not detected. A significant correlation was noted between SGLT1 and Glut4 in DM-pts ($p < 0{,}0001$) which was not the case for DM+ pts (p = 0.07).
Conclusion: Besides the common Glut1 and Glut4, SGLT1 not SGLT2 plays a role in glucose transport in CMP. The identification of higher SGLT1 gene expression in DM+ CMP and the lack of any relationship between SGLT1 and Glut4 might suggest that glucose uptake is differentially regulated in DM+ pts compared to DM-pts.

P1269

Decreased longitudinal left ventricular contraction after acute myocardial infarction in a porcine model revealing the opportunity for new treatments with mechanical circulatory support devices

J Karlsson[1]; K Solem[2]; E Heiberg[1]; M Kanski[1]; D Nordlund[1]; R Jablonowski[1]; S Kopic[1]; C Xanthis[1]; S Bidhult[1]; H Engblom[1]; D Erlinge[3]; H Arheden[1]; M Carlsson[1]
[1]Lund University, Department of Clinical Sciences Lund, Clinical Physiology, Lund, Sweden; *[2]Syntach AB, Lund, Sweden*; *[3]Lund University, Department of Clinical Sciences Lund, Cardiology, Sweden, Lund, Sweden*

Funding Acknowledgements: Swedish foundation for strategic research, Swedish research council, The Swedish Heart-lung foundation

Introduction: Decreased systolic atrio-ventricular plane displacement (AVPD) towards the apex independently predicts mortality. In humans, 60% of left ventricular (LV) stroke volume (SV) is generated by the AVPD and longitudinal displacement is decreased after an acute myocardial infarct (AMI). How an AMI changes AVPD and LVSV at the individual level is not known from patient studies. Such information could motivate the design of future treatments and devices aiming to improve the AVPD.
Purpose: To investigate the relationship between the AVPD and LVSV in an experimental AMI model.

Methods: Nine pigs (landrace, circa 40 kg) were studied with cardiac MRI before AMI (baseline) and 2 hours after AMI reperfusion. AMI was induced by a selective coronary occlusion with a PCI-balloon under fluoroscopy guidance for 40 minutes in the left anterior descending artery (LAD) with varied distances distal to the first diagonal branch (D1). Cardiac MRI at baseline and 2 hours post-AMI included short axis and long axis cine images for function and volumes. Late gadolinium enhancement (LGE) were acquired post-AMI in the same image planes for infarct size. MR images were analysed using the post-processing software Segment v2.1 (http://segment.heiberg.se). The AVPD was measured in the 2-chamber, 3-chamber and 4-chamber cine images. Values are given as mean ± SD, results were compared using Pearson correlation and paired t-test.
Results: LAD occlusion caused an infarct size of 30.0 ± 9.8% (range 19.5-45.0%) and significant decrease in ejection fraction (EF) from 46.0 ± 6.4% to 33.0 ± 7.3% ($p < 0.001$). LV end-diastolic volume decreased (95.1 ± 12.2ml to 83.9 ± 17.1 ml) and end-systolic volume increased (51.1 ± 7.2ml to 56.3 ± 13.5 ml) 2 hours post-AMI. AVPD was significantly correlated to LVSV ($p < 0.0001$, $R = 0.82$) (Fig 1) and cardiac output ($p = 0.038$, $R = 0.49$). AMI caused decreased AVPD (9.3 ± 1.4mm to 6.0 ± 1.5mm) and LVSV (43.9 ± 9.6ml to 27.6 ± 7.8ml) in all pigs compared to baseline ($p < 0.001$ for both) (Fig 2 & 3). The correlation between relative decrease in AVPD and infarct size did not reach statistical significance ($p = 0.09$, $R = 0.59$).
Conclusions: This study has shown that AMI causes concomitant decrease in LVSV and AVPD and a strong correlation between LVSV and AVPD within the same population. The coefficient of determination ($R^2 = 0.67$) is similar to the 60% contribution of AVPD to LVSV found in humans. The relationship between decreased AVPD and LVSV after AMI in this porcine model enabels testing of future treatment options with mechanical circulatory support devices designed to improve AV-plane motion.

Fig 1. Stroke Volume vs AVPD

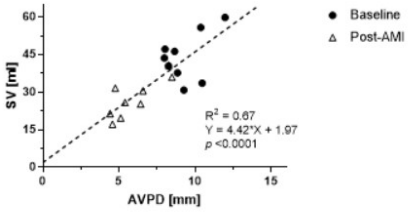


Fig 2. AVPD: Baseline vs Post AMI

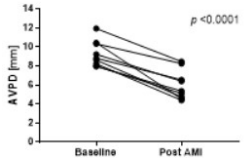
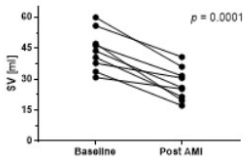


Fig 3. Stroke Volume: Baseline vs Post AMI

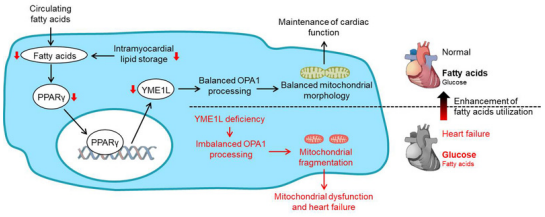


P1270

Enhancing fatty acid utilization ameliorates mitochondrial fragmentation and cardiac dysfunction via rebalancing OPA1 processing in the failing heart

X Xing Zhang[1]; Y Guo[1]; F Gao[1]
[1]*Fourth Military Medical University, Xi'an, China People's Republic of*

Background: Heart failure is characterized by reduced fatty acid (FA) utilization associated with mitochondrial dysfunction. Recent evidence has shown that enhancing FA utilization may provide cardioprotection against heart failure. However, the underlying mechanism of lipoprotection in the failing heart is poorly understood.
Purpose: Our aim was to investigate the effects and the underlying mechanisms of cardiac FA utilization on cardiac function in response to pressure overload.
Methods: Transverse aortic constriction (TAC) was used in C57 mice to establish pressure overload-induced heart failure.
Results: TAC mice fed on a high fat diet (HFD) exhibited increased cardiac FA utilization and improved cardiac function and survival compared with those on control diet. Such cardioprotection could also be provided by cardiac-specific overexpression of CD36. Notably, both HFD and CD36 overexpression attenuated mitochondrial fragmentation and improved mitochondrial function in the failing heart. Pressure overload decreased i-AAA protease YME1L expression and induced the proteolytic cleavage of the dynamin-like guanosine triphosphatase OPA1 as a result of suppressed FA utilization. Enhancing FA utilization upregulated YME1L expression and subsequently rebalanced OPA1 processing, resulting in restoration of mitochondrial morphology in the failing heart. In addition, cardiac-specific overexpression of YME1L exerted similar cardioprotective effects against heart failure to those provided by HFD or CD36 overexpression.
Conclusions: These findings demonstrate that enhancing FA utilization ameliorates mitochondrial fragmentation and cardiac dysfunction via rebalancing OPA1 processing in pressure overload-induced heart failure, suggesting a unique metabolic intervention approach to improving cardiac functions in heart failure.



Schematic figure

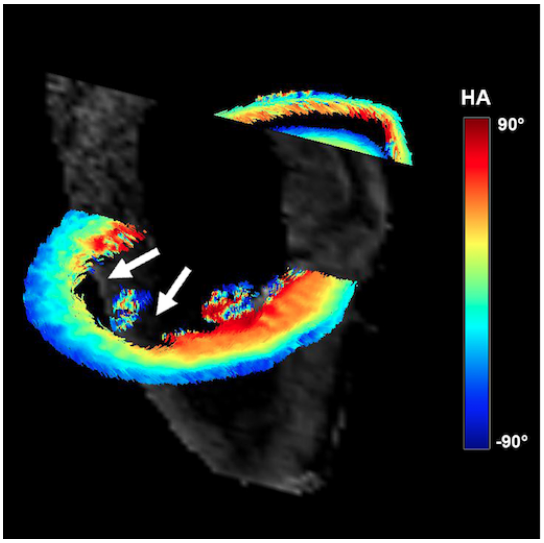
P1271

The role of subendocardial form and function in heart failure with preserved ejection fraction

N Beyhoff[1]; D Lohr[2]; A Foryst-Ludwig[1]; E Smeir[1]; R Klopfleisch[3]; LM Schreiber[2]; U Kintscher[1]
[1]*Charité - Universitätsmedizin Berlin, Center for Cardiovascular Research, Berlin, Germany*; [2]*University Hospital Würzburg, Comprehensive Heart Failure Center (CHFC), Chair of Cellular and Molecular Imaging, Würzburg, Germany*; [3]*Free University, Department of Veterinary Pathology, Berlin, Germany*

Funding Acknowledgements: Supported by the DZHK (German Centre for Cardiovascular Research) and by the BMBF (German Ministry of Education and Research)

Background: The subendocardium is highly susceptible to injury and is therefore considered to be the earliest myocardial layer affected during cardiovascular disease



Diffusion tensor imaging analysis.

development. Several studies have postulated the involvement of subendocardial damage in heart failure with preserved ejection fraction (HFpEF), especially at subclinical state. However, morphologic-functional studies regarding the impact of subendocardial status in HFpEF are currently lacking.
Purpose: To identify the role of subendocardial damage in HFpEF.
Methods: 129/Sv mice were injected with a high-dose of Isoproterenol (ISO) to induce isolated subendocardial damage, or saline as appropriate control. Animals were challenged with a graded exercise test protocol to determine exercise capacity. Two weeks after final treatment with ISO/saline, comprehensive echocardiographic examinations and gene expression analyses were performed. Myocardial microstructure was assessed by histologic analyses and diffusion tensor magnetic resonance imaging (Picture).
Results: ISO-treatment led to pronounced fibrotic lesions, predominantly in the subendocardial layer, which was accompanied by increased atrial natriuretic peptide

levels ($p < 0.05$ vs. control). Left-ventricular ejection fraction and fractional shortening were comparable among both groups. Global Longitudinal Strain and -Strain Rate were markedly impaired due to ISO-treatment, whereas radial and circumferential strain values remained unaffected. Subendocardial fibrosis induced a moderate diastolic dysfunction and increased estimated filling pressures in the absence of lung congestion or reduced exercise capacity.
Conclusion(s): Isolated subendocardial fibrosis alone is able to induce several characteristics of HFpEF, however, does not lead to heart failure symptoms or signs under experimental conditions. Diagnostic assessment of subendocardial form and function may contribute to early assessment of cardiac damages in subclinical patients at risk to develop HFpEF, and may consequently improve prevention of functional impairment.

P1272

Impact of aging and obesity on cardiac function in female mice

C Aad Withaar[1]; C Gehlken[1]; HHW Sillje[1]; SPC Lam[1]; RA De Boer[1]
[1]*University Medical Center Groningen, Experimental Cardiology, Groningen, Netherlands*

Background/Introduction: Advancing age, female gender, and obesity are well-recognized as key risk factors in heart failure. Aging and co-morbidities are believed to drive cardiac dysfunction, by impacting the loading conditions and by inducing systemic inflammation, which may partly explain why elderly obese woman are at higher risk. Despite this knowledge, female sex is largely neglected in pre-clinical research. We aimed to develop a murine model of heart failure based on the co-existence of these 3 risk factors
Purpose: To study the effects of aging and diet on cardiac function in female mice, and to determine the morphology and cardiac function assessed by echocardiography.
Methods: 4 and 18 months old female C57BL/6 WT mice were fed a low fat diet (LFD) or high fat diet (HFD) for 12 weeks. Cardiac function where determined before sacrifice by echocardiography and strain analysis where performed offline. Body mass composition and oral glucose tolerance were determined.
Results: Mice maintained on a HFD develop obesity and body mass exceeded LFD-fed control mice by 25% after 8 weeks ($p < 0.01$). HFD further significantly increased total fat mass compared to LFD-fed animals ($9{,}0 \pm 1{,}0$ vs $25{,}5 \pm 1{,}4$ g $p < 0.01$). HFD-fed mice had a significantly impaired glucose handling after oral glucose tolerance test (area under the curve, $p < 0.01$). Total heart weight to tibia length ratio (8.3 ± 0.5 vs $11{,}5 \pm 0.8$ $p = 0.018$) was increased in 18 month mice on HFD compared to LFD. Normal left ventricular ejection fraction and fractional shortening was observed in HFD and LFD-fed animals. Strain analysis shows myocardial alterations suggesting contractile dysfunction. This is associated with the development of heart failure, as evidenced by decreased effort tolerance on treadmill running between young and old animals, and further decreased by HFD.
Conclusion We conclude that a 'multiple hit' model in female mice exposed to long term HFD results in a phenotype that resembles heart failure as commonly observed in elderly human female patients.

P1273

Functional state of the rats myocardium in postinfarction and diabetic remodeling

D Dina Kondrat'eva[1]; SA Afanasiev[1]; SV Popov[1]
[1]*Research Institute of Cardiology, Tomsk Scientific Center, Tomsk, Russian Federation*

Background/Introduction: Diabetes mellitus aggravates of the cardiovascular diseases progression with a deterioration of the contractile function of the heart and serious violations of intracellular metabolism. This is determined by changes in energy metabolism, which is a trigger of functional and structural changes in the cardiomyocytes, including the alteration of the intracellular calcium handling proteins and, consequently, excitation-contraction uncoupling of cardiomyocytes.
Purpose: Aim of study is evaluate the relation between level of calcium handling proteins and energetic metabolism in contractile dysfunction of rat myocardium in postinfarction and diabetic damage.
Methods: Study was performed on adult Wistar rats with postinfarction lesion and diabetes mellitus alone and combined. The postinfarction lesion developed after 6 weeks of coronary artery occlusion. Diabetes mellitus was induced by single injection streptosotozine (60 mg/kg i.p.). Inotropic reaction on rest period (4 - 60 sec) were studied on papillary muscles, bathed at 37 C in oxygenated Krebs-Henzelait solution and stimulated at 0.5 Hz. The protein levels of SERCA2a and RyR2 in myocardium were determined by Western blotting. Oxygen consumption by mitochondria was measured using a Clark-type oxygen electrode. The activity of lactate dehydrogenase and succinate dehydrogenase were determined by histochemical method.
Results: Development of postinfarction damage alone in experimental animals led to depression of post-rest contraction. The force of post-rest twitches was better preserved in diabetic rats and postinfarction rats with diabetes mellitus. This post-rest behavior corresponded with alteration of calcium handling proteins level (RyR2, SERCA2a). The most decrease of RyR2 and SERCA2a levels were obtained in postinfarction rats. In rats with combined pathology preserving levels of calcium handling proteins were found. The development of monopathologies resulted in a significant decrease in the intensity of energy production. The energy production activity in diabetic rats was more significant decrease in compare with postinfarction rats, despite the fact that contractile disturbance of postinfarction rats was more severe. However, the development of the combined pathology resulted in the preservation of the energy production near the control level. The activity of succinate dehydrogenase (Krebs cycle key enzyme) and lactate dehydrogenase (glycolysis key enzyme), and mitochondrial respiration were most preserved in postinfarction rats with diabetes mellitus.
Conclusion: Development of diabetes mellitus in postinfarction rats facilitate preservation of inotropic reserve of myocardium, expressed by post-rest reaction, and expression of Ca2+-ATPase and ryanodine receptors and activity of key enzymes of glycolysis, Krebs cycle, and oxidative phosphorylation in comparison with postinfarction rat without diabetes mellitus.

P1274

Expression profile of the natriuretic peptide system in the heart of mice with myocardial infarction exposed to sangiovese grape juice.

B Svezia[1]; M Cabiati[2]; M Matteucci[1]; C Passino[3]; ME Pe'[1]; V Lionetti[1]; S Del Ry[4]
[1]*Sant'Anna School of Advanced Studies, Institute of Life Science, Pisa, Italy*; [2]*Institute of Clinical Physiology of CNR, Pisa, Italy*; [3]*Institute of Life Science, Scuola Superiore Sant'Anna, Fondazione Toscana "G. Monasterio", Pisa, Italy*; [4]*Institute of Clinical Physiology of CNR, Institute of Life Science, Scuola Superiore Sant'Anna , Pisa, Italy*

Funding Acknowledgements: Studio delle proprietá cardiorigenerative dei microRNA contenuti nelle bacche d'uva di sangiovese toscano nella prevenzione dello scompenso cardiaco

Background: Despite many studies were focused on the protective effect of grape and wine consumption on cardiovascular diseases, to the best of our knowledge the modulation of natriuretic peptides (NPs) system was not taken into account.
Purpose: to investigate the impact of grape juice (Vitis vinifera L., cv. Sangiovese) administration on the NPs system in a murine model of myocardial infarction.
Materials & Methods: Male and female C57BL/6J mice (n = 33) 10-12 weeks' old were randomly subdivided into 3 groups: 1) Sham (n = 7); 2) Mice with myocardial infarction (MI, n = 15); 3) MI fed for 4 weeks with a standard diet supplemented with 200 µl/die of Sangiovese juice25% vol/vol concentrated (MI+Sj, n = 11). Two-dimensional (2-D) echocardiography was performed on mice at baseline and 4 weeks after surgical procedures (MyLab 25, EsaoteSpA Genova, Italy). Cardiac function was evaluated by measuring left ventricle ejection fraction (LVEF). At the end of the protocol, the animals were sacrificed by isoflurane overdose and cardiac tissue collected for biomolecular and histological analysis. The transcriptomic profile of the NPs system in cardiac tissue of all animals was investigated by Real-Time PCR; histological analyses were also performed to assess myocardial fibrosis.
Results: The 2D- echocardiographic studies showed that infarcted animals developed progressive cardiac remodelling over 4 weeks from left anterior descending coronary artery ligation. LVEF% was significantly decreased in MI when compared to sham ($p < 0.01$). MI+Sj showed a partial recovery of LVEF. MI showed a higher expression level of ANP and BNP ($p = 0.0002$) compared to the sham. After Sangiovese grape juice administration to mice with myocardial infarction, ANP mRNA cardiac level decreased whereas BNP expression did not show any significant difference and CNP was significantly higher compared to sham ($p = 0.007$) and MI ($p = 0.03$). The mRNA cardiac expression of NPR resulted higher in MI than in the sham also if only NPR-B mRNA level was statistically significant ($p = 0.02$). In MI+Sj the mRNA expression of NPR-B ($p = 0.002$) and NPR-C showed a lower level with respect to MI, whereas NPR-A gene expression increased compared to MI. Masson's trichrome stain on infarcted heart tissue revealed a decrease in infarct size in MI+Sj as compared with MI ($p = 0.08$). In the MI+Sj, the fibrotic tissue was decreased compared to vital myocardium thereby indicating a reduction in cardiomyocytes death.
Conclusions: The data obtained suggest that in ischemic condition Sangiovese grape juice is able to modulate NPs system. In particular, CNP plays a direct cardioprotective effect through the activation of its specific receptor NPR-B but also acting as an EDHF by binding NPR-C. The data obtained suggest that in ischemic condition Sangiovese grape juice is able to mitigate fibrosis and to modulate NPs system.

P1275

Characterisation of a novel mouse-pacemaker model for mechanistic studies of dyssynchrony in heart failure

M Stahlberg[1]; R Nakagawa[2]; DI Lee[2]; B Lin[2]; DI Bedja[2]; G Zhu[2]; DA Kass[2]
[1]Karolinska Institutet, Stockholm, Sweden; [2]Johns Hopkins University of Baltimore, Department of Cardiology, Baltimore, United States of America

Funding Acknowledgements: National Institute of Health; American Heart Association; Swedish Research Council; Swedish Society of Medicine; Swedish Society of Cardiology

Purpose: Cardiac dyssynchrony plays an important role in clinical heart failure. However, the biological mechanisms underlying its detrimental effects are not well defined and have only been studied in larger mammals where genetic manipulation is not feasible. The purpose of this study was to develop a model of dyssynchronous heart failure in the mouse, a genetically modifiable animal, and to use this model to characterize the effect of dyssynchrony on phospho-kinase activation in failing hearts.
Methods: Moderate heart failure was induced in wild type (C57/Bl6) mice by ischemia-reperfusion (I/R). After recovery, an ECG-lead and a right ventricular pacing (RVP) lead was implanted Mice were then divided into two groups: (i) Dyssynchronous heart failure (DysHF - four weeks of continuous RVP) and (ii) Synchronous heart failure (SyncHF - no pacing). Nonfailing/instrumented wild type mice served as additional control (WT-CON). Fractional shortening (FS) and left ventricular end-systolic diameter (LVESD) were measured using echocardiography after pacemaker surgery and after four weeks. Mice hearts (DysHF, n = 8; SyncHF, n = 8; WT-CON, n = 5) were analyzed for relative levels of phosphorylation/activation of 46 kinase phosphorylationsites using a phospho-kinase array kit.
Results: QRS duration increased from 10 ± 1 ms in sinus rhythm to 15 ± 2 ms with RVP ($p = 0.002$). The septum-to-posterior wall motion delayed was prolonged with RVP (22 ± 6 ms) compared to sinus rhythm (3 ± 3 ms, $p < 0.001$). After four weeks FS was unchanged in the SyncHF group ($36 \pm 6\%$) but decreased in the DysHF group (24 ± 6, $p < 0.01$ vs. both others). LVESD was unchanged after four weeks in SyncHF mice (2.4 ± 0.4 mm) but was significantly increased in DysHF mice (3.1 ± 0.6 mm, $p < 0.01$). Eleven of 46 kinase phosphorylation sites had significantly higher level of phosphorylation/activation in the DysHF compared to SyncHF groups (Figure 1).
Conclusion: RVP induces left ventricular dyssynchrony in mice that when applied for four weeks accelerates heart failure remodeling in infarcted hearts. This is associated with phosphorylation/activation of kinases that regulate a range of cellular processes including cell survival, energy homeostasis and hypertrophy. This novel model can now be used to study the effect dyssynchrony on cellular signaling pathways in a genetically modifiable animal for the first time.

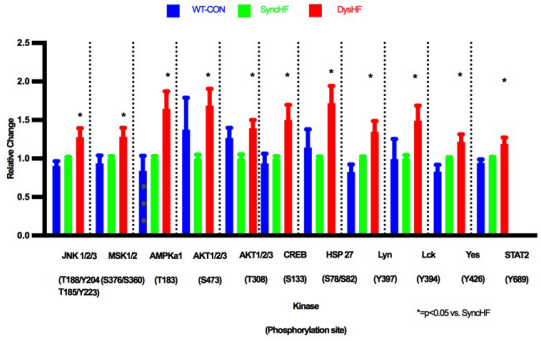


Figure 1

P1276

MIF deletion prevents heart failure after acute myocardial infarction by controlling macrophage polarization

PL Luedike[1]; MH Heisler[1]; U Hendgen-Cotta[1]; UF Floegel[2]; IH Hilgendorf[3]; JB Bernhagen[4]; TR Rassaf[1]
[1]University of Duisburg-Essen, West German Heart Center, Department of Cardiology and Vascular Medicine, Essen, Germany; [2]University Hospital Duesseldorf, Department of Cardiology, Pulmonology and Vascular Medicine, Duesseldorf, Germany; [3]University of Freiburg, Department of Cardiology and Vascular Medicine, Freiburg, Germany; [4]Ludwig-Maximilians University, Institute for Stroke and Dementia Research (ISD), Munich, Germany

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Objectives: This experimental study aimed to investigate whether genetic deletion of MIF influences the inflammatory healing and consecutive cardiac function after myocardial infarction.
Background: The fine-tuned recruitment of monocytes to the myocardium represents the first step of healing after myocardial ischemia. Damage-associated pattern molecules (DAMPs) are the first to initiate the sterile immune response via toll like receptors (TLR) like TLR4. MIF controls TLR4 expression in leukemia macrophages and is also released during myocardial I/R and exhibits
auto- and intracrine cardioprotective activities. However, MIF's role in cardiovascular disease is dual, as it also has a clear-cut cardioprotective role in the setting of myocardial I/R injury contrasting the bonafide negative function in the promotion of arteriosclerosis development. Whether MIF-mediated regulation of TLR4 expression in myocardial tissue might influence the inflammatory environment after myocardial ischemia is unknown.
Methods: Wild type (WT) and MIF-KO mice underwent myocardial ischemia (50min) and subsequent reperfusion in vivo. Functional magnetic resonance imaging (MRI) was performed before and after I/R (d0,d1,d3,d5,d7,d28). Detection of late gadolinium enhancement (LGE) was applied for infarct size quantification. MIF-dependent TLR4 expression was analyzed in bone-marrow derived monocytes (BMDM) in vitro and in Ly6Chi monocytes after myocardial I/R in vivo. Polarization behavior of WT and MIF-KO macrophages was analyzed after M-CSF-mediated differentiation of BMDM.
Results: Infarct sizes (LGE) were similar in MIF-KO and WT mice at d1 after I/R ($n = 9$; $p = ns$). Ejection Fraction (EF) of MIF-KO and WT mice did not alter before and at d1 after I/R, however at d7 MIF-KO mice showed an improved recovery of heart function that persisted until d28 after I/R ($n = 9$; $*p < 0.05$). Furthermore, pharmacological inhibition of MIF by MIF-antibody led to a decreased expression of TLR4 in BMDM in vitro. Moreover, pharmacological MIF inhibition through intravenous application of MIF-antibodies attenuated TLR4 expression measured by FACS analysis on immigrated Ly6Chi-monocytes at d1 after myocardial I/R injury in vivo demonstrated. In vitro experiments revealed that stimulation with IL-4 and DAMPs showed a distinctly attenuated polarization of MIF-KO macrophages into inflammatory subtypes with decreased iNOS and increased arginase 1 expression.
Conclusion: MIF deficiency promotes polarization of functionally beneficial macrophages after myocardial I/R injury, thus improves healing and prevents development of ischemic heart failure. These date give first insights into a potential cardioprotective role of MIF inhibition after prolonged ischemia and reperfusion injury.

P1277

Selective heart irradiation induces left ventricular hypertrophy and diastolic dysfunction with overexpression of the miR-212/132 cluster

M Sarkozy[1]; R Gaspar[1]; A Zvara[2]; L Kiscsatari[3]; Z Varga[3]; B Kovari[4]; M Kovacs[1]; G Szucs[1]; G Fabian[3]; G Cserni[4]; L Puskas G[2]; T Thum[5]; Z Kahan[3]; T Csont[1]; S Batkai[5]
[1]University of Szeged, Faculty of Medicine, Department of Biochemistry, Metabolic Diseases and Cell Signalling Group, Szeged, Hungary; [2]Biological Research Centre of Szeged, Laboratory for Functional Genomics, Institute of Genetics, Szeged, Hungary; [3]University of Szeged, Department of Oncotherapy, Szeged, Hungary; [4]University of Szeged, Department of Pathology, Szeged, Hungary; [5]Hannover Medical School, Institute for Molecular and Translational Therapeutic Strategies (IMTTS) , Hannover, Germany

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Background: A deleterious, late-onset side effect of thoracic radiotherapy is the development of radiation-induced heart disease (RIHD). It is characterized by left ventricular hypertrophy and diastolic dysfunction and often manifests as heart failure with preserved ejection fraction. The miR-212/132 family is a crucial regulator of pathologic cardiac hypertrophy and miR-132 has been proposed as a therapeutic target for heart failure.
PurposeTherefore, our aim was to investigate whether the miR-212/132 cluster and its hypertrophy associated targets play a role in the development of RIHD.
Methods RIHD was induced in a clinically relevant chronic rat model. A single dose of 50 Gy was delivered to the whole heart of the animals and 19 weeks later, cardiac function was assessed by transthoracic echocardiography and tissue samples collected for histology and molecular analysis.
Results: Echocardiography and histology revealed left ventricular hypertrophy with preserved ejection fraction, diastolic dysfunction and interstitial fibrosis in the irradiated group. The miR-212/132 cluster was overexpressed and FOXO3 mRNA was repressed in the irradiated hearts. In contrast, total FOXO3 protein level failed to decrease in response to heart irradiation. However, cardiac phospho-FOXO3 level and phospho-FOXO3/total FOXO3 ratio showed a non-significant increase in irradiated hearts. Cardiac total AKT level and the phospho-AKT/total AKT ratio failed to change in the irradiated hearts as compared to controls.
Conclusions: Cardiac overexpression of the miR-212/132 cluster might play a role in the development of cardiac hypertrophy in RIHD. The development of cardiac hypertrophy seems to be independent of the AKT/FOXO3 mediated pathways in RIHD.

P1278

Preclinical evaluation of a novel dual acting V1a/V2 vasopressin receptor antagonist by using a noninvasive cardiac output monitor

T Thomas Mondritzki[1]; P Boehme[2]; P Sandner[1]; W Dinh[2]; J Hueser[1]; H Truebel[2]; P Kolkhof[1]
[1]Bayer AG, Cardiovascular Research, Wuppertal, Germany; *[2]Bayer AG, Experimental Medicine, Wuppertal, Germany*

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Background/Introduction: Elevated levels of arginine-vasopressin (AVP) may mediate deleterious effects via renal V2 and vascular V1a AVP receptors. While the only outcome trial in HF with a selective V2 receptor antagonist (EVEREST-trial) showed no mortality benefit, a respective trial in HF patients with a dual V1a/V2 receptor antagonist has not been conducted so far. Preclinical studies suggest beneficial aquaretic and hemodynamic effects of a dual acting V1a/V2 antagonist. However, there is a lack of predictive diagnostic readouts used in experimental models in view of transferability in a clinical scenario.
Purpose: Noninvasive cardiac output monitoring with bioreactance can be used to identify and differentiate the hemodynamic effects of a dual acting V1a/V2 antagonist compared to a selective V2 antagonism avoiding hemodynamic changes induced by anesthesia which would be required for invasive assessment.
Methods: Healthy beagle dogs (n = 9) were instrumented with telemetric sensors for hemodynamics assessment. Additional surface sensors were attached for noninvasive cardiac output monitoring (CHEETAH NICOM™, USA) and bladder catheter were placed for investigations diuretic effects. We compared the hemodynamic effects of a novel, dual acting V1a/V2 vasopressin receptor antagonist, BR-6819 with the selective V2 antagonist tolvaptan during intravenous AVP challenge in conscious animals.
Results: BR-6819 (3 mg/kg) induced a significant increase of 0.26 l/min ($p = 0.029$ vs. placebo) in cardiac output (CO) and 0.58 (l/min)/m2 ($p = 0.018$ vs. placebo) in cardiac index (CI) during vasopressin challenge, whereas tolvaptan was without any significant effect, respectively. In addition, BR-6819 treatment significantly reduced (-36.4%, $p = 0.015$) total peripheral resistance vs. placebo. BR-6819 and tolvaptan significantly ($p < 0.05$) increased urinary volume.
Conclusion: This is the first study demonstrating the feasibility of noninvasive cardiac output monitoring to differentiate between V1a/V2 and selective V2 antagonism. Use of the dual V1a/V2 antagonist BR-6819 significantly improved CO and CI while tolvaptan was without any effect here. Noninvasive cardiac output monitoring has the potential to improve the transferability of preclinical findings to the clinics.

P1279

Enzyme activity evaluation and tissue distribution of Neprilysin in heart failure

MC Asensio Lopez[1]; MC Sanchez Perez[1]; A Hernandez Vicente[1]; E Cabrero Romero[2]; D Fernandez Vazquez[2]; DJ Vazquez Andres[2]; MT Perez Martinez[1]; E Fernandez[1]; DA Pascual Figal[2]; AM Lax[1]
[1]Biosanitary Research Institute of Murcia (IMIB-Arrixaca)., Cardiology, Murcia, Spain; *[2]University Hospital Virgen de la Arrixaca, Department of Cardiology, Murcia, Spain*

Background: Neprilysin is a ubiquitous enzyme involved in degradation of numerous vasoactive peptides, notably including natriuretic peptides (NP). Despite recent data indicate a substantial mortality reduction associated with use of neprilysin inhibition in patients with reduced ejection fraction, had no data about enzymatic activity and tissue distribution.
Purpose: To evaluated the enzymatic activity and tissue distribution of neprilysin in presence of myocardial infarction and heart failure.
Methods. Wistar rats underwent MI by left coronary artery ligation were sacrificed at 4 weeks after surgery (n = 5 per group). Sham-operated animals were also included. Frozen tissue (100 mg) was homogenized using N2 liquid in adequate buffer. Neprilysin enzyme activity was measured with a fluorometric assay for the generation of free dansyl-D-Ala-Gly (DAG) from N-dansyl-Ala-Gly-D-nitro-Phe-Gly (DAGNPG)., using 562 and 342 nm as wavelengths of emission and excitation, respectively. Unpaired t-test was used to compare neprisilin activity respect sham in each tissue and, for multiple comparisons between tissues, paired t-test with Holm-Bonferroni correction was used.
Results: Neprylisin activity exhibited a gradient between tissues, with the highest level in lungs ($p < 0.01$ for all comparisons) followed by liver ($p < 0.01$) compared with kidney and heart); whereas, kidney and myocardial tissues showed similar levels. This gradient was observed in both sham animals and infarcted animals after 4 weeks (Figure 1). Of interest, animals with myocardial infarction and heart failure showed higher levels in all non-cardiac tissues as compared with sham animals: lung (1375.8 ± 166.0 vs. 152.8 ± 15.6, $p = 0.0017$), liver (68.55 ± 2.49 vs. 12.66 ± 0.76, $p < 0.0001$), and kidney (16.23 ± 3.96 vs. 2.29 ± 0.79, $p = 0.023$). In myocardium, neprylisin activity was observed at higher levels than sham (1.61 ± 0.22) in both infarcted (29.85 ± 1.84, $p < 0.0001$) and ischemic border of left ventricle (29.0 ± 4.73, $p = 0.0044$); however no differences were observed in remote myocardium compared with sham (2.59 ± 0.76, $p = 0.28$) (Figure 1).
Conclusion: Neprilysin activity has a gradient of levels from lung, to liver and kidney/heart. In the presence of myocardial infarction and heart failure, an increase of neprylisin activity was observed in non-cardiac tissues, as well as infarcted and ischemic myocardium, but not in remote non-ischemic myocardium.

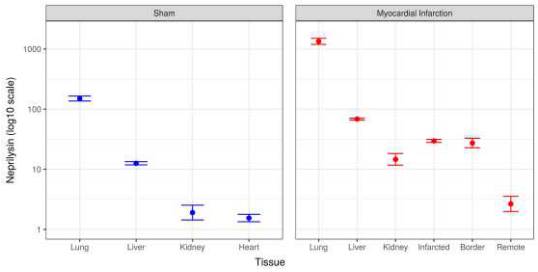

Figure 1

P1280

Different pathophysiological mechanisms for heart failure progressions in male and female mRen2 rats

N Nikolett Olah[1]; T Csipo[1]; A Kovacs[1]; GA Fulop[1]; I Edes[1]; Z Papp[1]; A Toth[1]
[1]University of Debrecen, Division of Clinical Physiology, Institute of Cardiology, Debrecen, Hungary

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Introduction: In view of the effectiveness of renin-angiotensin-aldosteron system (RAAS) inhibitors in heart failure (HF) therapy RAAS appears to play a crucial role in the pathomechanism of HF. Transgenic rats (mREN2) harboring an extra copy of renin gene develop fulminant hypertension at an early age which progresses into HF.
Purpose: Here we studied hypothetical gender dependent differences in the pathomechanisms in the mREN2 model of HF.
Methods: Mean arterial pressure (MAP) of transgenic renin overexpressing rats (mRen2) were high in both females (138.5 ± 11.7 mmHg) and males (168 ± 5.8). Internal non-transgenic wild type rats (WT) served as controls. To reveal the mechanisms contributing to HF progression, levels of RAAS activity in isolated tissues were studied in vitro.
Results: Male rats had higher mortality till 1 year of age (survival rate: males: 23% versus females: 75%). At 1 year rats exhibited signs of mixed systolic and diastolic cardiac dysfunctions, indicating the progression of hypertension to HF (EF in females: WT: 68.28 ± 2.1 versus mRen2: 68.26 ± 2.3; males: WT: 74.7 ± 6.1 versus mRen2: 60.2 ± 4.9; E/A: in females: WT: 1.74 ± 0.03 versus mRen2 1.47 ± 0.052; males: WT: 1.56 ± 0.01 versus mRen2: 1.06 ± 0.038). In parallel, a dysregulation of the tissue RAAS was observed. In particular angiotensin converting enzyme (ACE) activity was higher in male mREN2 left ventricles (9.5 ± 0.8 U/mg) than in those of their WT littermates (5.5 ± 0.2 U/mg), while no similar differences were observed in the lungs (71 ± 21 versus 76 ± 9 U/mg) and in any of the above parameters in females. Activities of angiotensin 2 eliminating ACE2 enzymes were similar in the left ventricles, lung, kidney of WT and mRen2 animals irrespectively of gender.
Conclusions: Our work illuminated important gender differences in the progression of hypertension to HF. In particular, our data implicate that left ventricular ACE activities increase in males more than in females. This is in accordance with the higher clinical effectiveness of ACE inhibitors and the higher HF risks in males than those in females.

P1281

Vanhoutte and Bowditch phenomena in heart failure: their relation to ischemia-reperfusion impact

L Tacu[1]; M Ivanov[2]; E Cobet[3]; A Rotaru[4]; L Ciobanu[2]; V Rotaru[1]; V Lutan[1]; IU Feghiu[1]; V Cobet[1]; M Popovici[2]
[1]State University of Medicine and Pharmacy, Chisinau, Moldova Republic of; *[2]Institute of cardiology , Chisinau, Moldova Republic of*; *[3]State University of Moldova , Biopharmaceutical chemistry , Chisinau, Moldova Republic of*; *[4]Harvard Medical School, Cambridge, United States of America*

Aim: Evaluation of both 15,16-epoxyeicosatrien (15,16-EET) induced coronarodilation and Bowditch's staircase in experimental heart failure (HF) as well as their

influence on ischemic contracture and functional recovery of isolated heart during repefusion.
Material and methods: HF was reproduced by doxorubicin administration in rat (16 mg/kg in 2 weeks). Vanhoutte's phenomenon was estimated by coronary flow raising rate in izovolumic isolated heart perfused by Langendorff method during action of 15,16-EET (10-4 M). Bowditch's staircase was assayed by electrically induced heart rate (HR) rise till maximal level suitable to left ventricle (LV) systolic pressure elevation (LVSP). Ischemic contracture was appreciated by LV end-diastolic pressure (LVEDP) at the end of global 20 min ischemia period followed by 30 min period of reperfusion when LVSP dynamics has been recorded. Likewise, ischemia-reperfusion impact was attested in condition of 15,16-EET action during pre-ischemia (20 min) and reperfusion as well as after maximal HR reaching.
Results: Coronarodilation effect of 15,16-EET has not been compromised in HF, because the coronary flow increased like in control comparatively to basal value (13,2 ± 1,2% vs 13,9 ± 1,1%). However, Bowditch's staircase was earlier interrupted in comparison to control according to maximal HR matching to positive slope of LVSD: 285 ± 22,6 vs 372 ± 29,4 1/min ($p < 0,05$). Maximal ischemic LVEDP was significantly higher in HR: 47,6 ± 3,3 vs 24,9 ± 1,8 mmHg ($p < 0,001$). On the other hand LVSP was at the end of reperfusion lower than control: 72,4 ± 6,5 vs 112,3 ± 7,5 mmHg ($p < 0,01$). Remarkably, 15,16-EET action before ischemia and during reperfusion notably improved dynamics of LVEDP and LVEDP in both control and HF (in the last even more evidently). Relative diminution of LVEDP measured 14,3 ± 1,4% in HF and 12,5 ± 1,2% in control, and LVESP increment: 15,1 ± 1,5% vs 13,7 ± 1,3%. If the ischemia-reperfusion onset started after frequency pacing ischemic contracture and functional LV recovery worsened similarly in both control and HF series: LVEDP increased by 19-20% while LVSP decreased by 17-18%.
Conclusions: 1. Derived (in cytochrome P450 biochemical way) from arachidonic acid 15,16-EET increases coronary flow in HF similarly to control and could be an important factor of coronary regulation by hyperpolarization mechanism in cases of endothelium dependent compromised coronary reactivity.
2. 15,16-EET mitigates ischemia-reperfusion impact in HF while HR elevation worsens ischemic contracture and LV contraction recovery in reperfusion.

P1282
A link between oxidative stress and CaMKII activity in post-ischemic failing hearts: a subcellular analysis with pathophysiological implications

T Tomas Rajtik[1]; A Szobi[1]; M Lichy[1]; J Hrdlicka[2]; P Galis[1]; J Neckar[2]; F Kolar[2]; A Adameova[1]
[1]Comenius University, Faculty of Pharmacy, Department of Pharmacology and Toxicology, Bratislava, Slovak Republic; *[2]Academy of Sciences of the Czech Republic, Institute of Physiology, Prague, Czech Republic*

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Background: Heart failure (HF) is generally associated with increased oxidative stress (OS) which has been suggested to be linked with detrimental activity of Ca2+/calmodulin-dependent protein kinase II (CaMKII) and thereby dysregulation of Ca2+-homeostasis. As CaMKII is widely localized in various cellular compartments throughout the cell, oxidative damage of these particular cellular fractions can underlie the increase in kinase activity observed in HF and thereby its influence on cellular function such as excitation-contraction coupling.
Purpose: To test this hypothesis, we measured the activity of CaMKII and various forms of oxidative stress in whole cell lysates, and subcellular fractions, such as cytoplasmic (Cy), membrane (Me) and mitochondrial (Mi) in left ventricles of failing hearts and sham operated hearts.
Methods: In male Wistar rats, a ligation of left descending coronary artery was performed to induce post-ischemic HF. Immunoblot analysis was used to assess the levels and activity of CaMKII (evidenced as p-Thr286-CaMKII). Lipoprotein oxidation, protein S-glutathionylation (PSSG) and protein carbonylation (PC) were evaluated by measuring the levels of TBARS, formation of glutathionylated proteins in non-reduced samples and carbonylated proteins detected in DNPH-derivatized lysates, respectively.
Results: In the whole cell lysates of failing hearts, oxidative stress evidenced itself as higher levels of PSSG and slightly increased carbonylated proteins. In the Me fraction of HF, only TBARS were increased. Despite the unchanged levels of PSSG in Me fraction in HF, there was a positive correlation with p-Thr286-CaMKII indicating a novel link between glutathione homeostasis and the kinase activity. In addition, a negative correlation of p-Thr286-CaMKII with PC was found in this fraction suggesting the abolishment of its activity under such conditions. In the mitochondria of diseased hearts, TBARS and PC were higher and were not in line with the active form of CaMKII.
Conclusions: This study has shown that the various types of OS are selectively upregulated in particular cellular compartments of failing hearts. Moreover, we have indicated for the first time that contractile dysfunction of post-ischemic HF might be, at least in part, linked with the activity of the membrane-bound CaMKII being dependent on protein S-glutationylation and carbonylation.

P1283
Lung diffusion capacity is positively correlated to pulmonary capillary wedge pressure in heart failure: a capillary volume effect?

T Tania Deis[1]; L Balling[1]; K Rossing[1]; E Wolsk[1]; F Gustafsson[1]
[1]Rigshospitalet - Copenhagen University Hospital, Copenhagen, Denmark

Background: Patients with heart failure (HF) are known to have a reduced pulmonary diffusion capacity for carbon monoxide (DLCO) but little is known about how hemodynamics relate to lung function. This study tested the hypothesis that pulmonary capillary wedge pressure (PCWP) is associated with alveolar volume adjusted pulmonary diffusion capacity (DLCO/VA) in patients with advanced chronic HF.
Methods: We retrospectively studied the data on 262 HF patients (mean age 51 ± 13) with a LVEF < 45 % referred non-urgently for evaluation for heart transplantation or LVAD, who underwent right heart catheterization and lung function testing. Univariate and multivariate linear regression models were constructed to examine the associations between DLCO/VA, FVC, FEV1 and hemodynamic parameters (PCWP, central venous pressure (CVP), cardiac index (CI), mean pulmonary artery pressure (MPAP) and mean arterial pressure (MAP)) as well as other factors known to affect lung function in HF.
Results: There was no significant correlation between hemodynamics and FVC or FEV1. DLCO/VA correlated positively with PCWP in both univariate ($p < 0,001$) and multivariate ($p = 0,012$) regression analysis but did not correlate to other hemodynamic factors. DLCO/VA was not a significant predictor of mortality. FVC and FEV1 were found to be significant predictors of mortality (HR for lower versus highest FEV1 and FVC tertiles 2,0 (1,4-2,9) and 1,9 (1,3-2,6)).
Conclusions: Surprisingly, PCWP was positively associated with DLCO/VA. This relation might be driven by increased lung capillary volume (Vc) in patients with lung congestion. Unlike dynamic lung parameters, DLCO did not predict mortality.

P1284
Quantitative estimation of extravascular lung water volume and preload by dynamic 15O-H2O positron emission tomography

R Roni Nielsen[1]; J Sorensen[2]; L Tolbod[2]; AKO Alstrup[2]; P Iversen[2]; CA Fredriksen[1]; J Frokiaer[2]; HJ Harms[2]
[1]Aarhus University Hospital, Skejby, Department of Cardiology, Aarhus, Denmark; *[2]Aarhus University Hospital, Department of Nuclear Medicine & PET center, Aarhus, Denmark*

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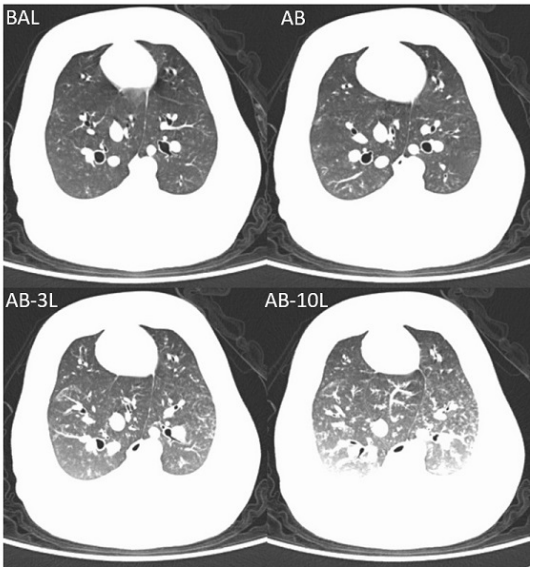
Background: Pulmonary congestion is an important finding in heart failure. It can be assessed invasively by the PICCO method using transpulmonary thermodilution to measure extravascular lung water content (EVLW) and preload by global



CT during the study of a pig

end-diastolic volume (GEDV) and pulmonary wedge pressure (PCWP) by pulmonary catheterization. However, at present, no reliable non-invasive methods are available for quantitatively measuring EVLW and preload.
Purpose: The present study was undertaken to evaluate whether measures derived from positron emission tomography (PET) performed to measure myocardial perfusion can be used to estimate EVLW and preload in a porcine model of pulmonary congestion.
Methods: Eight anesthetized and ventilated pigs were studied. Pulmonary congestion was induced by a combination of beta-blockers (BB), angiotensin-2 agonist (AT-2a) and saline infusion. Right heart catheterization, PICCO, computerized tomography (CT) and dynamic 15O-H2O-PET was performed. Transcardiac and transpulmonary transit times were measured by PET to calculate EVLW and GEDV.
Results: PCWP increased from 8 ± 2 mmHg at baseline to 29 ± 5 mmHg during intervention ($p < 0.001$). EVLW increased from 521 ± 76 mL to 973 ± 325 ml ($p < 0.001$) and GEDV from 1068 ± 170 ml to 1254 ± 85 ml ($p < 0.001$). 15O-H2O PET measures of EVLW increased from 566 ± 151 ml to 797 ± 231 ml ($p < 0.001$) whereas GEDV was lower than by PICCO but increased from 364 ± 60 ml to 524 ± 92 ml ($p < 0.001$). Both EVLW and GEDV measured with PICCO and 15O-H2O-PET correlated ($r2 = 0.40$, $p < 0.001$; $r2 = 0.40$, $p < 0.001$, respectively). EVLW correlated positively with Hounsfield units by CT (PICCO: $r2 = 0.36$ $p < 0.001$, PET: $r2 = 0.46$ $p < 0.001$) and GEDV with PCWP (PICCO: $r2 = 0.20$ $p = 0.01$, PET: $r2 = 0.29$ $p = 0.002$).
Conclusion: Here we demonstrate that preload and extravascular lung water content can be measured simultaneously and quantitatively during myocardial perfusions assessment using 15O-H2O-PET. Importantly, these parameters are spin-off during myocardial perfusion imaging and do not presuppose additional PET examinations. The prognostic implications of these quantitative measures can now be assessed non-invasively in outpatient settings.

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Risk score for heart failure with reduced ejection fraction

R Rajesh[1]; M Al Jarallah[1]
[1]*Sabah Al Ahmad Cardiac Center, Al Amiri Hospital, Cardiology , Kuwait, Kuwait*

Today in our day to day practice there are many such calculators available and we know very few physicians adhere to them during their practice. Its mainly due to time consuming and a number of variables that they have to enter into an app from the available risk score calculators. In such scenarios, we need a simple tool which is handy to all such physicians which can be easily used while seeing your ambulatory heart failure patients. Its important to decide in which category the subject belongs to and when to give them follow-up appointment. Such an easy systematic approach can help reduce frequent hospitalisations in such patients.
We are suggesting a new prognostic risk calculator for heart failure patients with reduced ejection fraction. The treating physicians should need to take only 3 variables for getting the prognostic score which is possible during the busy schedule. As we all know the vicious cycle where heart failure is linked to kidney diseases and anemia. Hence we developed a simple tool by encorporating the values which is more relevant to all three systems above mentioned. Here we need to find ejection fraction (EF,%), estimated glomerular filtration rate (e-GFR, ml/min) and haemoglobin levels (Hb, g/dL). (Table 1)
However, the above suggested HF risk model is yet to be validated in large clinical trials in its prediction of mortality in HF patients.
Seattle heart failure model (SHFM) is one among the available risk predicting calculator in heart failure. Here again the number of variables to be entered is more compared to ours. Our RHF score equation was derived while investigating the association of heart failure with various risk factors and its relevance to mortality. Anticipated population where this score is applicable is all patients with HFrEF. At present the cut off value is derived by calculating the severity of heart failure with other variables. It is too early to comment on the expected impact of treatment on this score. More details regarding cut off value and its impact on treatment will be published soon with the results after applying this score in a large cohort of heart failure patients.

Table 1 Rajan's HF risk score

	Rajan's HF risk score (R^{HF}Score) = (EF xe-GFR)/Hb	
#	Category	R^{HF}Score
1.	High Risk	0 - 50
2.	Moderate Risk	50 - 125
3.	Low Risk	125 - 250
4.	Minimal Risk	>250

EF = ejection fraction , e-GFR = estimated glomerular filtration rate, Hb = haemoglobin

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Age-related abnormalities in myocardial connexin43 expression, intercellular coupling and ultrastructure may facilitate heart dysfunction.

N Tribulova[1]; J Kohutova[2]; B Szeiffova Bacova[1]; T Egan Benova[1]; M Sykora[1]; P Weismann[3]; J Zurmanova[2]; E Goncalvesova[4]; M Barancik[1]
[1]*Slovak Academy of Sciences, Institute for Heart Research , Bratislava, Slovak Republic*; [2]*Charles University of Prague , Department of Physiology, Faculty of Science, Prague, Czech Republic,, Prague, Czech Republic*; [3]*Comenius University, Institute of Anatomy, Faculty of Medicine, Bratislava, Slovak Republic*; [4]*The National Institute of Cardiovascular Diseases, Department of Failing Heart, Bratislava, Slovak Republic*

Rationale: Heart failure is at the highest incidence in the elderly and often associated with atrial or ventricular rhythm disturbances. Myocardial gap junction (GJ) connexin (Cx) channels ensure action potential propagation and coordinated contraction. Age-related decline in Cx43 contribute to sinoatrial node dysfunction and ocurrence of atrial fibrillation. However, the role of Cx43 in deterioration of left ventricular function by ageing is poorly elucidated.
Objective: We aimed to explore whether ageing itself may facilitate heart dysfunction and increase a risk of malignant ventricular arrhythmias due to abnormal expression and/or distribution of Cx43 and alterations of the myocardial ultrastructure.
Methods: Analysis were carried out on left ventricle of the hearts of young 4-weeks-old and aged, 24-weeks-old, male and female guinea pigs. Cx43 expression, its phosphorylation and expression of PKCe were quantified using Western blot. Cryostat sections were processed for 'in situ' Cx43 immunofluorescence labeling and quantitative evaluation. Ultrathin sections of the left ventricle were examined in transmission electron microscope to reveal subcellular alterations of the cardiomyocytes and their junctions.
Key Results: The apparent differences in the distribution of Cx43 between young and old guinea pig heart were detected in males and females left ventricles. Besides intercalated disc-related 'end-to-end' type of Cx43-positive GJ, the abundant 'side-to-side' type on lateral cardiac cell membranes were observed in young animals. Lateral distribution was much less pronounced in old guinea pig heart ventricles. Both, quantitative image and western blot analysis revealed significantly lower expression of Cx43 in aging hearts of males (by 45%) and females (by 25%) guinea pigs. Likewise, functional phosphorylated forms of Cx43 were significantly decreased in old versus young male and female animals. In parallel, expression of PKCe was lower in old comparing to young guinea pigs ventricle. Ultrastructure examination revealed that enhanced extracellular collagen deposition in elder hearts is accompanied by shorter GJ profiles in comparison to young animals and also extracellular space between fascia adherens junctions increased from about 20 nm to more than 30 nm by aging. In addition, mostly electron-lucent mitochondria suggesting low energetic state were found in old hearts whereas electron-dense mitochondria reflecting high energetic state were observed in young male and female guinea pigs.
Conclusions: Unlike young guinea pig heart exhibiting high level of cell-to-cell coupling and mitochondria energetic state the old guinea pig heart are characterized by decline of Cx43 expression, impairment in intercellular coupling and reduced energetic state that likely contributes to increased propensity to ventricular arrhythmias and heart dysfunction.
This study was supported by VEGA 0076/16, 0167/15, 2/0160/18 grants, GACR 17-07748S and GAUK 940216

P1287

The role of TLR-9 in ischemia-reperfusion injury following acute myocardial infarction.

M Max Lenz[1]; A Kiss[2]; P Hohensinner[3]; K Krychtiuk[3]; J Wojta[4]; W Speidl[4]
[1]*Medical University of Vienna, Vienna, Austria*; [2]*Medical University of Vienna, Center for biomedical research, Vienna, Austria*; [3]*Medical University of Vienna, AKH - Department of internal medicine II - Cardiology, Vienna, Austria*; [4]*Medical University of Vienna, Core Facilities, Vienna, Austria*

Backround: Ischemia and subsequent reperfusion cause cell death within the reperfused tissue, followed by mitochondria leaking from the cells to the extracellular space. As recently demonstrated by experimental studies and clinical trials, circulating extracellular mitochondrial DNA (mtDNA) exhibits proinflammatory effects by binding to its corresponding receptor TLR-9. This activation causes chemotaxis and activation of neutrophils as well as monocytes which play a pivotal role in further damaging the infarcted tissue. Nonetheless, the exact role of TLR-9 in ischemia-reperfusion injury due to acute myocardial infarction remains to be unknown.
Methods: By ligation of the left coronary artery, ischemia was induced in male Wistar rats. After an ischemic period of 30 minutes, reperfusion was initiated by removal of the ligature. At this point, the animals were randomly divided into groups receiving TLR-9 antagonist ODN 2088 (bolus: 500μg and subsequently 1500μg over 24h via

subcutaneous pump) or ODN-control (bolus: 500μg and subsequently 1500μg over 24h via subcutaneous pump). Circulating neutrophil count was determined by flow cytometry 24h after the operation. Furthermore, hemodynamic measurements and histological analyses were performed 28 days thereafter.
Results: Rats receiving treatment with ODN 2088 showed significantly lower counts of circulating neutrophils after 24h compared to animals receiving ODN-control (ODN 2088: 22866 ± 7992/μl Vs. ODN-control: 35651 ± 15121/μl, p = 0.02). After 28 days, we analyzed for subsequent changes in cardiac repair in these animals. Though, hemodynamic parameters remained unchanged, left ventricular mass was significantly decreased accompanied by an enhanced aneurysm formation which was characterized by a 50% thinning of the left ventricular wall (ODN 2088: 0.93 ± 0.41mm Vs. ODN-control: 1.96 ± 0.75mm, p = 0.02).
Conclusion: We used the TLR-9 antagonist ODN 2088 to inhibit TLR-9 signaling within the first 24h following ischemia and reperfusion. This was in order to illuminate the involvement of TLR-9 in immune system activation and cardiac repair. Our presented data suggests that inhibiting TLR-9 results in a reduced activation profile of neutrophils 24h after the ischemic event. Furthermore it leads to changes in myocardial structure including a dramatic reduction of wall thickness and ventricular muscle mass. We speculate that these structural changes could cause severe defects including rupture at later stages of the healing process.

P1288

Is it possible the use of sacubitril/valsartan in HFrEF and hemodialysis?

J Jose Morgado[1]; AM Ana J Manovel Sanchez[1]; RL Raul Lopez Aguilar[1]; CCV Crecencio Camacho Vazquez[1]; FF Fernando Fernandez Giron[1]; BM Basilio Martinez Mora[1]; JF Jose Francisco Diaz Fernandez[1]
[1]Hospital Juan Ramon Jimenez, Cardiology, Huelva, Spain

Background/Introduction: Chronic heart failure (HF) is a major public health problem associated with high mortality rates.
Sacubitril/valsartan (S/V) acts by simultaneous inhibition of neprilysin (enhancement of natriuretic peptides) and inhibition of the effects of angiotensin II. It has cardiovascular and renal therapeutic effects, and has demonstrated the superiority over enalapril in reducing mortality and morbidity in patients with Heart failure with reduced ejection fraction (HFrEF) in PARADIGM-HF trial. It is unknown the use of sacubitril/valsartan in patients with end-stage kidney disease (ESKD).
Purpose: Describe our initial experience in our centre using sacubitril/valsartan in patients with HFrEF on long-term dialysis.
Methods: This study was performed as a prospective, single-center study from June 2017 to December 2017 in the University Juan Ramon Jimenez Hospital, Spain. We included three patients with this characteristics.
We describe it's safety and efficacy. Patients were verbally informed about this drug.
Results: Case 1: 68 year-old man with a medical history of hypertension, type II diabetes, end-stage renal disease (ESRD) due to diabetes, New York Heart Association (NYHA) class III-IV functional status, 34% LVEF due to ischemic heart disease. We decided to change valsartan to sacubitril/valsartan. Actually, 6 months later, he received maximum dose, and has improved his functional status (class II NYHA) with no changes in blood pressure and good hemodialysis tolerance.
Case 2: Patient 2 is a 62 year-old man with a medical history notable for systemic hypertension and ESRD due to uncertain etiology, (NYHA) class III functional status and 23% LVEF due to Non-ischemic heart disease. Because of sintomatology, losartan was changed to sacubitril/valsartan. Three months later, he received 24/26 mg with improvement in functional status and similar blood pressure and hemodinamic tolerance to dialysis.
Case 3: 53 year-old man with a medical history for systemic hypertension and diabetes, associated with ESRD due to uncertain etiology, (NYHA) class III functional status and 20% LVEF due to Non-ischemic heart disease. We added sacubitril/valsartan to his treatment, removing losartan. 1 month later, he remains asymptomatic and we have increased dose (maximum dose) with normal blood pressure
Conclusion(s): This study shows the efficacy and safety of sacubitril/valsartan in 3 patients with hemodialysis and HFrEF, with no adverse effects; although it is limited by the small number of patients.
It is necessary confirmatory studies to test this hypothesis.

P1289

How to predict thrombi formation in patients with apical aneurysms

R P Santos[1]; A Nunes Ferreira[1]; J Rigueira[1]; IS Goncalves[1]; JR Agostinho[1]; IA Ricardo[1]; T Rodrigues[1]; N Cunha[1]; R Placido[1]; C David[1]; FJ Pinto[1]; AG Almeida[1]
[1]Cardiology Department, Santa Maria Hospital, CHLN, CCUL, Lisbon University, Lisbon, Portugal

Introduction: The clinical relevance of left ventricular aneurysms (LVA) is based on the fact that they are preferred sites for arrhythmias and thrombus formation, which may secondarily imply severe thromboembolic complications. Thus, the identification of predictors of these complications may have an impact on the monitoring or therapy of patients at higher risk.
Purpose: To identify, in a population with a diagnosis of LVA, possible predictors of left ventricular thrombus (LVT) formation.
Methods: All patients diagnosed with transthoracic echocardiograms from January 2015 to December 2016 were selected. Clinical, electro / echocardiographic and therapeutic parameters prior to the echocardiogram were analysed and the relationship with the presence of LVT was evaluated through Kaplain-Meier analysis and cox regression.
Results: A total of 78 patients with LVA (80.8% males, age 63.9 ± 11.7 years) were identified. Most patients had ischemic heart disease (85%), followed by dilated cardiomyopathy (14%) and valve heart disease (1%). The left ventricular ejection fraction (LVEF) was 35.8 ± 10.8%, the left ventricular end-diastolic volume (LVEDV) was 87.7 ± 37.3 ml and the end-systolic volume (LVESV) was 58, 7 ± 31.6 ml. Regarding therapy, 19.5% of the stroke population were under anticoagulation and 39% under antiaggregation at the time of the echocardiogram, with LVT being present in 23% of the stroke population. The univariate analysis showed that the LVT formation was associated with advanced age (p = 0.006), LVEF (p = 0.013), increase in LVESV (p = 0.046), absence of anticoagulant or antiaggregation therapy (p = 0.001), dyslipidemia (p = 0.049) and coronary artery disease (p = 0.006). In the multivariate analysis of Cox regression, only therapy (anticoagulant or antiplatelet) was identified as an independent and protective factor for the formation of LVT (p = 0.001), with no difference between anticoagulation and antiaggregation therapy.
Conclusion: This study showed that the development of intraventricular thrombi is associated with older age, LVEF compromise, LVESV increase, dyslipidemia and coronary artery disease. On the other hand, chronic anticoagulation or antiaggregation therapy was the only independent and protective factor in the development of LVT.

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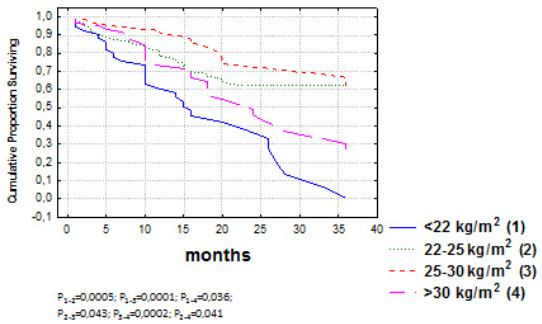
Body Mass Index as a predictor of mortality in Chronic Heart Failure

N Nataliya Tkach[1]; L Voronkov[1]; L Voronkov[1]; L Voronkov[1]; L Voronkov[1]
[1]NSC Institute of Cardiology M.D. Strazhesko, Heart Failure department, Kiev, Ukraine

Background: Despite good knowledge about predictors of long-term mortality in Chronic Heart Failure (CHF) the influence of body mass index (BMI) on the long-term mortality of these patients is still non-well investigated.
Aim: The purpose of study was to determine the effect of BMI on the mortality of patients with CHF and with reduced left ventricular ejection fraction (LVEF)
Methods: 267 CHF patients with reduced LVEF < 40 % were analyzed. Survival analysis was performed using the "STATISTICA for Windows. Release 6.0" program (Survival Analysis section) using the Kaplan-Meier method. To assess the impact on BMI life expectancy, patients were distributed for following groups: reduced body weight - BMI < 22kg /m2, normal - BMI 22-24.99 kg/m2; overweight - BMI 25-29.99 kg/m2 and obesity - BMI = 30 kg / m2.
Results: During the 1 and 3 years of follow-up the survival rate had a lower in patients with reduced BMI (52% after 1 year, after 3 years - 0%), somewhat better in obese patients - 71% and 25%, respectively, and the best predictor was characterized by patients with overweight BMI - 90% and 60% respectively; these differences were significant (p = 0.01).
At the same time, the groups of patients did not significantly differ among themselves by age, duration of the signs of CHF and severity of reduced LVEF. The prognostic information of the BMI was greater for survival of patients over three years (OR-5,992 (CI = 1,020-114,898)) in comparison to the first year of observation (OR-3,591 (CI = 1,001-112,359)).
Conclusions: the patients with low BMI (< 22 kg / m2) in CHF patients with reduced LVEF is the worst prognostic criterion, while at the same time, patients with overweight BMI (25-29.99 kg/m2) have the best survival indices for one and three years of follow-up.



P1291

Fibroblast-mediated atrial mechanical dysfunction in HFpEF and hypertensive heart disease.

D David Bode[1]; R Doerr[1]; D Lindner[2]; M Schwarzl[2]; D Westermann[2]; U Primessnig[1]; B Pieske[1]; FR Heinzel[1]
[1]Charite - Campus Virchow-Klinikum (CVK), Innere Klinik m.S. Kardiologie, Berlin, Germany; *[2]University Heart Center Hamburg, Hamburg, Germany*

Heart failure (HF) with preserved ejection fraction (HFpEF) is present in about 50% of HF patients and often related to metabolic syndrome. Atrial remodeling (AR) is common in HFpEF, associated with atrial mechanical stretch and increased fibrosis, leading to altered secretory activity. AR and mechanical dysfunction has been shown to independently increase patient mortality. We hypothesize that atrial cardiomyocyte function and interaction with fibroblast mediated extracellular matrix triggers is pivotal for the manifestation and progression of AR and dysfunction in heart failure.
Methods: Atrial mechanical function in-vivo was assessed using echocardiography. In-vitro, contractile function of atrial cardiomyocytes was evaluated by video edge detection in wild type (WT) and ZFS-1 rats without (Ln; hypertension) and with metabolic syndrome and AR (Ob; HFpEF, as previously shown). In addition, excitation-contraction-coupling (ECC) was examined using confocal and ratiometric Ca imaging (Ca transients; CaT) (Fluo4-AM/Fura2-AM, field stim) in atrial cardiomyocytes of Ln and Ob. CaT were recorded at 1 Hz after treatment with conditioned medium of their respective cultured unstressed or stressed (stretch-induced activation; Flexercell system) fibroblasts isolated from Ln and Ob.
Results: Under baseline-conditions at 21 weeks, Ob and Ln showed increased cell shortening compared to WT (6.449 ± 0.6761 vs. 11.46 ± 0.6247; $n = 48$ and 84 cells; $p < 0.05$; 6.449 ± 0.6761 vs. 10.84 ± 0.6144; $n = 49$ and 89 cells; $p < 0.05$) related to enhanced Ca release. In-vivo however, atrial function was impaired. Histology unveiled increased fibrosis in Ob and treatment with conditioned, activated medium vs. medium from unstressed fibroblasts was associated with increased cardiomyocyte diastolic Ca content (0.62 ± 0.02 vs. 0.068 ± 0.02; $n = 22$ and 34 cells; $p < 0.05$), prolonged cytosolic CaT time to peak (61 ± 5 vs. 77 ± 11 ms; $n = 19$ and 20 cells; $p < 0.05$) and Ca removal (209 ± 11 vs. 347 ± 52 ms; n= 19 and 20 cells; $p < 0.05$) in Ob.. In addition, while Ca spark frequency was unaltered, conditioned medium significantly increased amplitude (0.98 ± 0.03 vs. 1.1 ± 0.03; $n = 11$ cells/group; $p < 0.05$) and altered time to peak as well as duration and width. This indicates profound changes of ECC due to mechanical stress in metabolic syndrome mediated by fibroblast secretions, potentially contributing to decompensation. In Ln however, atrial in-vivo function was preserved and a shortening of Ca removal (357 ± 53 vs. 219 ± 16 ms, $n = 29$ and 18 cells: $p < 0.05$) could be observed after exposure to stressed fibroblast secretome.
Summary: During metabolic syndrome and HFpEF, impaired in-vivo atrial mechanical function might be related to adversely affected cardiomyocyte ECC due to fibroblast secretome and mechanical stress. In hypertensive AR, stressed fibroblasts enhance cardiomyocyte Ca removal and in-vivo atrial function is preserved.

P1292

Inhibition of the Na+/Ca2+ exchanger (NCX) improves cardiac remodeling and diastolic function in heart failure with preserved ejection fraction.

U Primessnig[1]; T Bracic[2]; P Pollesello[3]; B Pieske[1]; FR Heinzel[1]
[1]Charité - Universitätsmedizin Berlin, Campus Virchow-Klinikum, Department of Cardiology, Berlin, Germany; *[2]Medical University of Graz, Department of Cardiology, Graz, Austria*; *[3]Orion Pharma, Critical Care, Espoo, Finland., Espoo, Finland*

Background: Heart failure with preserved ejection fraction (HFpEF) is increasingly common but there are no therapeutic strategies available at the moment; mostly because the underlying cellular mechanisms are not well understood. Therefore, we investigated the chronical inhibition of the Na+/Ca2+ exchanger (NCX) with SEA0400 and ORM11035 in a rat model of HFpEF.
Methods: Young male Wistar rats were subjected to subtotal nephrectomy (NXT) or sham operation (SOP). Chronical treatment for 16 weeks with the NCX inhibitor SEA0400 or ORM11035 was started 8 weeks after intervention. At the end after 24 weeks the cardiac phenotype was evaluated using non-invasive blood pressure (NIBP) measurements, echocardiography and invasive pressure-volume loops (PV). Furthermore, heart morphometry as well as left ventricular (LV) cardiomyocytes were isolated and cardiomyocyte function and Ca2+ handling was measured.
Results: NXT rats (untreated) showed stable compensated renal impairment and signs and symptoms of HFpEF (hypertrophied left ventricle (LV), left- and upward shift of end diastolic pressure (EDP) volume relationship (EDPVR), increased lung weight/body weight ratio (LW/BW) indicating pulmonary congestion and preserved LV systolic function (EF, dP/dt)). In LV cardiomyocytes from untreated NXT Ca2+ transient amplitude was unchanged but time for early (50%) decay was significantly prolonged at 24 weeks and correlated with diastolic dysfunction (EDP) in vivo. In NXT treated with a NCX inhibitor cardiac remodeling and diastolic function improved. Moreover, congestion and NTproBNP was enhanced after chronic NCX modulation. Compared SEA0400 with the new, more specific NCX inhibitor, ORM11035 there were no negative inotropic effects and effects on blood pressure observed with ORM11035. Additionally, a potential antiarrhythmic effect of ORM11035 in LV cardiomyocytes was observed.
Conclusion: Chronic inhibition of the Na+/Ca2+ exchanger with ORM 11035 significantly attenuated cardiac remodeling and diastolic dysfunction without lowering systemic blood pressure in this model of HFpEF compared to SEA0400.

P1293

Aged hypertensive rats exhibit myocardial oedema: a link to HFPEF?

G Giacomo Rossitto[1]; A Harvey[1]; S Lacchini[1]; AC Montezano[1]; RM Touyz[1]; M Petrie[1]; C Delles[1]
[1]University of Glasgow, Institute of Cardiovascular and Medical Sciences, BHF Centre for Research Excellence, Glasgow, United Kingdom

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Introduction: Salt is associated with progression of hypertensive heart disease through left ventricular hypertrophy and diastolic dysfunction, which are often precursors and/or determinants of HFpEF. Recently, Na+ was shown to accumulate in peripheral tissues with advancing age and resistant hypertension; in rodent models, glycosaminoglycans (GAGs) were identified as the putative binding site and lymphatic vessel networks have been implicated as fine-tuning buffering systems.
Purpose: This study was set out to investigate sodium accumulation and its determinants in the heart of hypertensive animals.
Methods: Heart samples from hypertensive young and old rats (SHRSP; 20 and 52 weeks old, respectively) and normotensive age-matched controls (WKY rats; n = 6-10 per group) were used for: i) chemical analysis of tissue Na+ and K+ content by flame photometry; ii) gravimetric measurement of water content, as the difference between wet (WW) and dry weight (DW); iii) histologic quantification of GAGs content by alcian blue staining (A.B., pH 2.5) of mid-myocardial tissue (A.B. positive area, %); iv) comparison of the gene expression of lymphatic-specific markers and growth factors (Lyve-1; Podoplanin; VEGFc; VEGFR3).
Results: Myocardial Na+ content and concentration were increased in SHRSP old compared to SHRSP young and age-matched WKY (0.190 ± 0.040, 0.133 ± 0.011, 0.139 ± 0.027 mmol/gDW and 54.5 ± 4.1, 45.8 ± 5.5, 46.6 ± 3.6, mmol/l, respectively), paralleled by an increase in water (76.7 ± 0.9 vs 74.4 ± 1.0 and 73.5 ± 1.5 %WW, respectively). K+ concentration showed a mirror-pattern decrease, leading to an overall similar [Na+ + K+] concentration across groups. Relative gene expression of Lyve-1 and Podoplanin or VEGFc-VEGFR3 axis was not increased in rats showing tissue Na+ accumulation. Myocardial GAGs increased with aging, but was higher in both SHRSP young and old rats compared to WKY.
Conclusion: Na+ accumulates in the heart of aged hypertensive rats and is putatively bound to the increased sulphated GAGs observed with aging, particularly in hypertension. This accumulation is overall isotonic and paralleled by water, suggestive of tissue oedema, which has been previously shown to impact on myocardial function in animal models. These processes may play a role in the development of HFpEF phenotype.

P1294

Dapagliflozin ameliorates diastolic function in an animal model of hypertensive heart disease in the absence of diabetes

K Konrad Urbanek[1]; D Cappetta[1]; A Micciche'[1]; G Esposito[1]; LP Ciuffreda[1]; A Cozzolino[1]; D D'amario[2]; F Crea[2]; S Naviglio[3]; F Rossi[1]; A De Angelis[1]; L Berrino[1]
[1]University of Campania "Luigi Vanvitelli", Department of Experimental Medicine, Naples, Italy; *[2]Catholic University of the Sacred Heart, Department of Cardiovascular and Thoracic Sciences, Rome, Italy*; *[3]University of Campania "Luigi Vanvitelli", Department of Biochemistry, Biophysics and General Pathology, Naples, Italy*

Background: The results of trial with SGLT2 inhibitors raised possibility that this class of anti-hyperglycaemic drugs may provide cardiovascular benefits independently from their anti-diabetic effects. Although it has not been specified whether patients with significantly reduced risk for HF hospitalization had any particular form of HF, it is possible that heart failure with preserved ejection fraction (HFpEF) patients were appreciably represented. HFpEF is a challenging clinical syndrome and represents yet unresolved pathophysiological continuum with a consequent perception of lack of effective treatments. Moreover, HFpEF often share co-morbidities like hypertension and diabetes.
Purpose: Following noted dissociation between control of glycaemia and cardiac outcome, we have selected a hypertensive, non-diabetic model of HFpEF.to examine

the effects of SGLT2 inhibitor dapagliflozin on the progression of experimental heart disease independently from its effects on diabetes.
Methods: Seven-week-old Dahl salt-sensitive (Dahl/SS) rats were fed a high salt diet (8% NaCl) for 5 weeks to induce hypertension. Then, rats continued with a high salt diet and were orally administered with either dapagliflozin (0.1 mg/kg/day) or vehicle for the following 6 weeks. Diastolic and systolic function were monitored by echocardiography.
Results: The animals progressively developed hypertension and after 5 weeks of high-salt diet, before initiation of pharmacotherapy, LV hypertrophy was already evident while systolic parameters were unchanged. However, diastolic function was compromised as documented by decrease of E/A ratio along with increase of E deceleration time and isovolumetric relaxation time. During 6 weeks of the treatment with dapagliflozin, blood pressure remained markedly elevated, with a slight reduction observed only during last two weeks. At completion of dapagliflozin treatment, hypertrophied LV had systolic parameters within a normal range while diastolic parameters were partially recovered. These results define an improved ventricular relaxation. Additionally, animals on high-salt diet had an increased urine albumin-to-creatinine ratio (UACR). An improved cardiovascular profile following treatment with dapagliflozin was confirmed by the reduction of UACR.
Conclusions: Dapagliflozin positively modulates diastolic compliance with cellular and molecular mechanisms yet to be identified. Although a slight reduction in blood pressure may have participated in functional and structural modifications, these changes cannot exclusively account for the beneficial effects of the drug. Because of a non-diabetic nature of our model and unaltered blood glucose levels, the protective action of dapagliflozin lays beyond its effect on glycaemia.

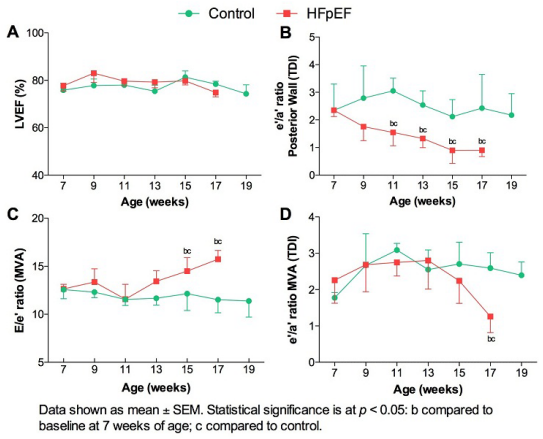
P1295

Doppler evaluation of radial myocardial tissue relaxation: an early marker of disease progression for heart failure with preserved ejection fraction

A Giraldo[1]; J Talavera[2]; MJ Fernandez-Del-Palacio[2]; G Brooks[1]
[1]University of Reading, Institute for Cardiovascular and Metabolic Research, Reading, United Kingdom; [2]University of Murcia, Department of Small Animal Medicine and Surgery, Veterinary School, Murcia, Spain

Funding Acknowledgements: University of Reading, United Kingdom.

Background: Heart failure with preserved ejection fraction (HFpEF) is highly prevalent. There are no effective therapies, and there is a lack early markers of disease progression/prognosis in populations at risk of HFpEF (e.g. hypertensive, obese, diabetic). Evaluation of diastology with tissue Doppler imaging (TDI) has mainly focused on longitudinal myocardial tissue relaxation at the mitral valve annulus (MVA).
Purpose: We hypothesized that radial motion of the myocardium using TDI in a preclinical model of HFpEF, may add valuable information to the evaluation of diastology during the progression of this condition.
Methods: Male Dahl salt sensitive hypertensive rats were fed a high salt diet (8% NaCl) from 7 weeks of age (HFpEF group). Another cohort of male Dahl rats was fed a diet containing 0.3% NaCl (Control group) throughout the study protocol until 19 weeks of age. Blood pressure was evaluated by the tail cuff method. A complete echocardiographic evaluation was performed at baseline, repeated every 2 weeks thereafter, and included amongst other parameters: mitral valve inflow velocities, longitudinal myocardial tissue relaxation via TDI with the sample volume placed at the MVA in an apical 4 chambers view, and radial myocardial tissue relaxation by placing the TDI sample volume at the posterior wall in a parasternal short axis view (papillary muscles level).
Results: Rats in the HFpEF group developed severe hypertension, whilst the control group remained normotensive. Both the HFpEF and control groups exhibited normal left ventricular ejection fraction throughout the whole study (Figure 1A). Significantly, in the HFpEF group, alterations in radial myocardial tissue relaxation velocities (reduced e', increased a' and reduced e'/a' ratio (e' reversal pattern) (Figure 1B)) occurred early, relative to commonly evaluated Doppler parameters of diastolic function (E/e' and e'/a' at MVA) (Figure 1C-D). Of note, animals that presented earlier alterations in radial myocardial tissue relaxation, also exhibited earlier development of HFpEF and deterioration of health status. No alterations in diastolic function were found in the control group.
Conclusion: Our detailed time course evaluation of myocardial tissue relaxation via TDI in the Dahl salt sensitive hypertension-induced model of HFpEF, suggests that alterations in the radial myocardial tissue relaxation pattern is an early marker of disease progression in HFpEF. Complementary studies are necessary to further validate this technique as well as to evaluate its prognostic value in patients with established or at risk of developing HFpEF.



Data shown as mean ± SEM. Statistical significance is at $p < 0.05$: b compared to baseline at 7 weeks of age; c compared to control.

Figure 1

P1296

Assessment of myocardial contractile function by tissue doppler echocardiography in patients with chronic heart failure with preserved systolic function

VA Barbuk[1]; MI Belskaya[1]; AN Zhuiko[1]; NV Semyonova[1]; ID Kozlov[1]
[1]Republican Scientific and Practical Centre of Cardiology, Chronic CAD Laboratory, Minsk, Belarus

Objectives: to assess myocardial contractile function in patients with chronic heart failure (CHF) of ischemic origin with preserved systolic function.
Study Methods: 65 patients with post-infarction cardiosclerosis complicated by NYHA FC II CHF aged 48 - 70 y.o. (mean-age 61.9 ± 8.09) have been examined. All patients received cardiac ultrasound examination using Vivid - 7 device (GE, USA - Belgium) in ?, ? - modes and tissue Doppler (TD) with 3.5 MHz transducer with the assessment of key structural and volumetric indices, contractility and left ventricular (LV) myocardial longitudinal deformation (strain).
Results: the results suggest that patients with post-infarction cardiosclerosis complicated by NYHA FC II CHF showed evidently reduced global longitudinal systolic left ventricular myocardial deformation (-12.3 ± 1.98%; ? <0.05) compared to normal values (-16%) secondary to preserved or slightly decreased LV ejection fraction (EF) (mean EF 50.1 ± 4.79%) suggesting the presence of chronic contractile dysfunction of heart muscle. Simultaneously, these patients showed a positive correlation between the degree of myocardial longitudinal deformation and LV EF in ? and ?-modes (r = 0.58, r = 0.74; ? <0.05, respectively). It is noteworthy, that impaired longitudinal systolic function in patients with post-infarction cardiosclerosis was discovered both in the scarring area, and in areas of preserved myocardial kinetics which some authors think is predicated by the development of subendocardial dysfunction due to fibrosis formation and microvascular disorders.
Conclusions: Thus, despite preserved LV systolic function, patients with post-infarction cardiosclerosis complicated by NYHA FC II CHF showed decreased longitudinal deformation of heart muscle suggesting the presence of ischemic contractility disorders and increased LV myocardial stiffness and may be a prognostically adverse factor in this group of patients.

P1297

Right ventricular function as a predictor of exercise tolerance in patients with chronic left ventricular failure

S M Salah Mohamed Ibrahim[1]
[1]university, cairo, Egypt

Background: Few clinical studies suggested an important role for the pulmonary circulation and right ventricular functions in determining the exercise capacity in patients with chronic left ventricular failure (CHF). No correlation has been found between resting left ventricular ejection fraction (LVEF) and exercise capacity in these patients.
Purpose: Our aim was to delineate the role of the right ventricular function in determining of the exercise capacity in such patients.
Methods: Forty subjects were included in this study; thirty male patients with CHF secondary to ischemic cardiomyopathy (16 patients) or dilated cardiomyopathy (14 patients) fulfilled the inclusion criteria for this study and ten normal subjects matched for age and weight.

Following thorough history and clinical examination; the patients underwent first pass radionuclide study for the determination of the resting right ventricular ejection fraction (RVEF), two-dimensional echocardiography and Doppler study to study both left and right ventricular systolic and diastolic function, and a progressive multi-stage breath by breath cardiopulmonary exercise test using treadmill with incremental increase in the workload to a symptom limited point, to determine the maximal exercise capacity and maximal cardiopulmonary exercise test parameters.
Results: It was found that the LVEF did not correlate at all with any of the exercise capacity predictive parameters, whereas the RVEF correlated significantly to these parameters. There were however a striking abnormalities of the ventilatory response to exercise, in the form of increased ventilation in response to given rate of CO2 production, and this excessive ventilation correlated significantly with the increase in dead space ventilation in the affected patients. While the VE/VCO2 and the VD/VT max correlated significantly with VO2max, they also correlated significantly with RVEF. The correlation between RVEF and exercise capacity may be explained by the perfusion/ ventilation mismatch resulting from chronic pulmonary changes.
Conclusion: The study showed that the exercise capacity in CHF is not related either to etiology, NYHA functional class or exercise end point.

P1298

Heart failure associated with chronic kidney disease - a reality: clinical characteristics and outcomes

T Tatiana Duarte[1]; S Goncalves[1]; M Fonseca[1]; C Sa[1]; R Marinheiro[1]; J Farinha[1]; R Rodrigues[1]; S Correia[1]; D Ferreira[1]; A Lourenco[1]; R Caria[1]
[1]Hospital Center of Setubal, Cardiology, Setubal, Portugal

Introduction: Heart failure (HF) and chronic kidney disease (CKD) share several risk factors and often coexist. Chronic kidney disease is associated with increased morbidity and mortality in heart failure and conditions use of drugs with a prognostic impact.
Treatment recommendations for patients with HF and CKD are insufficient, because the patients with severe renal impairment are excluded from most studies.
Aim: To determine the prevalence of renal dysfunction in a population with HF and to characterize these patients.
Methods: Consecutive patients from a HF clinic were evaluated. The creatinine clearance was calculated according to the Cockcroft-Gault equation.
The population was divided into 5 groups according to the degree of renal dysfunction: Group 1: GFR> 90; Group 2: < 89 and = 60; Group 3: < 59 and = 30; Group 4: < 29 and = 15; Group 5: < 15 ml / min / 1.73m2.
The population was characterized according to baseline characteristics, therapy and events - cardiovascular death and hospitalizations for HF.
Results: One hundred and seventy-eight patients were studied (male - 71% (N = 127), mean age 67 ± 11 years). Ninety-four patients (53%) had a GFR = 60.
Patients with renal dysfunction are significantly older, but without predominance of gender and ischemic etiology to HF. (Table I)
The majority of patients with renal impairment have ACE inhibitors, but not spironolactone.
Hospitalizations by HF were significantly associated with patients with renal dysfunction (GFR < 60: 34 vs 17; p = 0.019), however, the same was not found for death (10 vs 4, p = 0.146).
Conclusion: The majority of our population has associated with HF a degree of renal dysfunction.
In this sample, renal dysfunction did not affect the use of some drugs with a prognostic impact (ACEI and beta-blocker), but the same was not observed for spironolactone, which is used more cautiously in this group of patients.
More studies are needed in patients with HF and CKD for better surveillance and therapeutic orientation.

Variable	Group 1 (GFR> 90) (N=22)	Group 2 (GFR 89 - 60) (N= 69)	Group 3 (GFR 59-30) (N=58)	Group 4 (GFR 29-15) (N= 18)	Group 5 (GFR <15) (N=11)	p-value
Male (n)	19	51	38	11	8	0,3
Age (years)	54 ± 9	67 ± 11	70 ± 10	74 ± 5	65 ± 10	<0,001
Ischemic etiology (n)	7	34	26	8	6	0,65
LVEF (% median; IQ)	43(34;46)	43(35;49)	44(30;52)	40(19;55)	44(38;56)	0,001
Hospitalizations by HF (n)	4	16	14	10	7	0,006
Death (n)	2	2	4	3	3	0,146
ACEI (n)	20	56	42	8	8	0,11
Betablocker (n)	21	56	56	14	11	0,17
Spironolactone (n)	12	33	18	0	0	0,013

Heart failure according CKD

P1299

Heart failure with "recovered function": clinical characteristics and outcomes

T Tatiana Duarte[1]; S Goncalves[1]; M Fonseca[1]; C Sa[1]; R Marinheiro[1]; J Farinha[1]; S Correia[1]; D Ferreira[1]; A Lourenco[1]; R Rodrigues[1]; R Caria[1]
[1]Hospital Center of Setubal, Cardiology, Setubal, Portugal

Introduction: Patients with systolic dysfunction that improve/recover their left ventricular systolic ejection fraction (LVEF) present a more favorable clinical profile when compared to patients that maintain dysfunction, although the therapeutic.
The characteristics and outcomes of patients with "recovered function" are not fully described, and more studies in these patients are necessary.
Aim: To determine in a population with heart failure (HF) the prevalence of patients that improved/recovered LVEF and characterize this sample according to clinical characteristics and outcomes.
Methods: Patients followed at a HF clinic with initial LVEF < 40% were retrospectively evaluated. The population was divided into 3 groups according to the LVEF:

Variable	Group 1 (LVEF < 40%) (N=89)	Group 2 (LVEF> 50%) (N=35)	Group 3 (LVEF 45-50%) (N=31)	p-value
Male (n)	73	16	23	0,034
Age (years)	67 ± 1	68 ± 2	66 ± 2	0,9
Ischemic etiology (n)	52	9	13	0,041
Death (n)	14	2	4	0,5
HF hospitalization (n)	43	16	13	0,6
Composite endpoint (n)	45	16	14	0,8
BNP pg/ml (median; IQ)	257 [93; 558]	109 [22;172]	118 [35;268]	0,032

Group I - did not recover function (LVEF < 40%); Group 2 - recovered function (LVEF> 50%); Group 3 partially improved the function (LVEF between 45-50%).
The groups were characterized according to baseline characteristics, comorbidities, therapeutics and outcomes - death for cardiovascular cause; hospitalizations for HF; composite endpoint.
The prevalence of "recovered function" and predictive factors were evaluated.
Results: One hundred fifty-five patients were studied (male 72% (n = 112), mean age 67 ± 10 years). In 43% (66) of the patients there was an improvement in systolic function: LVEF> 50%: 53% (35); LVEF between 45 and 50: 47% (31).
Patients that did not improve the systolic dysfunction are predominantly male.
The non-ischemic etiology was associated with greater ventricular remodeling with improved function. The patients that improved/recovered function had less events but non-statistically significant. Median levels of BNP were lower in the two groups that improved function. (Table I)
Conclusion: The improvement/recovery of LVEF was frequent in this sample, especially in patients with non-ischemic etiology. This group of patients keeps a reasonable number of events that suggests the persistence of a risk profile and need of surveillance.
More studies in patients with "recovered function" are necessary, to determine predictors of "improved/recovered function" and to optimize therapeutics.

P1300

Combined inhibition of the renin-angiotensin system and neprilysin enhances skeletal muscle oxidative capacity and ameliorates cachexia in tachypacing-induced heart failure

A Dietl[1]; I Winkel[1]; M Paulus[1]; R Deutzmann[2]; A Bruckmann[2]; J Schroeder[3]; A Luchner[4]; LS Maier[1]; C Birner[1]
[1]University Hospital Regensburg, Department of Internal Medicine II, Regensburg, Germany; *[2]University of Regensburg, Department of Biochemistry I, Regensburg, Germany*; *[3]University Hospital Regensburg, Electron Microscopy Core Facility, Institute for Pathology, Regensburg, Germany*; *[4]Klinikum St. Marien Amberg, Department of Internal Medicine I, Amberg, Germany*

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Background: Cachexia of skeletal muscles (SKM) occurs early in heart failure. A multi-omics approach of early and advanced tachypacing-induced heart failure in rabbits was performed, revealing impaired oxidative capacity linked to natriuretic peptides. In a second step, we assumed beneficial effects of neprilysin inhibition.
Methods: Incremental tachypacing was sustained for 30 days. Left ventricular function was evaluated by echocardiography. In a first series of experiments, SKM (M. quadriceps femoris) and diaphragm tissue specimens were harvested in healthy controls (CTRL), asymptomatic left ventricular dysfunction (ALVD) and overt heart failure (CHF, n = 4 in each group) to analyse the molecular setup. In a second series of experiments, drinking water was either substituted with the RAS-/NEP-inhibitor

omapatrilat (50mg/kg/d) or placebo (n = 7 in each group). Muscle fibres were distinguished by ATPase staining. Tissue was subjected to custom-made PCR arrays and to difference in gel-electrophoresis with protein identification by tandem mass-spectrometry. In isolated mitochondria, abundance and activities of the electron transport chain complexes were assessed. The expression of natriuretic peptide receptor levels (NPR-A/B/C) and PGC1a was analysed by real-time PCR.
Results: Fractional shortening was reduced in ALVD and CHF (FS = 38.0 ± 1.4%/28.2 ± 1.9%/21.1 ± 2.2% CTRL/ALVD/CHF, $p < 0.05$ Bonferroni post-test with $p < 0.001$ for 1way ANOVA). Whereas body weight remained unchanged due to fluid retention, protein content of SKM decreased (8.7 ± 0.4% vs. 7.0 ± 0.5%, CTRL vs. CHF, $p < 0.05$) and a slow-to-fast fibre type switch occurred in CHF (slow fibres 31.9 ± 0.9% vs. 16.4 ± 1.2%, $P < 0.0001$). In ALVD and CHF, proteomic analysis revealed a dominance of catabolic pathways comprising glycolysis, the Krebs cycle, glycogenolysis and lipolysis. The diaphragm mirrored these changes. Transcriptomic analysis of SKM specimens indicated up-regulation of major mitochondrial transmembrane shuttles of fatty acids. In isolated SKM mitochondria of CHF animals, the expression levels of all complexes of the electron transport chain were reduced, which translated into diminished activities of complexes II and IV. NPR-A and B levels were reduced, whereas the clearance receptor NPR-C was increased in CHF. Albeit omapatrilat did not change systolic function, it mitigated the slow-to-fast fibre type switch, amplified the expression of enzymes involved in beta-oxidation and increased the activity of the electron transport chain. PGC-1a was on the transcriptomic and the protein level reduced in CHF animals. Omapatrilat prevented the reduction. Conclusion: For the first time we could show, that progressive tachycardia-induced heart failure entails profound and very early molecular changes of both SKM and the diaphragm muscle. Furthermore, our data provide first in vivo evidence for beneficial effects of a combined RAS-/NEP-inhibition on SKM in CHF, which is likely mediated by increased PGC-1a.

P1301

Correlation of various molecules involved in cellular traffic with the severity of heart failure in patients undergoing cardiac transplantation

M Ezzitouny[1]; I Sanchez-Lazaro[1]; M Rivera[2]; M Portoles[2]; E Rosello-Lleti[2]; L Almenar[1]; R Lopez-Vilella[1]; M Ferre-Vallverdu[1]; J Sanz-Sanchez[1]; V Donoso-Trenado[1]; P Arenas-Martin[1]; S Lozano-Edo[1]; L Martinez-Dolz[1]
[1]Hospital Universitario y Politécnico La Fe, Department of cardiology, Valencia, Spain; *[2]Hospital Universitario y Politécnico La Fe, Health Research Institute La Fe, Valencia, Spain*

On behalf of: Myocardial Dysfunction and Cardiac Transplant Unit (Research Institute La Fe)
Funding Acknowledgements: Health Institute of Carlos III

Objective: Analyze different molecules involved in cellular traffic (exportins, importins, RAN regulators and nucleoporins) to assess whether their levels are related to the severity of heart failure (HF) in patients undergoing heart transplantation.
Method: From a prospective cohort of patients with advanced HF collected between 2009 and 2015, we have analyzed 64 peripheral blood samples obtained at the time prior to the heart transplant. We compared the levels of the following molecules (determined by ELISA): IMPORTIN5 (IMP5); ATPaseCaTransp (ATPCa); NUCLEOPORIN153kDa (Nup153); RANGTPaseAP1 (RanGAP1) and EXPORTIN4 (EXP4), between two groups: urgent or elective transplant; need for ECMO or not.
Results: Of the 64 patients, 67.2% were corresponded to elective transplants and 32.8% urgent; Of the latter, 76% have undergone circulatory support (ECMO). Significantly elevated levels of IMP5 and ATPCa have been observed in patients undergoing urgent transplantation (compared to elective transplant), and have needed circulatory support with ECMO (versus patients without ECMO), also in the group with ECMO it have seen high levels of Nup153 and RanGAP1 (Table 1).
Conclusion: Patients with advanced HF in a critical situation (who have needed circulatory support or have undergone an urgent transplant) have presented a different pattern of molecular expression in the nucleic-cytoplasmic protein transport compared to those patients in a more stable clinical situation prior to transplantation. It remains to be seen whether the determination of these markers would facilitate the early identification of patients with short-term evolution to a critical situation that requires circulatory assistance, or if the alteration of these markers occurs as a consequence of circulatory support.

Table 1

	N	Mean	Std. Deviation	P	
Nup153	ECMO	16	32,905	18,053	0,032
No ECMO	48	22,898	15,049		
IMP5	ECMO	16	7,776	3,478	0,004
No ECMO	48	4,894	3,332		
RanGAP1	ECMO	16	34,759	18,103	0,007
No ECMO	46	21,990	14,701		
EXP4	ECMO	10	22,520	20,692	0,006
No ECMO	29	68,866	47,927		
ATPCa	ECMO	16	1,073	0,321	0,010
No ECMO	47	0,749	0,452		

P1302

Study of molecules involved in cellular traffic in advanced heart failure: are there differences in the nivels of these molecules between ischemic heart disease and idiopathic dilated cardiomyopathy?

M Ezzitouny[1]; I Sanchez-Lazaro[1]; M Rivera[2]; M Portoles[2]; E Rosello-Lleti[2]; L Almenar[1]; R Lopez-Vilella[1]; J Jimenez-Aguilella[1]; A Cervero-Rubio[1]; V Rosello-Perez[1]; P Pastor-Jover[1]; L Martinez-Dolz[1]
[1]Hospital Universitario y Politécnico La Fe, Department of cardiology, Valencia, Spain; *[2]Hospital Universitario y Politécnico La Fe, Health Research Institute La Fe, Valencia, Spain*

On behalf of: Myocardial Dysfunction and Cardiac Transplant Unit (Research Institute La Fe)
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Objective: Evaluate differences in the pattern of alterations of molecules involved in nuclear-cytoplasmic transport (exportins, importins, RAN regulators and nucleoporins) and related to ventricular function in patients with advanced heart failure with different underlying pathology (ischemic heart disease and cardiomyopathy dilated idiopathic).
Method: From a prospective cohort of patients with advanced heart failure collected between 2009 and 2015, we have analyzed 58 peripheral blood samples obtained at the time prior to heart transplantation. The levels of the following molecules were determined by means of ELISA: IMPORTIN5 (IMP5); ATPaseCaTransp (ATPCa); NUCLEOPORIN153kDa (Nup153); NUCLEOPORIN160kDa (Nup160); RANGTPaseAP1 (RanGAP1) and EXPORTIN4 (EXP4). Then, they were compared between 2 groups of pathology: Ischemic heart disease and idiopathic dilated cardiomyopathy.
Results: Of the 58 patients with advanced heart failure, 57% had ischemic heart disease and 43% had idiopathic dilated cardiomyopathy. We have observed significantly higher levels of IMP5, EXP4, RanGAP1 and Nup153 in patients with dilated idiopathic myocardiopathy compared to patients with ischemic heart disease (table 1).
Conclusion: In idiopathic dilated cardiomyopathy the alterations of nucleocytoplasmic transport are more pronounced with respect to ischemic heart disease. The usefulness and applicability of this finding remain to be determined in subsequent studies.

Table 1

	N	Mean	Std.Deviation	P	
NUCLEOPORIN153kDa	Ischemic	33	21,074	11,925	0,025
Dilated	25	31,379	19,520		
IMPORTIN5	Ischemic	33	4,829	2,897	0,018
Dilated	25	7,088	4,153		
NUCLEOPORIN160kDa	Ischemic	33	270,424	187,355	0,327
Dilated	25	312,365	203,260		
RANGTPaseAP1	Ischemic	32	21,818	15,403	0,033
Dilated	25	31,330	17,480		
EXPORTIN4	Ischemic	22	44,495	26,307	0,044
Dilated	14	76,687	64,478		
ATPaseCaTransp	Ischemic	32	0,912	0,509	0,102
Dilated	25	0,716	0,335		

P1303

Differential expression of plasma microRNA fingerprint in patients with heart failure with reduced ejection fraction responding or not to exercise training

I Witvrouwen[1]; AB Gevaert[1]; N Possemiers[1]; PJ Beckers[1]; H Heidbuchel[1]; SJ Van Laere[2]; AH Van Craenenbroeck[1]; EM Van Craenenbroeck[1]
[1]University of Antwerp Hospital (Edegem), Laboratory of Cellular and Molecular Cardiology, Department of cardiology, Antwerp, Belgium; *[2]University of Antwerp, Translational Cancer Research Unit, Department of Medical Oncology, Antwerp, Belgium*

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Purpose: Exercise training significantly improves morbidity and mortality in patients with heart failure with reduced ejection fraction (HFrEF), but 20% of patients show non-response. Since genetic and epigenetic regulatory mechanisms are key determinants of aerobic capacity (VO2peak), we hypothesize that a circulating microRNA (miRNA) profile can distinguish exercise responders (ER) from exercise non-responders (ENR).
Methods: A miRNA microarray was performed in 18 male HFrEF patients (LVEF <40%) prior to 12-week endurance training; 9 patients were ER (?VO2peak >20%) and 9 were ENR (?VO2peak <5%). Data were normalized using geNorm. MiRNA expression was assessed with unsupervised prediction analysis (pamr package), correlation with ?VO2peak and fold change (2-?Cq). Linear regression analysis was performed to predict ?VO2peak. Statistical analysis was performed in R (v3.3.3).
Results: ER and ENR were comparable with regard to age (58.6 vs 59.9 yrs), BMI (30.5 vs 30.4 kg/m2), resting heart rate (68 vs 76 bpm) and baseline VO2peak (17.5. vs 17.2 ml/kg/min), all p>0.05. Unsupervised clustering analysis of the circulating miRNA expression profiles resulted in a distinction of the ER-group and ENR-group with 83% accuracy. A total of 57 miRNA were differentially expressed: 31 upregulated in ER, 26 upregulated in ENR. Of these, 6 miRNA correlated well with ?VO2peak (all Spearman ? abs. >0.72, p <0.001). These miRNA (miR-23a, miR-140, miR-302c, miR-551b, miR-636 and miR-346) are known to play a role in heart failure, left ventricular hypertrophy, exercise (up- or downregulation) or skeletal muscle atrophy. MiR-140 independently predicted ?VO2peak in linear regression (ß -1856 ± 384, p <0.001).
Conclusions: We found a differential expression pattern of miRNA in HFrEF patients responding or not to exercise training, which could distinguish both groups with 83% accuracy. A fingerprint of 6 miRNA could serve as biomarkers for training response and needs prospective validation in a larger cohort of HFrEF patients.

P1304

A novel method for high precision aortic banding in mice

A O Arne Olav Melleby[1]; A Romaine[1]; JM Aronsen[1]; I Veras[1]; L Zhang[1]; I Sjaastad[1]; IG Lunde[1]; G Christensen[1]
[1]Oslo University Hospital, Institute for Experimental Medical Research, Oslo, Norway

Experimental pressure overload is a commonly used model system in rodents to investigate disease mechanisms in cardiac remodeling and failure. Thoracic aortic constriction (TAC), where a suture is used to restrict blood flow through the ascending or transverse segment of the aorta, has been a valuable tool in cardiac research for three decades. However, there are limitations to TAC with regards to mortality and reproducibility. Additionally, the suture-based method has not allowed precise grading of the stenosis. Here we present a novel method for high precision aortic banding in mice, where fixed diameter micro o-rings were used to induce various degrees of reproducible cardiac remodeling and failure.
Male C57BL6/J wild-type (n = 105) and FVB/J NFAT-luciferase (n = 28) mice were subjected to mild, intermediate or severe o-ring aortic banding (ORAB) of the ascending aorta using o-rings with various inner diameters. Post-surgical assessment of cardiac structure and function was performed with MRI and echocardiography. Hearts were harvested at 2, 4 and 20 weeks post-ORAB for molecular analysis. Post-ORAB survival was 97%, i.e. only 4 technically-related deaths from 133 operations. All ORAB-operated groups developed left ventricular (LV) hypertrophy within one week of operation, assessed as increased LV mass and wall thickness by MRI and echocardiography. Hypertrophic remodeling in the severe ORAB group was more prominent. Over the 20 weeks following surgery, the severe ORAB mice gradually developed reduced cardiac contractile function and declining LV ejection fraction, followed by LV dilatation, whereas the mild and intermediate ORAB groups maintained a compensated LV function. Mice subjected to severe ORAB presented with heart failure, assessed as increased lung weight and left atrial dilatation at 20 weeks. mRNA levels of signature molecules of heart failure (NPPA, NPPB) and hypertrophy (ACTA1, MYH7) were upregulated at 2, 4 and 20 weeks in all group and with a graded response to o-ring inner diameter. Similarly, signature signaling pathways (MAPK and NFAT) associated with LV remodeling and failure were activated in a graded manner. LV fibrosis, measured by collagen mRNA (COL1A2, COL3A1) and Masson's trichrome staining, was more pronounced in mice with severe ORAB. When performed by two independent investigators, comparable structural, functional and molecular cardiac phenotypes where obtained, suggesting that ORAB surgery is inter-surgeon reproducible.
In conclusion, we have developed a novel method for experimental pressure overload in mice using fixed diameter micro o-rings. ORAB allows for inter-surgeon, inter-mouse line, graded cardiac remodeling and heart failure progression, with low mortality and post-surgical exclusion. Thus, choosing ORAB over TAC in experimental protocols is likely to increase the precision of the study and to reduce the number of mice used.

P1305

Epigallocatechin-3-gallate lowers increased calcium sensitivity in cardiac muscle strips of hypertrophic cardiomyopathy patients

F Felix Friedrich[1]; N Kresin[1]; S Stuecker[1]; E Kraemer[1]; G Mearini[1]; G Muench[1]; M Patten[1]; T Eschenhagen[1]; L Carrier[1]
[1]University Medical Center Hamburg-Eppendorf, Hamburg, Germany

Background: Hypertrophic cardiomyopathy (HCM) is a primary disease of the myocardium and mainly caused by mutations in sarcomeric genes. Many forms of HCM show an increased myofilament Ca2+-sensitivity, which could account for compromised diastolic relaxation. Concerning mutations identified in HCM patients this observation has mainly been made in mouse models, reconstituted myofilament systems and isolated cells, but not multicellular tissue from patients. We therefore investigated myofilament Ca2+-sensitivity in multicellular cardiac muscle strips derived from septal myectomies or explanted heart of HCM patients. We furthermore evaluated the potential use of epigallocatechin-3-gallate (EGCg), a known Ca2+-desensitizer.
Methods: We isolated cardiac strips from cardiac tissue of nine HCM patients with either single heterozygous (MYBPC3, MYH7, ACNT2, PLN), or double heterozygous mutations (MYH7/MYBPC3, MYH7/LAMP2, MYBPC3/FLNC). After permeabilization we performed contractility measurements ± 30 μM EGCg to obtain maximal force (Fmax), force-Ca2+ curves and the Hill coefficient (nH). We furthermore evaluated gene expression with the NanoString technology using a customized heart-failure gene panel.
Results: Compared to strips from a non-failing control (NF), Fmax were not different in HCM strips except for two samples carrying MYBPC3 mutations with higher Fmax. Force-Ca2+ curves revealed a higher myofilament Ca2+-sensitivity in HCM patients' strips derived from myectomies, whereas failing explanted heart strips (PLN mutation) were not different. Strips with double heterozygous mutations showed a higher Ca2+-sensitivity than strips with single heterozygous mutations. NH as the indicator of cooperativity was different in all patients' myectomy derived strips, but not in failing explanted heart strips. 30 μM EGCg shifted the force-Ca2+curves of all strips to the right indicating myofilament Ca2+-desensitization. EGCg application induced a more pronounced shift in MYBPC3 strips than in the other genotypes and in strips from patients with truncating mutations. Compared to NF samples, gene expression analysis revealed differences in heart-failure, hypertrophy and fibrosis markers. Differences between NF and HCM samples with higher Ca2+-sensitivity were more prominent in heart-failure and hypertrophy markers, whereas fibrosis markers were more upregulated in tissue with no difference in Ca2+-sensitivity (explanted heart). NPPA and NPPB levels were markedly higher in tissue from patients with double heterozygous compared to tissue with single heterozygous mutations, and in tissue with missense vs. truncating mutations.
Conclusion: We confirmed previous results of an increased Ca2+-sensitivity in native multicellular cardiac strips of HCM patients. Findings suggest that EGCg might be useful for treatment of HCM-associated diastolic dysfunction. Moreover, EGCg could have differential effects depending on the underlying genotype and consequence of the mutation.

P1306

Yin-Yang 1 transcription factor modulates sST2 on adverse cardiac remodeling post-myocardial infarction

MC Asensio Lopez[1]; AM Antonio Manuel Lax[2]; MJ Fernandez Del Palacio[3]; Y Sassi[4]; R Hajjar[4]; DA Pascual Figal[2]
[1]Biosanitary Research Institute of Murcia (IMIB-Arrixaca)., Cardiology, Murcia, Spain; *[2]University Hospital Virgen de la Arrixaca, Department of Cardiology, Murcia, Spain*; *[3]Department of Animal Medicine and Surgery, Murcia, Spain*; *[4]Icahn School of Medicine at Mount Sinai, Cardiology, New York, United States of America*

Rationale: The cardioprotective effects of metformin in the setting of myocardial infarction remain poorly defined. IL33/ST2L signaling is a novel cardioprotective

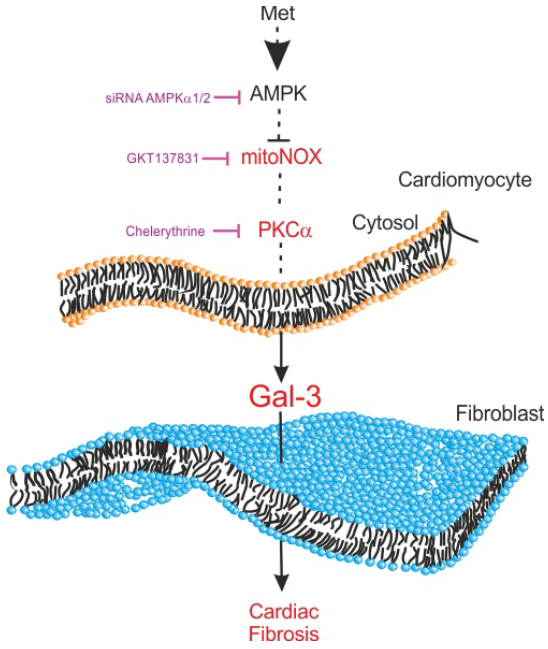
system, which is antagonized by the soluble isoform sST2. No data exist about the regulation of ST2 expression.
Objective: To evaluate the pathophysiological implication of Yy1/HDAC4 system in the expression of soluble ST2 isoform.
Methods and Results: Myocardial infarction and left ventricular dysfunction in rats were induced by permanent ligation of the left anterior coronary artery. Animals randomly received metformin or saline (control). Our results point to improved post-infarction cardiac remodeling induced by metformin, associated with an increase in IL-33 and reduced sST2 expression. Metformin therapy modulates the activity and significantly reduces intranucleus protein levels of the transcription factor Yin-Yang 1. Moreover, metformin blocked the HDAC4 phosphorylation induced by myocardial infarction preventing its export from the nucleus to the cytosol. Dephosphorylated HDAC4 in the nucleus acts as a co-repressor of Yin-Yang-1, which leads to repress the expression of sST2.
Conclusions: Metformin prevented myocardial remodeling after MI by blocking the nuclear-cytosol shuttling of HDAC4, acting as co-repressor of Yin-Yang 1, which leads to suppresses the soluble isoform of the ST2 gene. Manipulation of this pathway might offer new therapeutic options for adverse cardiac remodeling.

P1307

Pharmacological inhibition of the mitochondrial NADPH oxidase 4/PKC/Gal-3 signaling pathway attenuates adverse cardiac fibrosis, following myocardial infarction

M C Maria Del Carmen Asensio[1]; A Lax[1]; MJ Fernandez Del Palacio[2]; MC Sanchez Perez[1]; Y Sassi[3]; R Hajjar[3]; DA Pascual Figal[4]
[1]Biomedical Research Institute Virgen de la Arrixaca (IMIB-Arrixaca), University of Murcia, Cardiology, Murcia, Spain; *[2]Veterinary Teaching Hospital, Veterinary Medicine and Surgery Department, University of Murcia, Cardiology, Murcia, Spain*; *[3]Mount Sinai School of Medicine, Cardiology, New York, United States of America*; *[4]Hospital Clínico Univeristario Virgen de la Arrixaca, Cardiology, Murcia, Spain*

Background: The antifibrotic mechanism of metformin is not completely understood. Our aim, therefore, was to characterize the possible involvement of NADPH oxidase 4 (mitoNox), PKC and Gal3 in this mechanism, given that each has been separately related with myocardial fibrosis and they could represent therapeutic targets.
Methods: Rats were subjected to MI by permanent ligation of the anterior descending coronary artery, and randomized into four experimental groups: (1) placebo-treated sham group; (2) placebo-treated MI; (3) Metformin-treated MI and (4) Metformin-treated sham group. Rats received MET (250 mg/kg/day) or normal saline for 4 weeks. An experimental model of biomechanical strain and a coculture, to allow cross talk between primary cultures of cardiomyocytes and cardiac fibroblasts (all obtained from C57BL6J mice using a Langendorff system), were established to characterize the underlying molecular mechanisms involved in the MET antifibrotic actions. The role of AMPK was determined via siRNA-mediated knockdown while those of mitoNox and PKCa were determined using the inhibitors GKT137831 and Chelerythrine, respectively. The mRNA and protein expression of different markers were measured by quantitative RT-PCR and Western blot, respectively.
Results: Long-term metformin treatment (4 weeks) following MI was associated with: i) a reduction in myocardial fibrosis, Gal3 mRNA and protein levels, as well as macrophage infiltration; ii) an increase in AMPK a1/a2 levels ($p < 0.001$), and an inhibition of both mRNA expression and enzymatic activities of mitoNox and PKCa ($p < 0.001$, in all cases). Following MI, the increase in expression and activity of both enzymes was associated with an increase in the accumulation of the superoxide anion ($p < 0.001$) which positively correlated with mitoNox and PKCa activities ($rs = 0.362$, $p = 0.018$), as well as an increase in the lipid peroxidation ($p < 0.001$) and the activation of the apoptotic death program characterized by the activation of initiatory procaspase 9 ($p < 0.001$) and effectory procaspase 3 ($p < 0.001$). MET therapy was associated with lower superoxide accumulation ($p < 0.001$), lipid peroxidation ($p < 0.001$) and caspases activation ($p < 0.001$). These findings were replicated using a biomechanical strain model. The silencing of AMPK expression (siRNA) blocked the ability of metformin to protect cardiomyocytes from biomechanical strain in terms of mitoNox and PKCa activities, Gal3 levels, cells viability and proliferation, and reactive oxygen species levels ($p < 0.001$, in all cases). The use of specific inhibitors supported the idea that PKC is downstream of mitoNox, and the activation of this pathway results in Gal-3 up-regulation. The Gal-3 secreted by cardiomyocytes has a paracrine effect on cardiac fibroblasts, inducing their activation.
Conclusion. A metformin-induced increase in AMPK improves myocardial remodeling post-MI, which is related to the inhibition of the mitoNox/ PKCa/Gal-3 pathway.



P1308

Investigation of novel derivatives of dexrazoxane reveals topoisomerase II beta interaction as a pre-requisite for effective protection against anthracycline cardiotoxicity

P Brazdova[1]; Z Pokorna[1]; E Jirkovsky[1]; G Karabanovich[2]; J Roh[2]; H Piskackova[2]; M Adamcova[1]; T Simunek[2]; P Sterbova-Kovarikova[2]; M Sterba[1]
[1]Charles University in Prague, Faculty of Medicine in Hradec Kralove, Hradec Kralove, Czech Republic; *[2]Charles University in Prague, Faculty of Pharmacy in Hradec Kralove, Hradec Kralove, Czech Republic*

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Purpose: Anthracyclines (ANTs) rank among the most effective, but also most cardiotoxic anticancer agents. The morbidity and mortality of ANT-treated cancer survivors may be affected by the irreversible damage to the heart resulting potentially into heart failure. The only cardioprotectant approved for prevention of development of ANT cardiotoxicity is dexrazoxane (DEX). It has been traditionally considered as a pro-drug of metal chelating agent ADR-925, nevertheless newer data highlight the interaction of the parent molecule with topoisomerase II beta (Top2b), which has been proposed as a key molecular target for ANTs in the heart. So far, only very few DEX derivatives have been tested for their cardioprotective effects. Furthermore, mechanisms of cardioprotection and structure-activity relationships remain unclear. Aim of this work was to study cardioprotective effects of two newly synthetized DEX derivatives very close in chemical structure to the prototype molecule (N, N‘–dimethylderivative - GK-627 and iso-methylderivative - GK-580) on a model of chronic ANT cardiotoxicity. Furthermore, the mechanisms required for effective protection were investigated.
Methods: Cardiotoxicity was induced in rabbits in a well-established schedule by daunorubicin (DAU, 3 mg/kg/week for 10 weeks) and cardioprotection was achieved by DEX (60 mg/kg before each DAU dose). New DEX derivatives were administered in the same dose and schedule as DEX. In other set of experiments, DEX and its derivatives were administered as a single dose to rabbits to study their pharmacokinetics and ability to interact with Top2b in the heart.
Results: Indeed, DEX completely protected rabbits from mortality (related to heart failure) and effectively prevented induction of the left ventricle (LV) dysfunction as assessed by both echocardiography and LV catheterization. In contrast, neither of its close derivatives was able to do the same. Mortality due to heart failure was 25% and 37.5% in GK-627 and GK-580, respectively (vs 30% in the DAU group). Furthermore, LV dysfunction and expression of natriuretic peptides in the LV were found to be similar as in the DAU group. Also biomarkers of cardiac damage (cTnT) and cardiac histopathology revealed significant damage in both groups which sharply contrasted with the DEX group. Further study confirmed that the difference between DEX and its derivatives is not due markedly altered plasma pharmacokinetics. Instead, the additional experiments revealed the striking difference is in pharmacodynamics - in particular, in ability of the studied agents to interact and deplete Top2b in the heart.

Conclusions: Interaction with Top2b seems to be essential for effective cardioprotection induced by DEX and similar compounds. Cardioprotective effects of DEX are tightly associated with the structure of piperazinedione rings and even small change to this part of molecule can completely abolish both Top2b effects in the heart and effective cardioprotection.

P1309

Study of cardioprotective effects of the ACE inhibitor perindopril against chronic anthracycline cardiotoxicity on dexrazoxane-validated in vivo model

Z Pokorna[1]; P Brazdova[1]; E Jirkovsky[1]; M Adamcova[1]; Y Mazurova[1]; M Sterba[1]
[1]*Charles University in Prague, Faculty of medicine and pharmacy, Hradec Kralove, Czech Republic*

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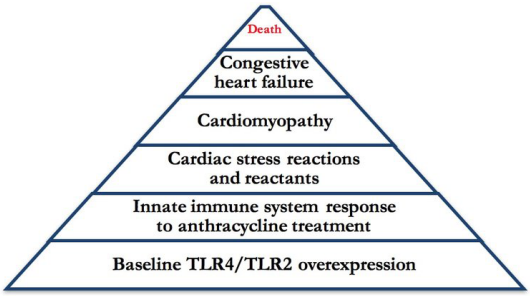
Purpose: Chronic anthracycline (ANT) cardiotoxicity and resulting heart failure are feared complications of cancer chemotherapy. In this indication, dexrazoxane (DEX) is the only drug with well-established cardioprotective effects in both experimental and clinical settings. However, its clinical use is currently restricted because of concerns about its adverse effects. Angiotensin-converting enzyme inhibitors (ACEi) are commonly used to treat ANT-induced cardiac dysfunction and recently been suggested to possess also cardioprotective effects when used prophylactically. However, it is unclear whether ACEi can induce true and sustained cardioprotection similarly as DEX which will not diminish after the withdrawal of the protectant. Hence, the aim of this study was to evaluate cardioprotective effects of perindopril (PER) on a DEX-validated model of chronic ANT cardiotoxicity.
Methods: Chronic cardiotoxicity was induced in DEX-validated model in rabbits with daunorubicin (DAU, 3 mg/kg, weekly for 10 weeks). PER was administered in drinking water in clinically relevant doses (0.05 and 0.1 mg/kg/day) starting a week before 1st DAU dose and withdrawn 3 days after the last dose. After another 4 days when PER was largely eliminated, survivors were randomized for LV catheterization and sacrifice or for subsequent 3 weeks drug-free follow up (FU).
Results: In the treatment period, PER prevented DAU-induced mortality (0 vs. 36 %) and echo examination showed no significant decline in systolic function. LV catheterization revealed significant decline in dP/dtmax in PER co-treated animals as compared to controls, but there was found a significant improvement as compared to the animals receiving DAU alone. Histopathological examination revealed lower cardiomyocyte degeneration and fibrosis at the end of treatment period in PER co-treated animals. In the FU period, PER prevented or markedly reduced ongoing DAU-induced mortality and incidence of sings of blood congestion, but echo examination revealed significant decline in LV systolic function in both doses of the drug. While DAU-induced raise of plasma cardiac troponin T was significantly suppressed by PER in the treatment period, gradual and significant release was observed in the FU to almost match the DAU group at the end of the study. Furthermore, LV expression of ANP, BNP and collagen I was then increased in both groups similarly to the DAU group.
Conclusions: ACEi treatment showed remarkable protection against different parameters of chronic ANT cardiotoxicity during the treatment period, but the effect was found to be progressively diminishing after the withdrawal of the drug. The latter findings are strikingly different to those previously obtained with DEX on the same model and the augmentation of the dose of ACEi showed no benefit in this regard. Estimation of overall benefit of cardioprotective intervention with ACEi against chronic ANT cardiotoxicity requires further study with longer FU period.

P1310

A non-biopsy genetic risk detection method from peripheral human blood for early detection of doxorubicin induced cardiotoxicity

M Trofenciuc[1]; D Darabantiu[1]; RM Christodorescu[2]; HS Branea[2]; A Pop-Moldovan[1]
[1]*Vasile Goldis Western University, Arad, Romania*; [2]*University of Medicine Victor Babes, Timisoara, Romania*

The purpose of the study was a better risk stratification and treatment management and individualization for each of the patients treated with doxorubicin without the usage of miocardial biopsy, which is (was) considered (until now) to be a “gold standard" for cardiotoxicty detection.
This was a prospective study on 25 oncological patients undergoing doxorubicin chemotherapy in which we determinated and correlated TLR2 and TLR4 (tool-like receptor) gene expression with diastolic and systolic echocardiographic parameters concerning cardiotoxicity monitoring.
Material and Methods: Our study included 25 consecutive patients who received treatment with doxorubicin for leukemia, lymphomas or multiple myeloma, aged 18-65, with a survival probability > 6 months and with left ventricular ejection fraction > 50% who expressed their informed consent. Exclusion criteria consisted of previous anthracycline therapy, previous radiotherapy, history of heart failure or chronic renal failure, atrial fibrillation, pregnancy.
Echocardiographic parameters recorded were those of left ventricular diastolic and systolic function (ventricular volumes, ejection fraction, pulsed and tissue Doppler analysis).
Results: Out of the 25 patients, 13 (52%) were males and 12 (48%) were females. Mean age was 56,9 years. The mean dose of doxorubicin administered ranged between 100 - 250 mg/m2, the doxorubicin clearance being 1443 ± 114 ml/min/m2. The average amount of gene expression units was 0.113 for TLR4 (range 0,059-0,753) and 0,218 for TLR2 (range 0,046-0,269).
After 6 months, for 4 patients (16%) left ventricular ejection fraction decreased from 64% to 45%, the other 21 patients having preserved ejection fraction. In patients with decreased of ejection fraction the mean values for TLR4 were 0,18885 and TLR2 at 0,2751 gene expression units.
Criteria for diastolic dysfunction were present after 6 months in 16 patients (64%). In these patients the mean value for TLR2 was 0,30 ± 0,19 and for TLR4 0,15 ± 0,04. Values for the patients who did not develop diastolic dysfunction were 0,16 ± 0,07 for TLR2 (p = 0.01) and 0,11 ± 0,10 for TLR4 (p = 0.2).
Mean E/e’ ratio was 15 ± 0,5 in patients with diastolic dysfunction and 7,8 ± 1,2 in those with normal diastolic function. Patients with E/e’ ratio > 15 had a mean TLR2 expression of 0,39 ± 0,2 compared with 0,23 ± 0,04 in patients with E/e’ = 15.
Conclusions: Our study suggests that TLR4 and TLR2 expression is higher in patients under doxorubicin therapy which develop diastolic dysfunction. The patients with the highest gene expression values were those with more severe diastolic dysfunction.
In all patients, in fasting state, a blood sample was drawn for the assessment of TLR2 and TLR4 gene expression. Gene expression was assessed by qRT PCR.
After 6 months of doxorubicin therapy patients were reevaluated.



Cardiotoxicity immunomodulation

P1311

Nitro oleic acids attenuated systolic heart failure in a murine model of hypertensive heart disease with reduced systolic function

D Dennis Mehrkens[1]; S Geissen[1]; M Adam[1]; M Pekarova[2]; L Kubala[2]; K Manchanda[1]; AK Schaetzle[1]; M Mollenhauer[1]; B Freeman[3]; A Klinke[1]; S Baldus[1]; V Rudolph[1]
[1]*Cologne University Hospital - Heart Center, Department of Cardiology, Cologne, Germany*; [2]*Academy of Sciences of the Czech Republic, Institute of Biophysics, Brno, Czech Republic*; [3]*University of Pittsburgh, Department of Pharmacology and Chemical Biology, Pittsburgh, United States of America*

Purpose: Hypertensive heart disease is a result of chronic arterial hypertension and ranks within the top 10 causes of death in the world, especially prevalent in industrial nations. Cardiac remodeling such as hypertrophy and fibrosis characterize its early progression. Persistent high pressure and volume overload leads to left ventricular dilatation and heart failure with reduced ejection fraction (EF). Nitro oleic acid (OA-NO2) is an endogenously produced nitroalkene which was shown to have antiinflammatory effects as a therapeutic in various animal models of cardiac disease. Recently, we reported the reduction of angiotensin II (Ang II) induced atrial fibrillation and atrial fibrosis by OA-NO2 treatment. Herein, we investigated the effects of OA-NO2 on the morphology and function of the left ventricle and underlying mechanisms in a murine model of hypertensive heart disease with impaired systolic function.
Methods and Results: Wild-type C57BL6/J mice (WT) were subjected to Ang II and additionally, to vehicle (polyethylene glycol/ethanol, AS treatment) or nitro-oleic acid (OA-NO2) via subcutaneous osmotic minipumps. All animals received a salt diet of 1% NaCl dissolved in drinking water for 28 days. Untreated WT mice of the same age were used as a control. Echocardiographic analysis showed a reduced EF in AS treated mice, an effect which was diminished in AS + OA-NO2 treated animals. Histological analyses showed a significantly larger cross-sectional area of cardiomyocytes and a higher grade of fibrosis in the left ventricle in AS

mice, as compared to AS + OA-NO2 treated mice. Of notice, heart weight was significantly increased in AS treated animals but not in the OA-NO2 group. mRNA expression analysis of left ventricular tissue showed activation of a cardiac fetal gene program in the AS treated group, primarily indicated by a shift in a-MHC/ß-MHC ratio, which was absent in OA-NO2 treated mice. Similar results were obtained in a second approach with 14 days of AS pre-treatment, which was followed either 14 days of AS or AS + OA-NO2 treatment. Mice subjected to AS + OA-NO2 showed no further decrease in EF, while AS treatment led to highly reduced EF. Invasively measured blood pressure was significantly elevated in AS and OA-NO2 treated mice compared to WT, but showed no difference between AS and OA-NO2 treatment. Mechanistically, protein and mRNA analyses of ventricular tissue and Ang II stimulated 3T3 fibroblasts indicated an OA-NO2 mediated inactivation of the STAT3 pathway and reduced expression of miR-21 in vivo and in vitro, factors which where both highly upregulated in AS treated mice.
Conclusions: The current data demonstrate that OA-NO2 reduces the cardiac effects of Ang II and high salt treatment and mitigates the progression of hypertensive heart disease due to prevention of STAT3 activation followed by reduced miRNA-21 expression.

P1312
The failing heart stimulates tumor growth by circulating factors

WC Wouter Meijers[1]; M Maglione[2]; SJL Bakker[3]; S De Jong[4]; AR Lyon[5]; DJ Van Veldhuisen[6]; BD Westenbrink[1]; P Van Der Meer[1]; HHW Sillje[1]; RA De Boer[1]
[1]University Medical Center Groningen, Department of Experimental Cardiology, Groningen, Netherlands; *[2]Innsbruck Medical University, Department of Visceral, Transplant and Thoracic Surgery, Innsbruck, Austria*; *[3]University Medical Center Groningen, Department of Internal Medicine, Groningen, Netherlands*; *[4]University Medical Center Groningen, Department of Oncology, Groningen, Netherlands*; *[5]Imperial College London, Heart and Lung Institute, London, United Kingdom*; *[6]University Medical Center Groningen, Department of Cardiology, Groningen, Netherlands*

Purpose: Heart failure (HF) survival has improved and nowadays many patients with HF die from
non-cardiac causes, including cancer. Our aim was to investigate whether a causal relationship exists between HF and the development of cancer.
Methods: HF was induced by inflicting large anterior myocardial infarction (MI) in APCmin mice, which are prone to develop precancerous intestinal tumors, and tumor growth was measured. In addition, to rule out hemodynamic impairment as a cause for potential HF-induced effects, a heterotopic heart transplantation model was employed, where an infarcted or sham-operated heart was transplanted into the cervical area of a recipient mouse, while the native heart was left in situ. After 6 weeks, tumor number, volume, and proliferation were quantified in all mice. Candidate secreted proteins that were previously identified to be associated with (colon) tumor growth in post-MI proteomic studies and studies related to intestinal epitopes. Myocardial gene expression levels of these selected candidates were analyzed, as well as their proliferative effects on HT-29 (colon cancer) cells. We validated these candidates by measuring them in plasma of healthy subjects and HF patients. Finally, we associated the relation between the HF surrogate marker NT-proBNP and new-onset cancer in a prospective general population cohort.
Results: The presence of failing hearts, either native or heterotopically transplanted, resulted in significantly increased intestinal tumor load of 2.4 fold in both animal studies (all $P < 0.0001$). The severity of left ventricular (LV) dysfunction and fibrotic scar strongly correlated with tumor growth ($P = 0.002$ and $P = 0.016$, respectively). Identified proteins were elevated in human patients with chronic HF ($N = 101$) compared to healthy subjects ($N = 180$, $P < 0.001$). Functionally, SerpinA3 resulted in marked proliferation effects in human colon cancer (HT-29) cells. Finally, elevated NT-proBNP levels in apparently healthy humans ($N = 8319$), being a surrogate for preclinical HF, were predictive for new-onset cancer ($N = 1124$), independent of adjustment for known risk factors for cancer, including age, smoking status and body mass index.
Conclusion: We demonstrate that the presence of HF is associated with enhanced tumor growth and this is independent from hemodynamic impairment and could be due cardiac excreted factors.

Poster Session 2 - Clinical Cases

Chronic Heart Failure–Pathophysiology and Mechanisms

P1313

A patient with symptomatic heart failure with preserved left ventricular ejection fraction and right sided heart failure treated with LCZ696

M Cafka[1]; J Xhanaj[1]; E Zace[1]; A Duka[2]; J Seiti[2]; I Balla[2]; A Goda[1]
[1]University Hospital Center Mother Theresa, Department of Cardiology & Cardiac Surgery, Tirana, Albania; *[2]University Hospital Center, Intensiv Care Unit, Tirana, Albania*

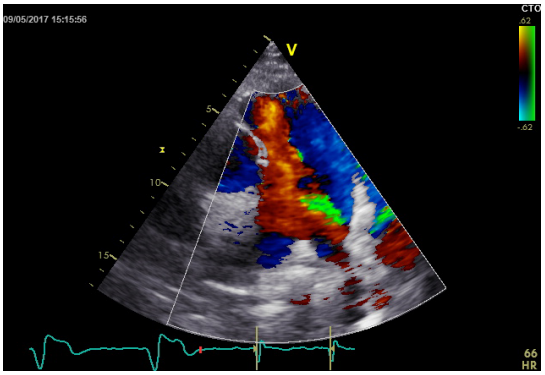
Introduction: Nowdays, where the place of LCZ696 in the treatment of heart failure with reduced systolic function is well established , there are no data about the effect of LCZ696 in patient with symptomatic heart failure with preserved ejection fraction. We present a complex case of a patient with acute cardiac decompensation, with right–sided heart failure but with preserved left ventricular ejection fraction , and chronic renal failure.
Materials : N.H 63 years old, female, presented at the hospital complaining of shortness of breath, fatigue, cough, fever. She had a history of two weeks with symptoms above, gradually worsening. The patient has a known history of repaired septal atrial defect (1990), mechanical prosthesis in aortal and mitral position (2011), a chronic atrial fibrillation, hypertension, insulin dependent diabetes mellitus, chronic renal failure. Vital signs : temperature 37.5 grade/celcius, heart rate 100-110/bpm,blood pressure 130/80 mmHg,respiratory rate 24 breaths/minute, O2 sat 90%. On cardiac examination: ortopnoe position , bibasilar pulmonary inspiratory crackles, elevated jugular venous pressure, hepatic congestion, peripheral edema. TTE revealed normal mechanical mitral and aortal prosthesis (no imaging positive for infective endocarditis). LVEDD 62 mm with LVEF 52% (evaluated by Simpson method), left atrium area 30cm2, right chamber dilated,advanced tricuspidal regurgitation, PSAP 55 mmHg. On the labs : WBC 11 200/mm3, creatininemia 1.7 mg/dl, uremia 215 mg/dl, C reaktiv protein 99 mg/dl, NT -pro BNP 1819 pg/mL, D-Dimer 583ng/ml, steril hemoculture.
Assuming that pulmonary infection and acute deterioration of chronic renal disease(Cardio-renal syndrome type 5) cause acute decompensation of heart failure in NYHA class IV, we begin the treatment with intravenous diuretics, MRA, Antibiotics .When fever is controlled (CRP 20mg/dl) and with stable with renal parameters (creatinine 1.3 mg/dl , creatinine clirence of 43 mL/min) we restart ARB and Beta blockers with minimal dose and up titrating them. Nevertheless the patient remain symptomatic, NT -pro BNP (1142 pg/mL) , so we decided to start LCZ696 50 mg 2 times a day. After 5 days the patient begin to feel better and after 2 weeks she was able to move without symptoms on normal effort; NT-pro BNP reduced to 998pg/ml.
The patient nowdays remain in NYHA Class II, tolerating 100 mg LCZ696 a day. No changes in parametres and systolic function of both ventricle, also in the LA area, was found, but a reduced of PSAP around 40 mmHg.
In Conclusion: This represent a combination of heart failure with preserved ejection fraction and right side heart failure , and chronic renal failure stade 3, where the addition of LCZ696 result in obvious clinical improvement which remain stable nowdays (for about 10 months after discharge) associated with reduction of value of BNP and reduction of pulmonary systolic pressure.

P1315

Unexpected blood flow from pulmonary veins during cardiopulmonary bypass for mitral valve surgery in a 62-year-old woman

N Nicolas Verheyen[1]; G Stoschitzky[1]; J Binder[1]; K Ablasser[1]; O Dapunt[2]; I Knez[2]; A Gamillscheg[3]; R Maier[1]
[1]Medical University of Graz, Clinical Department of Cardiology, Graz, Austria; *[2]Medical University of Graz, Department of Cardiac Surgery, Graz, Austria*; *[3]Medical University of Graz, Division of Pediatric Cardiology, Department of Pediatrics, Graz, Austria*

A 62-year-old lady was acutely referred from an external surgery department where open mitral valve annuloplasty had been cancelled directly after cardiopulmonary bypass connection and cardioplegia because the pulmonary veins had continued to deliver blood into the left atrium. At admission she reported about breathlessness on exertion equivalent to NYHA class III-IV, despite optimal medical therapy for heart failure including a loop diuretic. Auscultation revealed a grade 2/6 systolic-diastolic murmur in the aortic area. She had signs of cardiopulmonary congestion (elevated jugular venous pulse, leg edema). Further comorbidities included osteoporosis and depressive mood disorder.



Regurgitation jet in pulmonary trunk

Office blood pressure and heart rate were 160/60 mmHg and 81 bpm, respectively. An electrocardiogram showed atrial fibrillation and complete left bundle branch block and was otherwise unremarkable. Echocardiography showed a dilated and diffuse hypokinetic left ventricle (end-diastolic diameter 66mm, left-ventricular ejection-fraction 39%, global longitudinal strain –12.6 %) and severe mitral regurgitation (MR) secondary to mitral annulus dilatation. The right ventricle had normal dimension and mildly reduced function (end-diastolic diameter 35mm, TAPSE 15mm) and estimated systolic pulmonary artery pressure (sPAP) was 46 mmHg. In parasternal short axis view with focus on the RVOT, the pulmonary trunk was severely dilated (41 mm). Color Doppler revealed a massive regurgitation jet originating from the left-sided wall of the pulmonary trunk (Figure 1).
A patent ductus arteriosus Botalli (PDA) was confirmed by computed tomography. Simultaneous right and left heart catheterization revealed both post-capillary pulmonary hypertension (mean pulmonary capillary wedge pressure 22 mmHg), as a consequence of dilated cardiomyopathy and MR, and pre-capillary pulmonary hypertension (PAP 67/27 [mean 47] mmHg), due to chronic volume overload of the pulmonary arterial system. Surgical PDA closure and concomitant mitral valve annuloplasty were successfully performed. Three months after surgery the patient's symptoms were markedly improved and estimated sPAP declined to 34 mmHg.
This case illustrates congenital heart disease as a rare and potentially reversible cause of dilated cardiomyopathy and functional MR underlining the importance to perform a comprehensive echocardiographic examination in the early diagnostic work-up of heart failure.

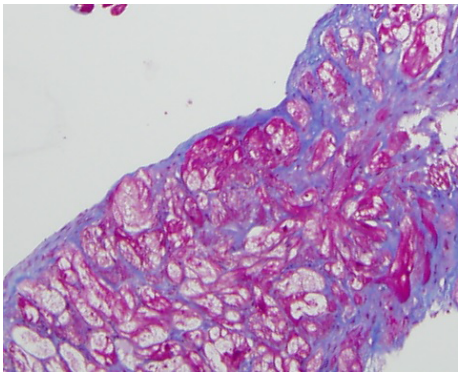
P1316

Chloroquine induced cardiomyopathy

K Krisztina Kosa[1]; B Muk[1]; D Vagany[1]; M Szabo[1]; J Papp[1]; G Bartha[1]; ZS Kiss[2]; T Borsanyi[1]; RG Kiss[1]; N Nyolczas[1]
[1]Medical Centre, Hungarian Defence Forces, Cardiology, Budapest, Hungary; *[2]Medical Centre, Hungarian Defence Forces, Department of Pathology, Budapest, Hungary*

Introduction: Chloroquine (CQ) and hydroxychloroquine are widely used in the treatment of autoimmune diseases. Long-term use of these drugs can induce a rare, but life-threatening toxic side effect, such as cardiomyopathy with restrictive dysfunction that is associated with left ventricle hypertrophy and conduction disorders. The background of the disease is a drug-induced, acquired lysosomal storage disorder. Henceforth we present three clinical cases of CQ induced cardiomyopathy.

Clinical case: In case of pt1 (64 years old) and pt2 (71 years old) long-term (13 and 12 years, respectively) CQ treatment was given due to Sjögren's syndrome and pt3 (67 years old, 16 years CQ treatment) due to SLE. They were admitted to our Cardiology Department with severe heart failure (NTproBNP pt1: 23815 pg/ml, pt2: >35ooo pg/ml, pt3: 33342 pg/ml). Before their hospitalization permanent pacemaker was implanted in all pts because of third degree atrioventricular block (pt1: 1 year, pt2: 6 years, pt3: 1 year earlier). In all cases severe hypertrophic left ventricle and restrictive dysfunction was shown by transthoracic echocardiography. Echocardiographic results suggested cardiac amyloidosis, but further studies have excluded the possibility of it. Due to long-term CQ therapy in the patients' history drug-induced cardiomyopathy was suggested. To confirm this diagnosis endomyocardial biopsy was performed in all three cases. Histological examination showed extreme cytoplasmic vacuolisation that is typical for CQ induced cardiomyopathy. Afterwards CQ therapy was stopped in each patient. One patient showing the most severe clinical symptoms died three months after the diagnosis (pt2). The other two patients are regularly controlled in our Heart Failure Outpatient Clinic. Currently they are clinically stable, but due to the long exposure period, their status seems irreversible. In case of advanced CQ induced cardiomyopathy, heart transplantation is a therapeutic alternative, although in our two patients it is contraindicated due to comorbidities.
Conclusion: CQ induced restrictive cardiomyopathy is underdiagnosed. Early diagnosis and CQ therapy withdrawal is a key point in reversibility, before the development of severe heart failure. Therefore, cardiologic follow-up of patients receiving CQ therapy is essential.



Histology

P1317

Myocardial impairment due to cardiotoxicity after stem cell transplantation: a case report.

R Badr Eslam[1]; S Kufova[1]; B Ozturk[1]; M Krauth[2]; T Binder[1]; IM Lang[1]; J Bergler-Klein[1]
[1]Medical University of Vienna, AKH - Vienna, Cardiology Clinic, Internal Medicine II, Vienna, Austria; [2]Medical University of Vienna, Internal Medicine I, Division of Hematology and Hemostaseology, Vienna, Austria

Introduction: Cardiac toxicity is induced early or late damage to the heart frequently occurring in patients undergoing chemotherapy and oncology treatments. Early detection and treatment of cardiovascular toxicities is highly important for the further outcome. This is a case report of a 63y old female with Multiple Myeloma after receiving stem cell therapy and irradiation, referred for cardiac evaluation ongoing therapy of lenalidomid combined with dexamethasone, and previous bortezomib cancer treatment, regarding cardiotoxicity.
Purpose: Aim of the presentation is to discuss the echocardiography, spiroergometry and clinical findings in context of treatment and prognosis impact.
Methods: Transthoracic echocardiography was performed to assess of myocardial impairment. Ventilation and pulmonary gas exchange as well as cardiac parameters were measured during cardiopulmonary exercise testing (CPET) using a cycle ergometer (VYNTUSTM CPX, Carl Rainer Austria). A ramp protocol, adapted to reach maximal exercise capacity after 8-10 minutes was chosen for the test. The parameter of main interest was maximal oxygen uptake (VO2 max. ml/min.), the major factor known to limit exercise capacity in heart failure.
Results: Transthoracic echocardiography revealed a reduced left ventricular (LV) global longitudinal strain and global circumferential strain by 2D speckle-tracking (GLPS -15%; GE Vivid System) despite LV systolic ejection fraction in normal range (55%), with abnormal basal and mid- interventricular septal motion and diastolic impairment. The patient had no cardiac history and reported fatigue.
Aerobic exercise capacity was slightly reduced: VO2 max. was 16.6 ml/kg/min (= 1162 ml/ min= 83% of percent predicted). Heart rate (HR) response to exercise was slightly below reference value (resting HR 96 b/min, HR end of exercise 130 b/min = 82% of age-predicted) (Figure 1).
N-terminal pro-B-natriuretic peptide level was elevated (241.9 pg/ml).
VO2 max, global longitudinal strain and NT-proBNP have been shown to predict outcome in heart failure, and were well related in this case of cardiotoxicity after allogenic bone marrow transplantation and chemotherapy. These 3 parameters can easily be determined in the clinical setting and appear useful for the cardiac follow-up of cancer pts. Furthermore, VO2 max improvement by exercise training has been shown to improve outcome in cancer pts and heart failure.
Conclusion: Longitudinal speckle tracking strain and peak oxygen consumption are important variables identifying cardiotoxicity non-invasively. Our report should encourage health care professionals to promote exercise testing for pts undergoing chemotherapy to identify development of early myocardial impairment and start treatment as well as exercise programs.

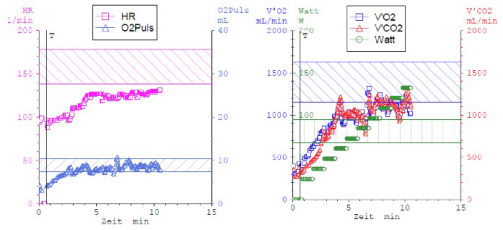


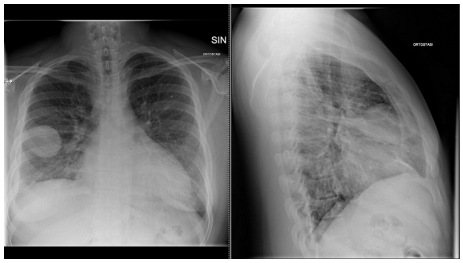
Figure 1

P1318

Late anthracycline - induced cardiotoxicity: a case report

M Marco Schiavone[1]; M Squillace[1]; E Gherbesi[1]; C Gobbi[1]; G Malanchini[1]; F Lombardi[1]
[1]IRCCS Fondazione Ca' Granda Ospedale Maggiore Policlinico, Cardiovascular diseases, Milan, Italy

Background: Chemotherapy with anthracycline is a mainstay for treating Acute Promyelocytic Leukemia (APML), due to its significant survival benefit. Nevertheless, treatment with anthracycline may result in progressive myocardial dysfunction and heart failure (HF), with a pattern of dilated cardiomyopathy. Currently, three types of anthracycline-induced cardiotoxicities are described: acute, early or late (median 7 years).
Case report: A 25-year-old male with a previous history of APML, treated 5 years before with All-trans retinoic acid and Idarubicin (cumulative dose >90 mg/m2) without a subsequent cardiac follow-up, was admitted to our department due to progressive dyspnea, cough and fatigue.
Physical examination at admission revealed several signs of HF: ankle swelling, hepatojugular reflux, third heart sound with a gallop rhythm, tachycardia, pulmonary crepitations and signs of pleural effusion. NT-proBNP was 3583 pg/mL.
A chest x-ray showed right pleural effusion and an oval-shaped pulmonary opacity (8 cm) in the right middle lobe which a subsequent CT scan described as a loculated pleural effusion.
An echocardiogram revealed a dilated left ventricle, diffuse hypokinesia (EF 25%) and moderate to severe mitral regurgitation.
High doses of iv Furosemide were started, together with Bisoprolol, Ramipril (both progressively titrated to the maximum dose, 10 mg o.d.) and Spironolactone 25 mg o.d..
A CMR confirmed the left ventricular dilation and the severe biventricular dysfunction (LVEF 28%, RVEF 35%) and did not show fibrosis.
During the admission, clinical conditions progressively improved and he was discharged after ten days, asymptomatic at rest.
A cycle of cardiac rehabilitation was started. During the follow-up, a CMR showed an almost complete recovery with normal left ventricular dimensions and an improvement in left ventricular function (LVEF 41% vs 28%); right ventricular function was normal (58% vs 35%).
The patient is still in our follow-up program.
Conclusion: Anthracyclines have been shown to be associated with dose-dependent cardiotoxicity, in about 5-18% of cases when the cumulative dose exceeds 90 mg/m2. Since this percentage is not negligible, screening and risk stratification are mandatory to develop early detection strategies, considering that anthracyclines toxicity is characterized by a continuous progressive decline in LVEF, as this case suggest.
These strategies need to be standardized and widespread, as the current Guidelines underline, in order to avoid hospitalizations due to acute heart failure or late therapy. This case emphasizes the importance of a multidisciplinary team of cardiologists and hematologists with expertise in drug induced cardiotoxicity, especially in patients affected by rare subtypes of acute leukemias, who are not scheduled for a strict follow-up program, as other patients affected by more common types of cancer, who are routinely evaluated in our clinic and echocardiography labs.



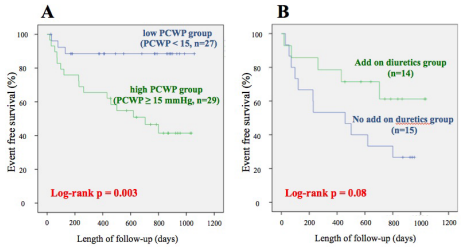
Chest x-ray

P1319

Residual hemodynamic congestion is related to poorer prognosis in patients with clinically compensated heart failure.

K Kazushi Sakane[1]; R Horai[1]; D Maeda[1]; K Akamatsu[1]; M Ozeki[1]; T Fujisaka[1]; K Sohmiya[1]; N Ishizaka[1]; M Hoshiga[1]
[1]Osaka Medical College, Cardiology, Osaka, Japan

Background: Residual clinical congestion is associated with worse prognosis in patients with heart failure. In the current study, we investigated the prognostic impact of hemodynamic congestion on the prognosis of clinically compensated heart failure patients after obtaining clinical compensation.
Methods: Among 250 patients admitted with acute decompensated heart failure, 75 patients underwent right heart catheterization. After excluding 19 patients with the condition of either persistent decompensated heart failure, 56 subjects were enrolled in the current study. Residual hemodynamic congestion was considered to be present when the mean pulmonary capillary wedge pressure (PCWP) was 15 mmHg or higher, and the major adverse cardiac events (MACE) were defined as either any cause of death, hospitalization due to worsening heart failure, implantation of the left ventricular assist devices.
Results: Among the study patients, plasma BNP value was not correlated with PCWP ($r = 0.08$, $p = 0.55$). Residual hemodynamic congestion was found in 29 patients (51.7%) even though symptoms were clinically compensated. Clinical characteristics including age, sex, blood pressure, renal insufficiency and left ventricular ejection fraction were not different between two groups. During the mean follow up period of 553 ± 341 days, 55.2% of patients with residual hemodynamic congestion ($n = 29$) had experienced MACE compared with 11.1% of those without ($n = 27$, Figure A). Among patients with residual hemodynamic congestion, MACE occurred more frequently in patients who did not add on diuretics before discharge compared with whose who added on diuretics (73.3% vs. 35.7%, $p = 0.08$, Figure B).
Conclusions: Residual hemodynamic pulmonary congestion in patients whose heart failure had already been clinically compensated was associated with higher risk for MACE. Hemodynamic assessment for the pulmonary congestion even after obtaining clinical compensation may have value for the long-term management of heart failure patients.



P1321

31 year old male presenting with unexplained HFrEF (LVEF 32%)-suspected DCM due to recreational steroid use, in-hospital acute ischemic stroke, improvement after ICD insertion & medical management

MM Marczewska[1]; M Kowalczyk[1]; A Sioma[2]; M Sinski[1]; L Mazurkiewicz[2]; B Nurowska-Wrzosek[1]; M Dabrowski[1]; A Kuch-Wocial[1]; M Maciejewska[1]; A Kaczynska[1]; J Tyszkiewicz[1]; C Szmigielski[1]; A Opuchlik[3]; B Kierdaszuk[3]; J Grzybowski[2]
[1]Public Central Teaching Clinical Hospital of the Medical University of Warsaw, Department of Internal Medicine, Hypertension and Vascular Diseases, Warsaw, Poland; *[2]Institute of Cardiology in Anin, Department of Cadiomyopathies, Warsaw, Poland*; *[3]Public Central Teaching Clinical Hospital of the Medical University of Warsaw, Department of Neurology, Warsaw, Poland*

On behalf of: Medical University of Warsaw, Institute of Cardiology, Warsaw, Poland

31y/oLS(male)presented to theInternalMedicineDept.with tachycardia & heart failure(HF)symptoms-a feeling of abdominal"fullness" & periodic chest discomfort,occurring irregardless of physical activity.For2-3wks he complained of decreased exercise tolerance & "shallow breathing."For3-4daysLS noted a wet cough.Beforehand he had considered himself to be fit,exercising regularly,and periodically taking dietary supplement & other substances intended to build muscle mass.Upon admission the physical exam showed tachycardia124bpm,BP120/80mmHg,a systolic murmur at the heart apex,with no other abnormalities.The initial work-up showed:ECG-sinus tachycardia120bpm;ECHO-enlarged heart chambers,LVEF 32%(Table1);laboratory studies-slightly increased troponin I,NTproBNP 2408pg/ml.The initial Dx was of dilated cardiomyopathy(DCM)of toxic or tachyarrhythmic etiology.Treatment(Tx)with low-doses of loop diuretic,bisoprolol & ramipril was begun.HolterECG registered sinus rhythm94bpm on avg.,with nocturnal episodes of atrio-ventricular dissociation with ventricular rate 40-60bpm.ABPM noted a tendency for hypotension.On theth day of hospitalization,LS presented motor aphasia & rt-sided neurological signs,which resolved spontaneously within25min.of onset.Based on the results of brainCT,CT-Angio & MRI,an ischaemic stroke of the lt hemisphere was diagnosed.TEEshowed no clots in the LAappendage nor signs of aPFO.No episodes of atrial fibrillation(AFib)were noted,but due to an enlarged LA & DCM,which were potential substrates forAFib,LSwas started on dabigatran.It was thought that the neurologic episode was due to a drop inBP,thusLSwas discharged 9days from admission with no diuretic.Three mo.s laterHolterECG registered nsVT of13beats with nocturnal bradycardia to37bpm,while a control ECHO showed a further fall ofLVEF to27%.Cardiac catheterization was normal.It seemed that the patient hadn't responded to initial conservativeTx,although optimalTx was limited by lowBP.ThusLS was transferred to a reference center for furtherTx & possible heart transplantation(HTx),where he was an in-patient for almost3mo.s.Initially,despite catecholamine & furosemide infusions,changing bisoprolol to carvedilol,the LVEFdecreased to16%. Pulmonary hypertension was diagnosed & sildenafil was added.The patient was qualified forICD implantation & placed on the urgent HTx list.He began to respond to conservativeTx afterICD placement,withLVEF25% at discharge(6mo.s after initial presentation [ptt]).In a control ECHOperformed 3mo.s later(9mo.s after initial ptt)theLVEF rose to36%.Four mo.s later(1yr.after initial ptt)theLVEFwas40%.The patient,following doctors' recommendations,had changed his lifestyle,stopped taking illicit substances&was able to continue daily functioning.This case illustrates the compensatory mechanisms toHF in a hitherto healthy,physically-fit young man.It also shows the dangers of using illicit substances.In addition it teaches doctors patience,in waiting for clinical improvement after optimal medicalTx.

Chronic Heart Failure–Treatment

P1322

Effectiveness of ARNI (Angiotensin II Receptor Blocker Neprilysin Inhibitor) therapy in advanced HFrEF in reduction of severe functional mitral regurgitation

J Joanna Berner[1]; M Lelonek[1]
[1]Medical University of Lodz, Department of Noninvasive Cardiology, Lodz, Poland

In 65-year old male with HFrEF, severe FMR, CAD (post CABG in 2016), arterial hypertension, DM type 2, in pursuance of HF therapy 2016 ESC guidelines, ARB was replaced with ARNI.
Patient was hospitalized due to ADHF (12/2016) - NYHA Class IV, peripheral edema, jugular veins overflow. Selected laboratory and TTE results are presented in Table. Optimal HF treatment was applied (LBA, ARB, diuretics, MRA). At discharged in 6-MWT patient covered the distance of 220m.
At ambulatory visit (02/2017) he maintained in NYHA Class III. Heart Team was performed with the decision of MitraClip procedure. ARB was replaced with sacubitryl/valsartan in start dose 49/51mg. After 1-month OMT ARNI dose was optimized to 97/103mg.
In TTE (6 months OMT with ARNI) significant reduction of FMR was observed. Heart Team re-evaluated the case and indications for MitraClip have subsided. Patient returned to work.
After 9-month OMT with ARNI (NYHA Class I), ergospirometry was performed up to the level of 150W, VO2peak:14,29ml/kg/min; VO2atAT: 11,21ml/kg/min. V02peak >14ml/kg/min and V02 at AT>11 ml/kg/min have favorable prognostic value.
This case report presents the effectiveness of optimal medical therapy with sacubitryl/valsartan in HFrEF accompanied by FMR. We documented significant reduction of FMR on ARNI.

Patient's parameters and pharmacotherapy				
	ADHF - at discharge	Start of ARNI	3 months on ARNI	9 months on ARNI
NYHA Class	III	III	II	I
NTpoBNP (pg/mL)	3692	3342	611	411
eGFR (mL/min/1.73m2)	42,5	81	83	85
K+ (mmol/L)	3.86	4.30	4.90	4.40
BP (mmHg)	125/90	125/80	102/70	124/80
EF (%)	31	-	23	35
LVDD/LVSD (mm)	67/53	-	65/56	61/55
LVEDV/ESV (mL)	-	-	193/149	176/114
LA vol. (mL)	70	-	79	68
TAPSE (mm)	8	-	10	16
PISA (mm)	3	-	7	3
HF Pharmacotheapy: Sacubitryl/Walsartan	-	2x49/51mg	2x 97/103mg	2x97/ 103mg
Bisoprolol	2,5mg	3,75mg	3,75mg	3,75mg
Torasemide	5mg	10mg	10mg	5mg
Eplerenon	25mg	25mg	12,5mg	12,5mg
Furosemide	40mg	40mg	40mg	-

P1323

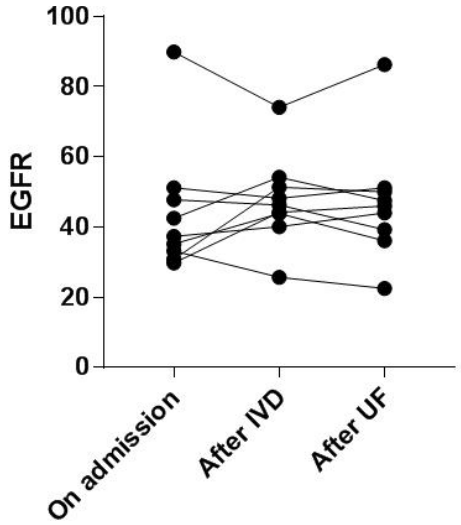
Successful use of ultrafiltration (UF) in patients with heart failure (HF) and diuretic resistant fluid overload - A 3 year experience in a District General Hospital

M Shanmuganathan[1]; K Saleh[2]; TP Chuah[2]
[1]Imperial College London, NHLI, London, United Kingdom; *[2]Royal Surrey County Hospital, Cardiology, Guildford, United Kingdom*

Introduction: Ultrafiltration (UF) is a non-pharmacological therapy for decompensated chronic heart failure (CHF). Its precise role in daily clinical cardiology remains undetermined. We report our experience of using UF in a district general hospital.
Method: UF treatment was delivered by the Aquadex Flexflow device via a central venous catheter. Data was prospectively collected between January 2014 to June 2017.
Results: 13 patients with decompensated CHF underwent UF. The mean age was 72 and mean LVEF was 27.5%. Median daily IV furosemide dose prior to UF was 180mg (120-240mg); 9 patients received metolazone and 2 received dobutamine infusions. Mean weight loss on IVD was 0.1kg/day over 9.67 days, indicating diuretic resistance. During UF, mean weight loss was substantially higher at 2kg/day, with a mean total weight loss of 6.75kg, over a median treatment duration of 2.4. The mean BNP level fell by 125pg/ml after UF. Mean EGFR (Renal function) was 44.21 ml/min/1.73m2. This remained stable after IVD (43.05, p = 0.48) and UF (40, (p = 0.60). There were no adverse events (bleeding or infection).
Conclusion: In our 3 year experience, UF was effective, safe in decompensated CHF with diuretic resistance. It was not associated with a deleterious effect on renal function.

Characteristics of patients		
	Mean value	Standard deviation SD)
Gender (M:F)	10:3	N/A
Mean Age (years)	72	8.24
LVEF (%)	29.29	0.12
On ARB/ACEi & Beta blocker & MRA	100%	N/A
Baseline eGFR (ml/min/1.73m2) n = 9	44.21	17.59
Post IV diuresis eGFR (ml/min/1.73m2) n= 13	43.05	12.9
Post UF eGFR (ml/min/1.73m2) n = 13	40	17.38
Post IV diuresis BNP (pg/ml)	1153	1426
Post UF BNP (pg/ml)	704	590
Pre UF Systolic Blood pressure (mmHg)	120	16
Post UF Systolic Blood pressure (mmHg)	118	15
Time on IV diuresis (days)	9.67	7.94
Time on Ultrafiltration (days)	2.4	0.49
Weight loss on IV diuresis (Kg)	1.73	3.8
Weight loss on UF (Kg)	6.75	2.16

LVEF - Left Ventricular Ejection Fraction, IV - intravenous, UF - Ultrafiltration, eGFR - estimated glomerular filtration rate, BNP - brain natriuretic peptide.



Renal function during treatment

P1324

Diagnostic and therapeutic challenges limit treatment options in heart failure due to complex congenital heart disease

M Luknar[1]; M Kovacova[1]; P Lesny[1]; E Goncalvesova[1]
[1]National Cardiovascular Institute, Bratislava, Slovak Republic

Background : Number of adult complex congenital heart disease (CHD) patients with heart failure (HF) is increasing. Their management is challenging due to numerous factors and treatment options are often limited. We present a case of a patient with corrected complex CHD and late left ventricular (LV) systolic dysfunction requiring advanced treatment.
Case: A young man (b. 1991) with a family history of heart failure (HF) at a young age and sudden death was born with D-transposition of the great arteries (TGA) and patent ductus arteriosus (PDA). Early after birth, balloon atrial septostomy was performed. Anatomic correction of the TGA, PDA ligation, and atrial septal defect closure were performed at 9 months of age. Due to progressive neo-aortic regurgitation with left ventricular (LV) dysfunction, Ross surgery was done in 2002. In later course, patient's condition remained mostly stable, with persisting mild LV dysfunction (LV ejection fraction 40%) as well as recurring atrial and ventricular tachyarrhythmias. Coronary angiogram was negative. In 2016, patient's condition worsened after an episode of atrial fibrillation and thyrotoxicosis. After immediate stabilization, he was referred to an HF centre in order to consider advanced treatment options. At admission, he was in functional class IV. There was LV dilation (82 mm) and extremely severe LV systolic dysfunction (LVEF 10%). Heart transplant (HTx) was considered but severe pulmonary hypertension (PH) with a predominant pre-capillary component (pulmonary vascular resistance of 5.0 Wood units) was a contraindication for listing. Pulmonary function testing revealed a restrictive pattern, however, subsequent imaging methods did not show any relevant lung pathology. LV assist device implantation was impossible due to right ventricular dysfunction. Total heart replacement as a bridge to HTx was not available. Despite sildenafil, unacceptable PH persisted and combined heart and lung transplant was considered. Unfortunately, status of the patient further deteriorated due to recurrent atrial fibrillation resistant to all treatments and he died of end-organ failure.
Case summary : We present a case of a patient with HF due to complex CHD. The most likely cause of LV dysfunction was concomitant dilated cardiomyopathy. Treatment decision making was challenging due to several complicating factors: cardiac (modified anatomy, right ventricular dysfunction, arrhythmia), cardiac-related (multi-factorial PH, repeated surgery), and non-cardiac (thyrotoxicosis, lung disease).
Conclusion: Treatment options for patients with HF due to CHD remain limited. Decision making must be individually tailored and depends on concomitant cardiac and non-cardiac conditions, as well as non-medical factors such as availability of

HTx programme, mechanical support, and other resources. Thorough identification and optimal management of these factors is warranted.

P1325

The heart- brain connection: tracking neurocognition from cardiogenic shock to heart transplantation

M R Robinson[1]; H Khalid[1]; M Khayata[1]; L Njoroge[1]; M Zacharias[1]; M Ginwalla[1]; CA Elamm[1]; M Moghbelli[1]; R Benatti[1]; GH Oliveira[1]
[1]*University Hospitals Cleveland Medical Center, Cardiology, Division of Heart Failure and Transplantation, Cleveland, United States of America*

Our patient is a 51 year old man with prior history non-ischaemic cardiomyopathy, left ventricular ejection fraction (15%, right ventricular systolic dysfunction, polysubstance abuse in remission for 15 years, left ventricular apical thrombus maintained on systemic anticoagulation and status post CRT-D implantation. He was known to have NYHA FC 4/ACC D heart failure for the preceding 3 years and was maintained on optimal heart failure pharmacotherapy. He had had recurrent hospitalisations for decompensated heart failure and cardiogenic shock requiring inotropic use in the recent past. He was admitted with progressive dyspnea and in cardiogenic shock. On presentation, he endorsed functional debility, but felt that his mental capacity was unchanged and within normal limits for him. In addition to heamodynamic (HD) assessment, we undertook serial testing of neurocognitive function (NCF) while he was medically and surgically managed for cardiogenic shock and report our findings leading up to and following orthotopic heart transplantation (OHT). On admission HD, central venous pressure (CVP) 10 mmHg, pulmonary artery pressure (PAP) 57/30 mmHg, pulmonary capillary wedge pressure (PCWP) 30 mmHg, cardiac index (CI) 1.5 L/min/m2, systemic vascular resistance (SVR) 2400 (dynes-sec/cm5), and pulmonary arterial O2 saturation (SvO2): 54%. Testing for depression and was negative and KCCQ suggested a poor quality of life (QoL). Figure 1 details change in MoCA score and CI as he was medically managed, transplanted and post heart transplantation.

Post-OHT, there was no biopsy evidence of rejection. At his outpatient follow-up visit on Day 73, he was able to do 10 METS of activity, continued to be free of depression and QoL testing was improved by 43 points (a 10 point change is considered clinically significant). Moreover his MoCA score continued to be normal.

Implications:

NC deficits are prevalent in cardiogenic shock. Little is known of the impact of HD changes of inotropic and medical optimisation on NCF. Similarly, there is a paucity of data on the evolution of NCF in patients following OHT. Despite subjective assessments to the contrary, our patient demonstrated abnormal NCF while in cardiogenic shock. Furthermore, as he was optimized with inotropic and medial therapy there was a step wise improvement in his NCF that was sustained following OHT. Larger studies are needed to explore the prevalence of this phenomenon. Comparative studies with other methods of cardiac support, e.g. temporary and durable left ventricular assist devices, will yield novel insights that can advise treatment choices.

Acute Heart Failure–Pathophysiology and Mechanisms

P1326

A case of reverse takotsubo cardiomyopathy presenting as acute pancreatitis.

SH Shareef Mansour[1]; O Abou Hassan[1]; A Zakharia[1]; H Isma'eel[1]; H Skouri[1]
[1]*American University of Beirut Medical Center, Cardiology, Beirut, Lebanon*

Case: A 44 year old hypertensive and diabetic lady presenting to the emergency department with severe epigastric pain of 2 days with palpitation and diaphoresis. Initial vitals were a BP of 150/90 and HR of 110 bpm. Patient became drowsy with cold extremities and developed severe dyspnea, desaturation and was intubated. Initial evaluation showed a WBC count of 31300 cu.mm, a creatinine of 1,8 and an amylase level of 6438 IU/L.

A bedside echocardiogram showed severely impaired LV systolic function (EF <20%), normal functioning apical segments with akinesia of mid and basal segments, suggestive of reverse takotsubo cardiomyopathy. Urgent coronary angiography was performed revealing normal coronaries. The LVEDP was 50 mmHg. See fig. 1 LV angiogram.

A Swan ganz catheter was inserted for pressure guided therapy. Her parameters cam as follow:

SBP:150/90; HR: 150 bpm ; CVP: 9 mmHg; SVR: 1800 dyn.sec.cm-5; PVR: 21 dyn.sec.cm-5; PAP: 21/11; COP: 2.88 L; CI: 1.8 L/m2

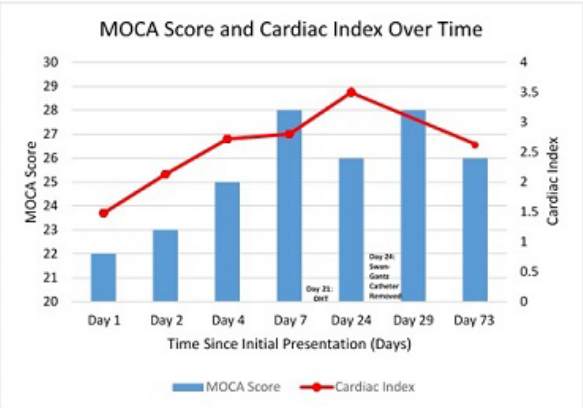


Figure 1: MOCA Total Score, pharmacotherapy, and cardiac index over time

Day 1, Prior to starting therapy

Day 2, Milrinone 0.5 mcg/kg/min, sodium nitroprusside 2.5 mcg/kg/min, spironolactone 12.5 mg QD

Day 4, Milrinone 0.5mcg/kg/min, digoxin 0.125mg QD, spironolactone 25mg QD

Day 7, Milrinone 0.5mcg/kg/min, digoxin 0.125mg QD, hydralazine 100 mg Q8H, isosorbide mononitrate 120 mg QD

Day 24, Milrinone 0.25 mcg/kg/min, hydralazine 50 mg Q8H, Prednisone, Tacrolimus, mycophenolate mofetil

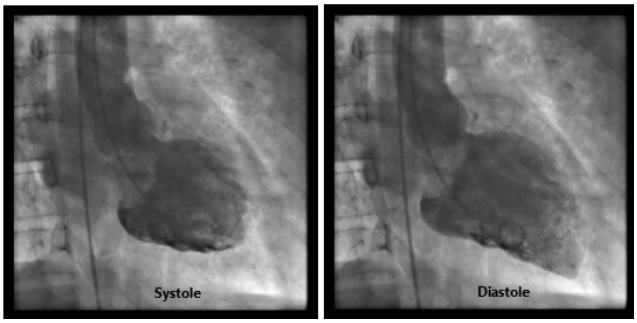
Day 29 , Hydralazine 50 mg TID, Lisinopril 10 mg QD, Nifedipine 60 mg QD, aspirin 81mg QD, Pravastatin 40mg QD, Prednisone, Tacrolimus, Mycophenolate Mofetil

Day 73, Lisinopril 10 mg QD, Nifedipine 60 mg QD, aspirin 81 mg QD, Pravastatin 40 mg QD, Prednisone, Tacrolimus, Mycophenolate Mofetil

Figure 1

Conclusion/Clinical

SBP: systolic blood pressure; CVP: central venous pressure; CO: cardiac output, PVR: pulmonary vascular resistance; SVR systemic vascular resistance, CI: cardiac index.
The patient was clinically in shock state, with evidence of organ hypoperfusion. She was comatose, cold, anuric, with severe worsening lactic acidosis and liver function. However she had a high blood pressure. She was started on nitroglycerine and



LV angiogram

furosemide drips with non adequate response. It was decided to start her on Levosimendan as inotrope. A CT abdomen showed a 5 x 6 cm left adrenal mass, suggestive of pheochromocytoma, so Doxazocin was added. However, Patient didn't show improvement, and went into multi-organ failure. Veno-arterial extracorporeal membrane oxygenator (VE-ECMO) was inserted for full hemo-dynamic support with CVVHD for acute renal failure.Patient started to show improvement until she was weaned from ECMO support after 6 days, and gradually regained her kidney function. Repeat echocardiogram showed complete recovery of LV systolic function. Pheochromocytoma was confirmed by MIBG scan and a surgical resection was performed when patient stabilized.
Discussion: The cardiovascular manifestations of pheochromocytoma can be mild as sinus tachycardia or lethal such as cardiogenic shock and Takotsubo cardiomyopathy especially the reverse type due to high level of circulating catecholamines.
Levosimendan, a calcium channel sensitizer and a vasodilator is a suitable for cardiogenic shock with systemic vasoconstriction as seen in pheochromocytoma.
Hyper-amylasemia is likely secreted by pulmonary endothelial cells under ischemic damage and hypoxia secreting the s-isoenzyme. ECMO allows a quick and full circulatory support in patients with cardiogenic shock, and is a very suitable option in phaeochromocytoma cases.

Acute Heart Failure–Diagnostic Methods

P1327
Eosinophilic myocarditis or arrhythmogenic cardiomyopathy? When neither the multimodal display decides.

E Eva Ozabalova[1]; J Krejci[1]; P Hude[1]; J Godava[1]; T Honek[1]; V Zampachova[2]; L Spinarova[1]
[1]St. Anne's University Hospital, Department of Cardiology, Brno, Czech Republic; *[2]St. Anne's University Hospital, Pathological –anatomical institute, Brno, Czech Republic*

Background: Myocarditis may be part of the ARVC pathophysiology, the manifestations of both diseases may also be similar. Multimodal imaging can help in differential diagnosis, but in some cases we can not do without endomyocardial biopsy.
The authors describe the story of a 47-year-old woman who has long been treated with rheumatoid arthritis, ulcerative colitis, chronic autoimmune thyroiditis and adrenal hypofunction after long-term corticotherapy. She was first hospitalized in 11/2015 at another hospital for paroxysmal atrial fibrillation. Pharmacologically restituted sinus rhythm. After 14 days she comes due to dyspnoea and fatigue, a junction rhythm is detected on the ECG. Echocardiography and laboratory are normal. After discontinuation of antiarrhythmics, no bradycardia was captured. 14 days later she was received for dyspnoea, signs of bilateral heart failure. According to ECHO, the left ventricular systolic function decreased slightly. MRI without signs of inflammation or other patology. There are large numbers of inflammatory cells present in the EMB, so the patient was treated with a pulse dose of corticoids. During the hospitalization the progression of right-heart failure was observed, temporary catecholamine support was needed. The junction rhythm is again present on the ECG. According to MRI, the most likely finding of arrhythmogenic cardiomyopathy, diagnostic kriteria were present than ICD was implanted. After improvement of the clinical condition the patient is able to dimise for oral corticotherapy, which is further reduced by the outpatient pathway. In 12 months, the patient is again admitted for total fatigue, shortness of breath, chest pain. Excluded acute coronary syndrome and pulmonary embolism. According to ECHO, signs of right heart failure with a slightly reduced systolic function of the left ventricle were present. EMB was performed again, where acute myocarditis with regressive cardiomyocyte changes and a higher proportion of eosinophils were reported. Cyclosporine and corticoid therapy was initiated with improvement in clinical status.
Conclusion: Echocardiography and especially MRI play a crucial role in the diagnosis of cardiomyopathy, in some cases, however, we can not do without invasive diagnostics. Treatment is mostly based on corticotherapy, in recurrent cases is a combination of immunosuppressant recommended. Arrhythmogenic cardiomyopathy is not available for pharmacological treatment, ICD implantation is necessary.

Acute Heart Failure–Treatment

P1328
Ivabradine in Acute Heart Failure, why not?

C Carmen Collado Moreno[1]; I Valiente-Aleman[2]; JC Rodriguez-Yanez[2]; FJ Morales-Ponce[1]
[1]Puerto Real Hospital, Department of Cardiology, Puerto Real, Spain; *[2]Puerto Real Hospital, Critical Medical Medicine, Puerto Real, Spain*

This is a 39 - year - old man patient with no personal or family history of heart disease or either cardiovascular risk factors. The patient suffered in the last 48 hours back pain, progressive dyspnea and febrile non-thermometer sensation.
At the time to hospital admission vital signs were No fever (36 °C), Blood pressure 100/65 mmHg, Heart rate 150 bpm, basal peripheral saturation of oxygen 85%, breathing frecuency 45 bpm. The patient was awake, oriented in time, space and person with Glasgow Coma Scale 15/15. Respiratory auscultation showed rales throughout the lung, cardiac auscultation was normal. No abdominal pain. No limbs abnormalities, peripheral pulses evaluated in extremities were normal.
Chest X-ray showed alveolar pattern, in transthoracic echocardiography severe left ventricular dysfunction (LVEF 30%) with akinesia in basal and mid septal segments which determined basal "ballooning" were appreciated, blood test showed elevation of ultrasensitive cardiac troponin and EKG ST-segment elevation in DI and aVL, so was firstly diagnosed of Acute Myocardial infarction with ST-segment elevation.
A coronary angiography was performed, which revealed normal arteries. The patient required admission to coronary intensive care unit (CICU) to be treated. During CICU stay sinus tachycardia (140 bpm) was treated with Ivabradine (5mg twice a day) due to low blood pressure (90/50 mmHg) so no vasoactive drugs were required. Acute pulmonary edema disappeared with Non-Invasive pulmonary ventilation, furosemide continuous intravenous infusion and heart rate control. On day 4 Ivabradine was remove due to moral opposition of physician, so the patient restarted to get on pulmonary edema although keeping the same treatment. Ivabradine was prescribed again 2 days later by all physicians agreement so the patient experimented clinical improvement that we could discharge him from the ICU in 48 hours. A cardiac MRI was performed on day 12 of hospital stay showing total normalization of LVEF and absence of late enhancements. Due to clinical evolution and complementary exams the most likely diagnosis was atypical Takotsubo Cardiomyopathy.
Conclusion: MINOCA should be considered as a working diagnosis in all patients who present myocardial infarction and normal coronary arteries. An overt cause should not exclude the physician to manage it as a MINOCA investigating the real cause although an apparent one has been presented.
Ivabradine seems to be a safe drug treatment for heart rate control in the onset of acute heart failure due to systo-diastolic disfunction.
Further clinical trials should be performed to reach best level of evidence.

P1329
A case of cardiac tumor of malignant B-cell lymphoma presented with heart failure due to cardiac tamponade

F Fumimasa Tabata[1]; T Koizumi[1]; S Taguchi[1]; I Tsutsumi[2]; C Yoshida[2]
[1]National Hospital Organaization Mito Medical Ceter, Cardiology, Ibaraki, Japan; *[2]National Hospital Organization Mito Medical Center, Hematology, Ibaraki, Japan*

Introduction: Primary cardiac tumor is only 1-2% among heart disease. 80% are benign and 20% are malignancy. Size, location, architecture of tumor are important factors for its treatment. There are many reports that could cause syncope, embolism, myocardial infraction and even sudden death so require to make early therapeutic strategies.
Case: A 80-year-old female presented heart failure. Cardiac echo revealed pericardial effusion and tamponade and pericardiocentesis was done.

Echo also pointed out 33 × 24mm mass at tricuspid valve annulus that are different from of thrombus, pedunculate tumor like myxoma or vegitation. Coronary artery CT showed no significant stenosis.
Effusion sample was bloody, cytologic diagnosis was class?b. Flow cytometry were CD45+,CD10+,CD19week, CD20-, CD79a week, that suggesting malignant B-cell lymphoma.
As get this data we thought malignant B-cell lymphoma and had started R-CHOP therapy.
This case final diagnosis is B-cell lymphoma, unclassifiable, with features intermediate between Diffuse Large B-Cell Lymphoma(DLBC) and Burkitt lymphoma, stage?B, high risk of International Prognostic Index (IPI). After chemotherapy mass vanished, no sign of refuel of pericardial effusion and his heart failure symptoms are improved.
Discussion: Cardiac tumor is rare disease in daily clinical world especially cardiac malignant B-cell lymphoma is about 1% among them and that reported rapidly progression and poor prognosis. This case cardiac tamponade is key turn for this patient's diagnosis and treatment. 6 cycle of R-CHOP has achieved complete remission now. It is difficult to diagnose DLBC accurately by Cardiologist. On the other hand Hematologist might difficult to control cardiac tamponade.

P1330
Successful extracorporeal resuscitation after intoxication with suicidal intent

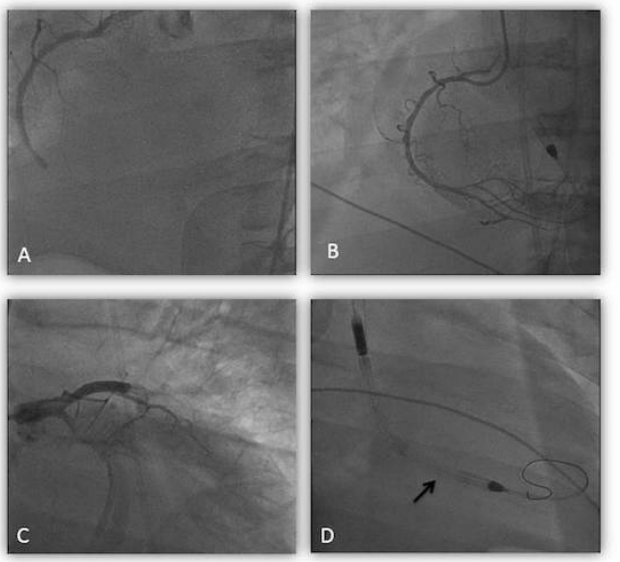
B Panholzer[1]; K Katharina Huenges[1]; M Eide[1]; G Hoffmann[1]; J Cremer[1]; A Haneya[1]
[1]University Medical Center of Schleswig-Holstein, Cardiovascular Surgery, Kiel, Germany

Background: Intoxication with suicidal intent is a possibly life threatening condition leading to a variety of symptoms with unpredictable severity. Here, we report from a case of successful extracorporeal resuscitation (eCPR) after intentional overdose of psychotropic drugs.
Methods and Results: A 24 year old female patient with a long history of depression was brought to hospital after intake of large quantities of pipamperone and citalopram. During transport and right after admission, the patient suffered from cerebral seizures, and emergency intubation had to be performed. Immediately afterwards, the patient developed ventricular fibrillation (VF), and cardiopulmonary resuscitation was inevitable. Electrocardiography revealed a pronounced long-QT- syndrome (LQTS), blood tests showed a massive metabolic disorder. Overall, the hemodynamic situation remained unstable with recurrent episodes of VF and high-dose catecholamine dependency. For immediate stabilization, veno-arterial extracorporeal membrane oxygenation (VA-ECMO) was percutaneously implanted into the femoral vessels using Seldinger's technique, and the patient was referred to our hospital. Within the following days, LQTS persisted, leading to continuous electrical storm, but under continuous VA-ECMO support, the patient remained stabile. After seven days, drug levels of pipamperone and citalopram normalized, and an additional administration of beta-blocker lead to a complete remission of VF. After eight days of support, ECMO could be explanted, and the patient was extubated two days later. Two weeks after ECMO explantation, the patient was discharged to a rehabilitation clinic.
Conclusion: eCPR using VA-ECMO is a highly effective way of achieving immediate location-independent stabilization with consecutive interhospital transfer. Our case could show that therapy with ECMO systems is a good option in unpredictable situations such as intoxication in suicidal intent.

P1331
Cardiogenic shock- bridging with multimodality short term mechanical circulatory support.

H Husnat Ahmed[1]; S Lim[1]
[1]University Hospital Birmingham, Cardiology, Birmingham, United Kingdom

A 46-year-old gentleman was transferred to our intensive care unit (ITU) for consideration of cardiac transplantation/left ventricular assist device (LVAD) due to severe left ventricular dysfunction and ongoing heart failure symptoms.
He had presented to his local hospital with left anterior descending artery (LAD) territory infarction and cardiogenic shock requiring percutaneous coronary intervention (PCI) to LAD and right coronary artery (RCA). His comorbidities included type II diabetes mellitus and hypertension.
On arrival, his observations were satisfactory.
His case was discussed at our transplant MDT and decision was made to work him up towards long term LVAD as bridge to cardiac transplant. Unfortunately, the following day he suffered further STEMI thrombosing LAD and RCA stents and a large obtuse marginal (OM) branch. Intra aortic balloon pump (IABP) was inserted and PCI to LAD initiated. Unfortunately, during PCI, he suffered cardiac arrest requiring prolonged cardiopulmonary resuscitation (CPR) with downtime of 60 minutes. Circulation was supported initially by an Impella 3.5 placed percutaneously into right common femoral artery and then laterally by peripheral veno-arterial extracorporeal membrane oxygenation (VA ECMO).



A: Occluded RCA stent; B: Restoration of RCA flow on ECMO; C: Occulded LAD stent; D: Impella (arrow)

Following ECMO, surprisingly, RCA showed spontaneous re-establishment of flow with some residual thrombus at distal end of stent. In order to preserve RV function and potentially avoid the need for biventricular assist device (BiVAD) implantation, RCA was wired and dilated using balloon with achievement of good TIMI 3 flow. As he needed an LVAD, it was felt that PCI to LAD and OM branch would not offer any additional benefit.
He was transferred back to ITU and after two days peripheral ECMO and Impella were removed and Centrimag short term LVAD was inserted. Post operatively, he was a bit slow to wake and there were concerns about his neurological prognosis. After detailed discussion with neurology colleagues, it was felt appropriate to keep supporting his cardiac care. Short term LVAD (provided support for 3 weeks) was therefore ex-planted and replaced with long term Heartmate III LVAD.
Patient made slow but steady progress post-op. He still has residual mild cognitive and mobility impairment. He has now been transferred to a neuro-rehabilitation centre and we remain hopeful that he will make enough progress to be discharged home.
Discussion: IABP, Impella and ECMO are viable short term interventions to manage cardiogenic shock secondary to severe LV dysfunction.
Uncertainty about neurological status following prolonged CPR and low flow state represents a challenging dilemma in clinical practice. Given our patient's young age and witnessed cardiac arrest we decided to support his circulation hoping that he would make meaningful neurological recovery.
Our case highlights good outcome from the use of a multimodality circulatory support in the context of severe cardiogenic shock, prolonged CPR and low flow state.

Coronary Artery Disease–Pathophysiology and Mechanisms

P1332
The role of transthoracic coronary arteries ultrasound in dyspnea differential diagnosis in a patient with chronic heart failure, atrial fibrillation and implanted permanent pacemaker

M V Agarkov[1]; O P Mamaeva[2]; S V Vlasenko[1]; D A Vorobyovskiy[1]; N E Pavlova[2]; O A Guseva[3]; A A Anton Khilchuk[1]; S V Lebedeva[2]; A M Sarana[4]; S G Scherbak[4]
[1]State City Hospital #40, Interventional Radiology, Saint-Petersburg, Russian Federation; [2]State City Hospital #40, Functional Diagnostics, Saint-Petersburg, Russian Federation; [3]North-west state medical university, Saint-Petersburg, Russian Federation; [4]Saint-Petersburg state university, Medical Faculty, Saint-Petersburg, Russian Federation

Introduction: new dyspnea onset in patients with long history of persistent atrial fibrillation and implanted permanent pacemakers is usually regarded as chronic heart failure progressing. Conducting stress-echo in order to diagnose significant stenosing atherosclerosis is difficult or impossible. We believe that transthoracic coronary arteries ultrasound is effective and specific diagnostic method to reveal hemodynamically significant coronary arteries stenoses with a further indication for coronary angiography without stress-test. Aim: to use personified approach in dyspnea differential diagnosis in a patient with multiple cardiac comorbidities. Materials: 66 years old male with rheumatic heart disease, artificial aortic and mitral valves on warfarin, implanted permanent pacemaker and persistent atrial fibrillation. Coronary angiography 5 years ago showed no stenotic lesions. Last 6 months patient has gradually worsening dyspnea after minimal exercise while on full medical therapy. We considered performing stress-echo early after transthoracic echocardiography but due to high pretest probability, high coronary diastolic flow velocity and persistent AFib with pacemaker we proceeded directly to coronary angiography.
Methods: we performed serial ECG and transthoracic echo registrations before referring the patient to the cardiac catheterization laboratory.
Results: ECG showed normo-tachisystolic persistent atrial fibrillation, TTE showed preserved systolic function with an absence of myocardium contraction abnormalities. Coronary ultrasound of middle left anterior descending artery (LAD) revealed high peak diastolic velocity (122cm/sec) which correlated with a hemodynamically significant lesion. Next day coronary angiography demonstrated hemodynamically significant critical stenosis of middle LAD, which was successfully stented in an elective way. The patient is totally fine at 90-day follow-up without dyspnea and any stable angina. Conclusion: we underscore feasibility and efficacy of hemodynamically significant stenosing atherosclerosis diagnostic with novel noninvasive ultrasound methods in patients with heart failure, persistent atrial fibrillation and implanted permanent pacemakers.

Coronary Artery Disease–Treatment

P1333
Pheochromocytoma with either myocardial infarction or myocarditis? That is the role of cardiac MRI

A Basuoni[1]; M El-Ramly[1]
[1]*Cairo University Hospitals, Cardiology , Cairo, Egypt*

Pheochromocytomas most commonly arise from the adrenal gland (90%) and are benign in 90% of cases.They produce characteristic systemic manifestations due to secretion of catecholamines, most commonly norepinephrine. Cardiac manifestations of pheochromocytoma include hypertension, myocardial hypertrophy, myocarditis, cardiomyopathy, pulmonary edema, cardiogenic shock, arrhythmias and rarely myocardial infarction. Hypertension is the most frequent cardiovascular manifestation of pheochromocytoma.
We reported a case of 31 year old female patient, was known to have hyperthyroidism, hypertension secondary to pheochromocytoma and supra-adrenalectomy 7 years ago. the patient presented with agonising chest pain. EKG showed lateral ST segment elevation with inferolateral ST segment depression. cardiac enzymes showed elevated high sensitive troponin with normal CKMB . emergency echo was normal. so cardiac MRI was recommended for suspected perimyocarditis. surprisingly, cardiac MRI showed lateral infarction so the patient underwent CA showed co-dominant LCX giving two large obtuse marginals, the second OM divided to two rami and there was a significant stenosis of one of the 2 rami most probably due to atherosclerosis. so the diagnosis was lateral MI for medical treatment, control of risk factors and searching for pheochromocytoma reactivity.
Pheochromocytomas have been rarely associated with acute myocardial infarction. Most of these cases have normal coronaries. The mechanism of myocardial infarction or segmental myocardial dysfunction associated with pheochromocytoma has been linked to coronary spasm or a direct toxic effect induced by catecholamines but in our case it could be due to acceleration of atherosclerosis. also Catecholamines increase left ventricular work by inducing left ventricular hypertrophy from hypertension and increase in heart rate. so in our case searching for activity of and recurrence of pheochromocytoma was mandatory for the diagnosis.

Myocardial Disease–Clinical

P1334
Putting the pieces together: a multimodality imaging approach to left-side pericardial agenesis diagnosis

C Catarina Ruivo[1]; R Ladeiras-Lopes[2]; R Faria[2]; N Ferreira[2]; V Gama[2]
[1]*Hospital Santo Andre, Cardiology, Leiria, Portugal*; [2]*Hospital Center of Vila Nova de Gaia/Espinho, Cardiology, Vila Nova de Gaia, Portugal*

A 56-year-old woman was referred to the Cardiology outpatient clinic complaining of atypical chest pain. Her physical examination was unremarkable. The chest radiograph (Figure 1) depicted flattening and elongation of the left heart border (Snoopy sign), right heart border superimposed on the spine and a radiolucent band. The apical four-chamber view of transthoracic echocardiogram (TTE) showed leftward position, exaggerated motion and bulbous ventricles. Suspicion of pericardial agenesis was raised.
Cardiac computed tomography (CCT) revealed extreme levoposition of the heart and interposition of lung parenchyma between the aorta and the pulmonary artery. Movement artifacts precluded accurate observation of the pericardium as well as exclusion of coronary disease. Better anatomic definition and temporal resolution were achieved with cardiac magnetic resonance (CMR). Axial T1-weighted imaging showed absence of left-side pericardium, while depicted the pericardium adjacent to right atria. Cine imaging in supine position confirmed the clockwise rotation of the heart, which assumed a near normal position (from 120° to 65°) after repositioning the patient in right lateral decubitus. Adenosine stress and late gadolinium enhancement imaging were normal. Associated non-cardiac and cardiac anomalies, including atrial septal defect, mitral valve stenosis or patent ductus arteriosus were ruled out. Given the benign prognosis, patient was managed conservatively.
This case highlights the incremental value of an integrated multimodality imaging approach. Left-side pericardial agenesis is exceedingly rare, generally found incidentally and can explain atypical symptoms1. Clinicians should be aware of the specific findings on chest radiograph and TTE. CCT aids in diagnosis and CMR stands the gold-standard. Repositioning the patient and real-time cine CMR show the hypermobility of the heart and might become part of the routine diagnostic work-up of pericardial agenesis.

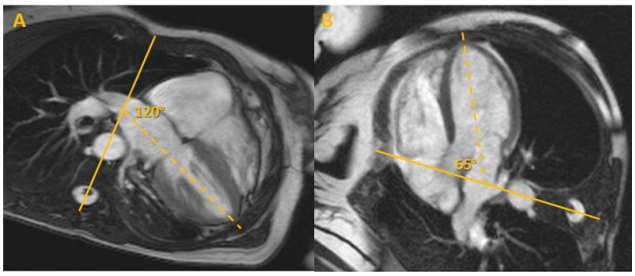


Figure 1: Cardiac magnetic resonance

P1335
A challenging case of cardiomyopathy and its clinical implications

A Antonio Xavier Fontes[1]; C Serena[1]; L Oliveira[1]; S Moura-Ferreira[1]; C Almeida[1]; C Machado[1]; R Dourado[1]; E Santos[1]; N Pelicano[1]; AM Pacheco[1]; A Tavares[1]; F Melo[1]; D Martins[1]
[1]*Hospital Divino Espirito Santo, Cardiology, Ponta Delgada, Portugal*

80-year-old female, was referred to our department in 2016 due to shortness of breath and in the last 3 months. Her past medical history included left bundle branch block (LBBB), hypertension (medicated with irbesartan 300mg and lercanidipine 20mg), diabetes, esophageal-gastric junction cancer in 2015 treated with surgery. She was considered to be cancer-free and lost 30kg (BMI = 22,2kg/m2).
She had performed an echocardiogram (ETT) in 2013 that showed calcification of aortic and mitral valves, with moderate mitral insufficiency. Patient gave birth 10 times (one daughter died suddenly at the age of 35 years old and 2 children died after delivery). Physical examination revealed a blood pressure of 126/70mHg, and systolic murmurs at the apex and left sternal edge. An electrocardiogram showed sinus rhythm and LBBB.
Patient repeated the ETT that showed dilated left ventricle with asymmetric hypertrophy of the inferior, infero-lateral and inferior septal walls (20mm), left ventricle ejection fraction (LVEF) = 25%, left atrium severely dilated, functional mild to moderate mitral regurgitation and mild pericardial effusion (PE). After the initial evaluation the main hypothesis were late-onset hypertrophic cardiomyopathy and cardiac amyloidosis. We started guideline based treatment with loop diuretic, spironolactone and beta-blocker (patient already taking irbesartan), with little improvement.
The next step considered was to perform cardiac magnetic resonance imaging. The findings in this exam were highly suggestive of amyloidosis (diffuse left ventricular wall thickening - maximum in anterior wall with 19mm, diffuse sub-endocardial and sub-epicardial heterogeneous increased signal on delayed contrast-enhanced and inability in obtaining an optimal null time on TI scout sequences).
Systemic light-chain amyloidosis has been excluded, cardiac biopsy was not performed due to the risks of the procedures and patient repeated the echocardiogram to evaluate ejection fraction 4 months after medical therapy (LVEF = 21%). We assumed senile cardiac amyloidosis.

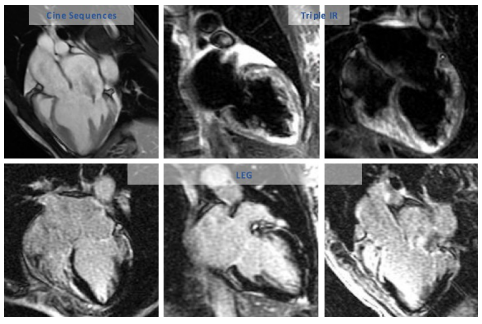
As she remained symptomatic we considered cardiac resynchronization therapy. This procedure was complicated with rupture of a great cardiac vein's collateral with consequent moderate PE. Tamponade physiology has not been developed. One month later the LVEF was 36% and the PE had mild to moderate dimension.
Cardiac amyloidosis is a clinical disorder caused by extracellular deposition of insoluble fibrils (approximately 7.5-10 nm wide) with beta-pleated sheet configuration. The cardiac involvement in the amyloidosis is, in most cases, secondary to a systemic disease. However an isolated cardiac involvement can occur. The gold standard for the diagnosis of a cardiac amyloidosis remains the endocardial biopsy, but this is an invasive procedure and is related to severe complications. A strong diagnostic suspicion can be made by identifying several specific bio-clinical and imaging findings.

P1336

An infectious cause of heart failure with increasing prevalence in Europe

AR Ana Rita Pereira[1]; AR Almeida[1]; I Cruz[1]; A Marques[1]; S Alegria[1]; AC Gomes[1]; D Sebaiti[1]; A Briosa[1]; N Marques[2]; H Pereira[1]
[1]Hospital Garcia de Orta, Cardiology, Almada, Portugal; *[2]Hospital Garcia de Orta, Infectious Diseases, Almada, Portugal*

We present the case of a 49-year-old woman, coming from the countryside of Brazil and living in Europe since about 10 years ago. She had clinical history of iron-deficiency anemia caused by menometrorrhagias and an unspecified cardiac disease, diagnosed 3 years before hospital admission and characterized by left ventricular (LV) moderate systolic dysfunction [LV ejection fraction (LVEF) 32%] evaluated by a transthoracic echocardiogram (TTE) and normal coronary arteries showed by a coronary computed tomography (CT) angiography. She was admitted in our Emergency Department with complaints of oppressive chest pain, palpitations and lipothymia with 3 days of evolution. She also reported progressive worsening exertional dyspnea (at admission, triggered by mild physical activity) with 1 month of evolution. At clinical examination, she was hemodynamically stable and an apical, grade II/VI, systolic heart murmur with axillary radiation were heard. Blood tests revealed haemoglobin 7,2 g/dL, high-sensitive cardiac troponin T 153 ng/L [normal range (NR) < 13 ng/L] and NT-proBNP 948 pg/mL (NR < 153 pg/mL). A 12-lead ECG showed sinus rhythm, 63 bpm, left anterior fascicular block and complete right bundle branch block. TTE demonstrated LV dilation with reduced wall thickness, diffuse hypokinesia and moderate systolic dysfunction (LVEF 35%), moderate functional mitral regurgitation and dilated inferior vena cava with decreased respiratory size variation.
The diagnostic hypotheses of type 2 acute myocardial infarction secondary to exacerbation of chronic anaemia and reduced LVEF heart failure (HF) of unknown cause were considered. During hospitalization, transfusion support and intravenous iron therapy was given and HF disease-modifying drugs were initiated and up-titrated. The initial laboratory studies revealed no abnormalities. To better clarification of clinical case, the patient (pt) underwent a cardiac magnetic resonance imaging that was suggestive of inflammatory dilated cardiomyopathy, namely, Chagas disease (CD) or sarcoidosis. On suspicion of these diagnoses, a chest CT was performed showing no relevant findings and serological tests to detect immunoglobulin G antibodies to Trypanosoma cruzi were requested. As two different serological tests were positive, the diagnosis of chronic chagasic cardiomyopathy was established. After discharge, the pt kept under follow-up (FU) in HF and Infectious Diseases appointments, completing 60 days of antiparasitic therapy with benznidazole.
As complication during FU, the pt was readmitted, hemodynamically unstable, owing to a monomorphic ventricular tachycardia. An implantable cardioverter defibrillator for secondary prevention was placed. Currently, she is in NYHA class I-II.
This clinical case illustrates and intends to make a brief review of an increasing cause of HF and arrhythmias in Europe, which is currently hosting large populations of migrants from Central and South America where the CD is endemic.

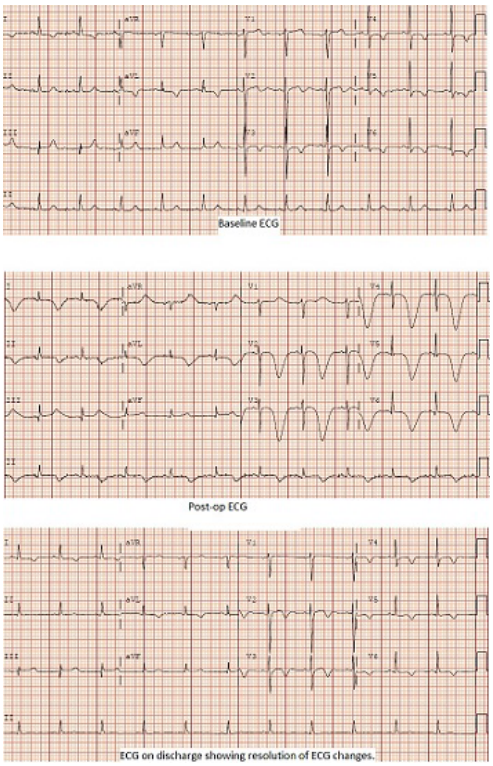


P1337

Takusubo cardiomyopathy: electrical cardiogram manifestation before myopathic changes.

C Li[1]; ZY Lim[2]
[1]Tan Tock Seng Hospital, Cardiology, Singapore, Singapore; *[2]Khoo Teck Puat Hospital, Cardiology, Singapore, Singapore*

Madam G.T is a 79-year-old Indian lady who presented with right neck swelling over the last few weeks. Her past medical history includes hypertension, hyperlipidemia,



impaired glucose tolerance and end stage renal failure on peritoneal dialysis. A transthoracic echocardiogram done a year ago showed normal left ventricular ejection fraction (LVEF), concentric left ventricular hypertrophy with no regional wall motion abnormality (RWMA). Baseline electrocardiogram (ECG) showed sinus rhythm and left ventricular strain pattern
She was admitted to Otolaryngology department for excisional biopsy of right cervical mass under general anaesthesia. Post-operatively, intravenous neostigmine and glycopyrronium bromide were given due to prolonged drowsiness but achieved only suboptimal effect and subsequently sugammadex was administered. Mrs G.T developed sinus tachycardia shortly after and was treated with intravenous beta blockers.
Serial electrocardiograms were undertaken and showed significant new T wave inversions in anterior and lateral leads which persisted despite the tachycardia settling and without any symptoms. Serial cardiac enzymes also demonstrated a dynamic rise in troponin T from 104 pg/ml to 249 pg/ml.
Based on the ECG changes and dynamic troponin rise, a provisional diagnosis of non-ST elevation myocardial infarction (NSTEMI) was made and an urgent echocardiogram was undertaken on the same day which was essentially unchanged from the previous year echo with normal LVEF and no RWMA.
Coronary angiography was also undertaken which showed normal coronary arteries and an echocardiogram was repeated. This time, it showed new apical akinesia and a depressed LVEF of 45%. The ECG changes resolved 4 days later and an echocardiogram performed 2 months later demonstrated resolution of the RWMA. These findings would fit with a diagnosis of takusubo cardiomyopathy.
Discussion: The interesting aspect of this case was the documentation of ECG changes preceding myopathic changes in keeping with Takusubo cardiomyopathy along with ECG resolution before the improvement in left ventricular function. This could have clinical implications for patients who have early investigations which could well be normal but in the presence of persistent ECG changes, a repeat left

ventricular assessment could help assist in the subsequent diagnosis of Takotsubo cardiomyopathy.

Hypertension–Other

P1338

Prognostic significance of clinical-anthropometric, biochemical, metabolic, vascular-inflammatory and molecular-genetic markers in the development of the first ischemic stroke.

V Veronika Shishkova[1]
[1]*Moscow Medical Centre Neurorehabilitation , Moscow, Russian Federation*

Aim: The study of the relationship between various parameters: clinical-anthropometric, biochemical, metabolic, vascular-inflammatory, molecular-genetic and the development of the first ischemic stroke, and the development of a prognostic model for determining the probability of its occurrence.
Material and methods. 196 patients who underwent the first ischemic stroke and 119 people who did not suffer a stroke, corresponding to age, place of residence and nationality to a group of patients, were examined. The main anthropometric, clinical, biochemical and metabolic parameters were assessed; markers of vascular inflammation and endothelial dysfunction. Genotyping of single nucleotide polymorphisms of genes: IL8, ADIPOQ, ADIROR, APOB, APOC-IV, BDNF, GRM3 using ready-made TaqMan probes was carried out.
Results: Based on the results of the correlation analysis, the following parameters were statistically significant with the first ischemic stroke: weight, BMI, WC, homocysteine, insulin, adiponectin, cystatin C, ApoA1, Apo B, OHL, XC-HDL, LDL, TG, CRB-sh , glucose, uric acid, IL-1b, IL-4, IL-6, IL-8, TNF-a, VEGF-A. The binary logistic regression method was used to construct the forecast model. The final independent model includes the following independent variables: weight, diabetes, adiponectin, Apo A1, IL-1b, IL-4, ADIPOQ (rs17366743), GRM3 (rs2228595), R2 value of Nagelkerk was 0.839. The percentage of agreement between the model and the "training sample" was 90.7%. The percentage of consent of the model with the "independent sample" was 87.1%, the overall percentage of the model's agreement for all patients was 89.8%. In accordance with the received data, the ROC-curve (Receiver Operating Characteristic) was constructed, the area under the ROC-curve was 0.92.
The conclusion: Based on the data obtained in this study, a probability model for the development of the first AI was obtained. Of all the parameters studied in the study, the largest contribution to the probability of development of the first AI, according to the model obtained, is made by the parameters: diabetes, adiponectin, Apo A1, IL-4.

P1339

Determination of knowledge levels about disease and treatment compliance in individuals with hypertension

S Oguz[1]; B Bayrak[1]; Ö Adadioglu[1]; B Akay[1]; G Camci[1]; B Kinali[1]; G Okur[1]; TE Sit[1]
[1]*Marmara University, Faculty of Health Sciences, ISTANBUL, Turkey*

Background: Hypertension is a risk factor for many chronic diseases, especially cardiovascular diseases. As individuals with hypertension become more knowledgeable about the disease, their treatment compliance increases.
Purpose: This study was planned as a cross-sectional and descriptive study to assess the level of knowledge about disease and treatment compliance in individuals with hypertension.
Materials and Methods: The study has been perfomed between January 15 and April 15, 2017 with 500 patients who were admitted to the cardiology clinic and hospitalized in cardiovascular ward of a hospital in Istanbul, were diagnosed with hypertension and had no communication problems. Data were gathered by using Questionnaire and Hypertension Knowledge Level Scale (HK-LS). The scale consists of definition, medical treatment, compliance, life style, diet, complication sub-dimensions. The highest total score of scale is 22. As the score from the scale increases, knowledge level of individuals increase. In our study, the cronbach alpha was found 0.78. Descriptive statistics, Student's T test and one-way ANOVA were used in the evaluation of research data.
Results: The mean age of the patients was 64.08 ± 12 and 56.6% of them were male, body mass index of 82.6% of them was 25 and above (BMI> 25) and %38.8 of participants were obese. 58.4% of individuals had comorbid disease and 55.8% of them had hypertension for 10 years and over. 58.8% measured blood pressure when their blood pressure was high, 40.6% drank lemon juice when their blood pressure rises, 44% did not took blood pressure medicine regularly and 43% forgotten to take their high blood pressure medication occasionally. The average score of the patients taken from the scale was 17.36 ± 3.47.
It has been found that women's medical treatment and high school graduates' definition, medical treatment, compliance, life style knowledge score was high ($p < .05$). And also it was seen total score, definition, compliance and complication knowledge score of employee and good income patients was high ($p < .05$). Total scale score, diet and complication knowledge score of patients living with family; definition, treatment, compliance, life style, diet and complication knowledge score of patients doing exercise and definition and diet knowledge score of patients without chronic disease were found to be high ($p < .05$)
Conclusion: Women, patients with good income, those living with family, those who exercise, those without chronic diseases, and those with a high education level had higher level of disease knowledge and compliance to treatment.

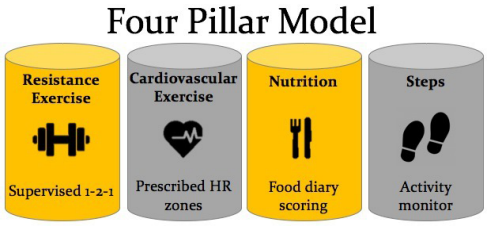
Cardiovascular Rehabilitation

P1340

A novel '4 pillar' model of clinical exercise training in a patient with heart failure

M Thompson[1]; YLD Rumble[1]; AC Groome[1]; SD Olden[1]; MAP Fawke[1]; IR Cradock[1]
[1]*Clinical Prevention and Rehabilitation, London, United Kingdom*

Background: It's classically known that physical training improves exercise tolerance, health-related quality of life and reduces hospitalisation rates in patients with heart failure, culminating in practical recommendations being published in 2011. The current case is a modern application of these guidelines using a novel '4 Pillar' model.
Case Description: A 72 year-old male with diagnosed heart failure (NYHA III) with reduced ejection fraction (25%). History of a complex multivessel PCI and dual



Four Pillar Model

chamber-defibrillator following an episode of cardiogenic shock. Subsequent severe mitral and tricuspid regurgitation and 4 chamber dilation with dyskinesis. The patient presented with exertional breathlessness and significant limitation in day-to-day activities. He was unable to climb one flight of stairs without stopping or walk on a flat gradient for 5 minutes.
Intervention
The patient underwent a 12-week personalised and intensive exercise and nutrition programme comprising twice-weekly one-to-one resistance-based exercise sessions, twice-weekly aerobic exercise sessions, on-going targeted step-count and nutritional monitoring and prescription. Exercise was prescribed and periodised into 'training blocks'. Stage 1: interval-based work, breathing mechanics and postural correction. Stage 2: muscular endurance, using time-under-tension theory, inspiratory muscle training and step count. Stage 3: muscular strength and hypertrophy, aerobic endurance and respiratory maintenance.
The patient experienced profound improvements in activities of daily living and breathlessness, moving from NYHA III to II. Exercise capacity increased to 4 flights of stairs and 45 mins of incline walking.
Conclusions: and implications for clinical practice
Additional research is required utilising this style of training to further elucidate optimal prescription. However, the current model may offer a development to the current guidelines and provide a blueprint for optimal exercise training in heart failure within the modern healthcare system.

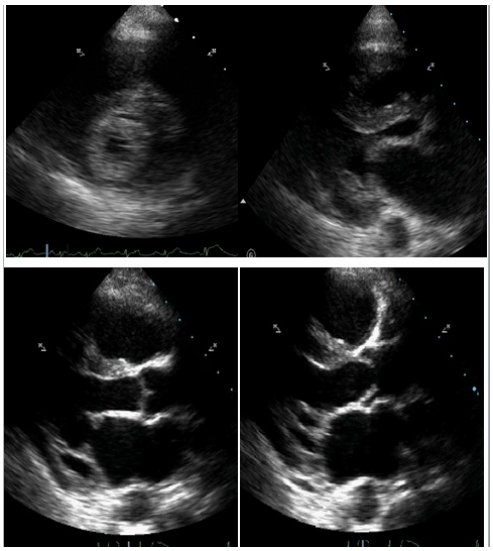
Valvular Heart Disease–Pathophysiology and Mechanisms

P1341

Non rheumatic mitral stenosis in a country with endemic rheumatic heart disease, Is it easy to judge?

AHMED Gaafar[1]; AMR Abdelaal[1]; HOSAM Magdy[1]; MAGDY Ismail[1]
[1]*Helwan University, Faculty of medicine, Cardiology department, cairo, Egypt*

Background: Mucopolysaccaridosis (MPS) is a rare inherited lysosomal storage disorder with multisystem manifestation due to systemic deposition of glycosaminoglycans (GAGs). Cardiac affection has been detected in all types of MPS syndromes and is a common cause of early mortality.
Description: young male patient from rural low socioeconomic area presented to cardiology clinic for assessment before planed surgery for inguinal hernia, he had characteristic features; He was dwarf, with coarse facies and abnormal gait. He complained from dyspnea (NYHA class III), easy fatigability and exertional palpitations with history of recurrent chest infections. No history of syncope, paroxismal nocturnal dyspnea, orthopnea or lower limb swelling.
On examination, patient was laying flat on bed, hisJugular venous pressure was



MPS syndrome

elevated , BP : 110/60, pulse: 90/min. regular. There was significant kyphoscoliosis, leading to absence of cardiac pulsations.On auscultation; cardiac sounds were distant with mid diastolic rumbling murmur hardly heard. ECG was unremarkable. X-ray revealed left atrial mitralization and deformed thoracic cage with spine deformities. Other systems revealed joint stiffness and deformities, kyphoscoliosis, large boxy skull, multiple ocular nerves paralysis with limited visual fields, large tongue, harsh voice, bilateral inguinal hernias and hepatoseplenomegaly. The lab results were within average.
Echocardiography revealed markedly thickened mitral leaflets with no evidence of calcifications and thickened sub-valvular apparatus causing severe mitral stenosis (MS), mitral valve area about 1.1cm^2 ; Bi-ventricular hypertrophy, thickened intra-atrial septum and dilated left atrium.
So the question was; Is it RHD case or these are manifestations of another systemic disease?IAS thickening, RVH in absence of significant pulmonary hypertension, LVH in absence of systemic hypertension or LVOT obstruction andwithout history of RH fever also his brother has the same manifestations in addition to valvular affection in form of grade 2 aortic regurgitation and mild AS which increased the doubt about RHD as the pathological process.So systemic storage disorder with cardiac manifestations became our main concern.The case was referred to an internist and an enzymatic assay was done for the patient, the result of which confirmed the diagnosis of MPS I Hurler-Sheie syndrome.
Management: A multidisciplinary team from cardiology, internal medicine and cardio-thoracic surgery was formed to determine and discuss the optimal line of management for the patient. Cardiac surgery in the form of mitral valve replacement was deferred by the cardio-thoracic team because of the associated risk posed by intubation and post-operative care issues.The next question was what is the appropriate management of this case? And can we apply Wilkin's score which was designed and applied for RHD in our case for suitability to perform balloon valvuloplasty?

Acute Heart Failure–Clinical

P1342
Recurrent takotsubo syndrome - case report

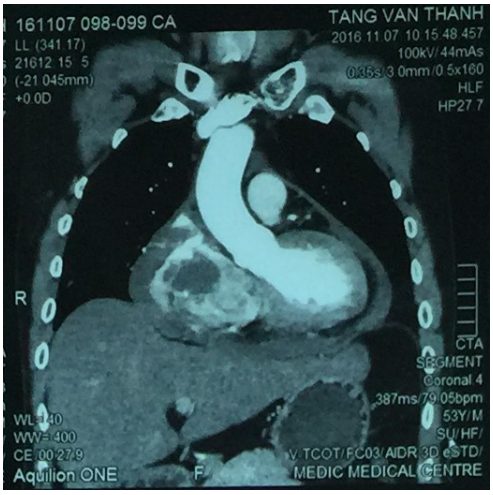
M Mariana Saraiva[1]; L Marta[1]; ML Pitta[1]; B Santos[1]; D Durao[1]; M Leal[1]
[1]*Hospital of Santarem, Cardiology, Santarem, Portugal*

Unravelling the etiology of left ventricular dysfunction is important for an appropriate therapeutic management of the patient. Many times, the differential diagnosis is challenging and meticulous. The authors present a case of Takotsubo Syndrome (TkS), peculiar for its recurrence, but also for the concomitance of coronary artery disease.
We report the case of a 67 year-old man, with arterial hypertension, anxiety and chronic obstructive pulmonary disease and active smoking. He presented to the hospital with shortness of breath and orthopnoea. Already at the hospital, he mentioned self-limited chest pain for a few minutes. On examination, he presented afebrile, with sinus tachycardia (s tach), hypoxemia and bilateral wheezing and lung rales. The most relevant findings were: s tach and nonspecific ST-T wave abnormalities in the electrocardiogram; significant elevation of myocardial necrosis biomarkers (MNB) and brain natriuretic peptide (BNP). The transthoracic echocardiogram showed severe systolic dysfunction of the left ventricle, akinesia of the anterior septum and anterior wall, hypokinesia of mid and distal segments of the other walls and hypercontractility of the basal segments of anterolateral, inferolateral and inferior walls, as well as the inferior septum. He underwent optimized treatment for acute heart failure and also antithrombotic therapy, considering the hypothesis of an acute coronary syndrome. During hospital stay, he revealed he had recently lost a family member. Coronary angiography showed a significant stenosis of the circumflex artery, where a drug-eluting stent was implanted. He evolved positively, with recuperation of left ventricular systolic function and no segmental kinetic changes at discharge. A diagnosis of TkS was considered the most likely.
Seven months later, he returned to the hospital, again with hypoxemia, acute congestive heart failure and self-limited chest pain. He mentioned the death of a previous co-worker the day before admission. For a second time, he presented a significant rise in MNB and BNP levels, and electrocardiographic and echocardiographic changes, both very similar to the ones described previously. He repeated coronary angiography which showed no relevant findings. Yet again, he had a favourable evolution and echocardiographic recovery at discharge. Pheochromocytoma and myocarditis were excluded.
Given the reversibility of these findings, the presence of a psychological stressor preceding the two episodes and the absence of other plausible causes to explain all these findings, a final diagnosis of recurrent TkS was made.

P1343
A case of hemorrhagic tamponade due to right atrium angiosarcoma

H Thai Hao Phan[1]
[1]*Pham Ngoc Thach University of Medicine, Cardiology, Ho Chi Minh, Vietnam*

Background: Primary cardiac angiosarcoma is rare. It is typically located in the right atrium and manifests as right-sided heart failure or cardiac tamponade. Most patients are symptomatic at presentation and when disease is discovered, it is often late in its course, resulting in a poor prognosis. We describe a case of hemorrhagic tamponade due to right atrium angiosarcoma.
Case presentation: A healthy 53-year-old man presented to lung diseases hosptital after one month of hemoptysis. He was started on antibiotics for suspected pneumonia. Over the next few weeks, the hemoptysis worsened and a chest computer tomography was performed.The result was a tumor in right atrium, then he was referred to our institution for further evaluation. Cardiac MS-CT showed a heterogeneous tumor in right atrium 6.5 x 8.0 x 8.0 cm in size suspected angiosarcoma, moderated pericardial effusion (Fig.) PET-CT showed hypermetabolic tumor in right atrium, paratracheal lymph nodes and intrapulmonary nodes. Over one week he suddenly developed dyspneic, hypotensive, and tachycardia. Examination revealed distended jugular veins, distant heart sounds, and diminished lung sounds at the bases. A transthoracic echocardiogram demonstrated a large circumferential pericardial effusion with evidence of cardiac tamponade. He was transfered to emergency surgery. A large amount of blood was found in the pericardial space. Direct invasion of the tumor to the pericardium detected. The tumor was located on the wall of the right atrium and extended over the epicardium. Bleeding from the tumor had ceased after sewing and blood drainage. A piece of tumor was resected and the pathological examination revealed primary cardiac angiosarcoma.
Discussion: Primary cardiac angiosarcomas are rare. Most patients present with symptoms related to heart failure and tamponade.The patient described here had numerous extensive pulmonary metastases, hemoptysis and tamponade. The majority of the primary tumor site is located in the right atrium, and the most common site for metastasis is the lung or the pericardium. Computed tomography scanning confirms the diagnosis of a cardiac mass.
Conclusion: Primary cardiac angiosarcomas-such as our patient's tumor-are highly aggressive and locally invasive. The tumor usually arises from the right atrium, with nonspecific symptoms and signs. Very rarely, the tumor presents with rupture, which leads to hemopericardium, cardiac tamponade, and a poor prognosis. In our patient, the surgery also controlled the bleeding and prevented death from cardiac tamponade; further, it provided a tissue specimen for diagnosis.



P1344

What may happen when you are expecting - a case of peripartum cardiomyopathy

T Theresa Glantschnig[1]; K Ablasser[1]; N Verheyen[1]; D Von Lewinski[1]; PP Rainer[1]
[1]Medical University of Graz, Cardiology, Graz, Austria

Introduction and description: A 29-year-old female presented with pulmonary edema and hypertension 5 days after delivering her first child and an uneventful pregnancy. Echocardiography (TTE) showed dilation of the left ventricle (LVEDD 68mm), reduced LVEF (40%) and severe mitral regurgitation. NT-proBNP was increased to 2496pg/ml and hsTnT to 27g/ml. Non-invasive positive airway pressure ventilation was administered, as well as loop diuretics and intravenous nitroglycerine. HF therapy with beta blockers, an ACE inhibitor, and aldosterone was initiated. Additionally, we gave low molecular weight heparin and bromocriptine. Cardiac MRI showed mild late gadolinium enhancement of the inferior LV wall. The patient was kept on bromocriptine for one week and symptoms improved. LVEF remained mildly impaired but recovered to near-normal values after 6 months.
Identification of the problem: Peripartum cardiomyopathy (PPCM) affects a particularly vulnerable collective. It occurs in late pregnancy or postpartally and is potentially fatal. Recovery rates are higher if LVEF is mildly reduced and response to HF therapy is present. These therapies prevent breastfeeding and may be established reluctantly. Antithrombotic prophylaxis is warranted for high risk of deep vein thrombosis (DVT). Recurrence of PPCM is possible, this necessitates prudent counseling of the patient.
Questions and differential diagnosis
1. What are important differential diagnoses and why can diagnosis be delayed?
2. How is PPCM treated?
Answers and discussion
1. DVT with pulmonary embolism is an important differential diagnosis. D-dimer levels are usually elevated after delivery, but TTE showing reduced LVEF without signs of right heart pressure overload may be helpful. Another factor delaying diagnosis is the common occurrence of dyspnea and leg swelling in pregnant patients. In such cases, risk stratification with NT-proBNP levels and, if elevated, echocardiography appears prudent. Other reasons for HF, including myocarditis, pre-existing cardiac disease, or ischemia should be excluded.
2. In addition to standard HF therapy, anti-prolactin therapy was effective in non-randomized clinical trials and case studies. Prevention of DVT is mandatory as these patients are at high risk of thromboembolic events. If PPCM occurs before birth close coordination with the obstetrician to time delivery is needed. In case of severely impaired LVEF and/or necessity of ICU treatment, we suggest referral to a center with capabilities of assist devices and heart transplantation and coordination with PPCM reference centers.
Conclusion: PPCM is a potentially fatal disease affecting young mothers. It requires early diagnosis and treatment, which is best executed in close coordination with specialized centers. Anti-prolactin therapy has been effective in small non-randomized trials and should be strongly considered in addition to standard HF therapy and antithrombotic prophylaxis.

P1345

Investigation of pulmonary edema revealed renal cell carcinoma growing into the right atrium

I Inna Rosenfeld[1]; T Levinas[1]; S Dabbah[2]; M Halabi[2]
[1]Sieff Government Hospital, Department of Cardiology, Safed, Israel; [2] Bar-Ilan University, The Faculty of Medicine in the Galilee, Safed, Israel

Background: The heart failure is a frequent morbidity in elderly age. The hypertension is a common cause for heart failure. We describe a case of heart failure due to very high blood pressure in elderly woman. Investigation of the causes showed advanced renal tumor as possible cause of hypertensive emergency.
Case report: A 84 years old woman with long history of hypertension was admitted to cardiology department complaining of severe dyspnea and weakness. Her physical examination was remarkable for signs of pulmonary edema with high blood pressure, 240/100mm Hg, HR 100/min. The patient was treated with IV diuretics , nitrates and CPAP mask with stabilization of blood pressure and resolving signs of pulmonary edema.
The diagnostic evaluation of causes for pulmonary edema was performed.
The acute coronary syndrome was excluded because absence chest pain, normal repeated troponin level and unchanged ECG.
Blood tests revealed normal for age creatinine level , normal thyroid function tests and potassium level.

Echocardiography examination showed good Left Ventricular function, EF 65%, Mild Left Ventricular Hypertrophy, Mild to moderate Mitral Regurgitation, Moderate Pulmonary systolic hypertension. An additional unexpected finding was mass in Inferior Vena Cava(IVC), suspected for thrombus .
The investigation was continued by CTA chest and abdomen that showed tumor in left kidney 4.7cm in diameter, dilated Left renal vein with tumor thrombus that continued in IVC up to entrance to the right atrium. The tumor was inoperable due to expansion . The patient declined biopsy and no chemotherapy was started.
Summary: Although acute heart failure due to hypertensive emergency is common condition, the thorough investigation of the causes may revealed uncommon finding like renal carcinoma .
The direct association between arterial hypertension and renal cell carcinoma unclear. Investigation secondary causes of hypertension recommended in patient with malignant hypertension like in our patient.

P1346

Acute heart failure and atrial fibrillation in case of myelodysplastic syndrome

S Severina Dakova[1]; K Ramshev[1]
[1]Military Medical Academy of Sofia, Cardilogy and Intensive care unit, Sofia, Bulgaria

Introduction: Cardiac involvement in patients with acute leukaemia is a well known finding, because of blast infiltration but in myelodysplastic syndroms(MDS) it is rarely reported in the literature. The symptoms may be due to presence of anaemia, iron overload or side effects of chemotherapy.
Case report: A 48-year-old male presented to intensive care unit, because of palpitations, chest discomfort, weakness, dry cough, shortness of breath, easy fatiguability and sweating started 1 day before. He described a loss of weight-20kg in one year. His vital signs were: BP 72/46, HR 153BPM- Atrial fibrilation,Temp 37,7 C and respiratory rate of 38/min, SpO2 of 77%. On examination, he was in mild respiratory distress, with signs of acute congestive heart failure, paroxysmal AF and suspected pulmonary embolism.ECG without signs of acute coronary syndrome.
He had a history of hypertension and myelodysplastic syndrome refractory anemia(MDS RARS 1) diagnosed 9 mothns ago, treated only with blood transfusions - last one 3months ago.
Laboratory tests were: HB-52 g/l, PLT-198,WBC-12,6;HCT- 0,24; RBC 2.4; TroponinI- 0.10ng/ml, NT BNP 254 pg/ml, D-Dimer slightly increased, Iron 34,1 mcmol/l, the other parameters were within normal range.
CT pulmonary angiography did not show any signs of PE, but had mild pulmonary edema.TTE showed EF 45%, with slightly increased LA volume- 33 ml/m2, diastolic disfunction type I and mild Mitral Regugitation.
He was treated with transfusion of 3U red blood cells, antibiotics, digoxin, amiodaron, diuretics,Low molecular Weight Heparins, corticosteroids. On the 5th day we performed TEE to evaluate thrombus in atrial appendage- no signs.
Conclusion: The patient was discharged on the 7th day in sinus rhythm, with normal vital signs.
We belived that cardiac problems in our patients were because of extreme anaemia and mild iron overload.
Do we need to have a long term anticoagulants in this patient?
CHA2DS2-VASc Score = 2 moderate-high risk of stroke
HAS BLED score = 2 moderate risk
ATRIA = 4 intermediate risk

According to those scores the answer is YES, but in our case we decided not to administer because of RARS 1-refractory anemia classified as a low risk MDS by WHO. It may remain stable for many years causing few symptoms, but also may progress rapidly into a different subtype of MDS or transform into an acute leukaemia. RARS is generally managed using the "watch and wait" approach with supportive care if or when required.
What would you do in your practice?
6 months later our patient is doing well, without AF, or any other cardiac problems except hypertension with excellent control.

P1347
Acute heart failure with more than one cause

N Mileva[1]; M Shumkova[1]; T Yaneva-Sirakova[1]; R Ivanova[1]; L Vladimirova[1]; D Vassilev[1]
[1]University Hospital Alexandrovska, Cardiology clinic, Sofia, Bulgaria

Case presentation: A 69-year-old man with past medical history of chronic hepatitis C infection, liver cirrhosis and esophageal varices, presented to our department with acute chest pain that started the same morning. On admission he was dyspneic and diaphoretic. Physical examination revealed bilateral jugular vein distention, tachypnea with respiratory rate of 18 breaths/min, tachycardia with heart rate of 100 beats/min, muffled heart sounds, blood pressure 90/60 mmHg and ascites. In the laboratory findings, anemia (haemoglobin 7,4 g/dl), thrombocytopaenia (85 G/l), hypoproteinemia (33 g/l), elevated spontaneous INR (2,1) were noted. Also cardiac biomarkers were elevated. The ECG was remarkable for diffuse ST-elevation V2-V6 and loss of the R-wave in the same leads. His echocardiography showed akinetic anterior wall segments, reduced left ventricular ejection fraction of 28%, pericardial effusion with interventricular interdependence with inspiration, early diastolic collapse of right ventricle, variability of left ventricular inflow (E wave) >25% and inferior vena cava dilation. Most probable diagnosis was acute coronary syndrome and coronary angiogram was performed. The examination showed thrombotic occlusion in mid-segment of left anterior descending coronary artery. We decided to perform thromboaspiration only, because of the high-bleeding risk in the patient and the unknown etiology of the pericardial effusion. The ventriculogram confirmed reduced ejection fraction with akinetic anterior wall segments. More importantly apical defect of the left-ventricle wall was noted. We proceeded with subxiphoid pericardiocentesis and evacuated 500 ml hemorrhagic fluid. It was decided to perform autohemotransfusion of the evacuated blood, considering the haemodynamic instability and the low haemoglobin of the patient. There was a significant improvement of the patients' condition, he was stabilised and promptly transferred to cardiac surgery department. The patient underwent surgery intervention and had full recovery. On follow up at 3 and 6 months he was clinically stable.
Discussion: We have described a case of a man presenting with acute heart failure due to acute myocardial infarction and cardiac tamponade in the context of apical rupture of the left ventricle at the same time. Patients with comorbid conditions can be challenging diagnostic problem and choosing the best treatment approach demands experience.
Conclusion: The presented case accentuates the importance of awareness that more than one cause for cardiogenic shock may be present at the same patient. Prompt diagnosis and decision on the right therapy approach may be challenging.

Chronic Heart Failure–Epidemiology, Prognosis, Outcome

P1348
64-Year-old man with left ventricule noncompaction cardiomyopathy

S Patino Velasquez[1]
[1]University of Puerto Rico, Hospital Cardiovascular de Puerto Rico y el Caribe , San Juan, Puerto Rico

While most cases of the patients who are recently diagnosed with heart failure develop clinical symptoms on the basis of previous known history of cardiovascular diseases, some in very unusual occasion experience new onset symptomatology without prior history or predisposing cardiovascular risk factors. Non-compaction cardiomyopathy (NCC) also called Spongy Myocardium is characterized by a prominent left ventricular trabeculae and deep intertrabecular recesses affecting majorly the left ventricular function causing clinical manifestation of heart failure.

We present the case of a 64 year old man with no past medical history who showed at our institution with 4-month history of dyspnea at mild exertion associated with recurrent heart palpitations. On physical examination, he had no significant cardiovascular finding except for an ECG with Left bundle branch block and bilateral diffuse crackles suggestive of pulmonary edema. Upon further questioning patient referred family history of non-specific cardiovascular diseases. A 2D- Echocardiogram diastolic dysfunction grade 3, moderate left ventricular dilation, LVEF of < 35% by Simpson criteria and evidence of mesh of endocardial trabeculations. Coronary angiography showing no evidences of CAD. A 24 hour holter monitor reported no arrhythmias, Cardiac MRI showed a large diastolic myocardial ratio of non-compacted to compacted thickness suggestive of NCC. In view of this findings, patient was recommended chronic anticoagulation to minimize the likelihood of cardio embolic event associated with this condition. He was started on optimal medical therapy.
This case shows an uncommon clinical manifestation of heart failure that lead to the unusual diagnosis of NCC. While the etiology in the general population is not known, it has been suggested that NCC may due to an intrauterine arrest of compaction of the loose interwoven meshwork that makes up the fetal myocardial primordium. The major clinical manifestations of NCC are heart failure, atrial fibrillation, ventricular arrhythmias, sudden cardiac arrest, and thromboembolic events, including stroke. There is a predominant genetic component among family member as evidence by our case were predominance for this cardiomyopathy was presumptively presenting among male family members.

Valvular Heart Disease–Epidemiology, Prognosis, Outcome

P1349
Heart failure and adult congenital heart disease: what's the relationship?

H Miranda[1]; I Almeida[1]; H Santos[1]; F Caetano[1]; D Mesquita[1]; J Chin[1]; C Sousa[1]; J Tavares[1]
[1]Centro Hospitalar Barreiro Montijo, Cardiology, Barreiro, Portugal

Introduction: Congenital malformations of the mitral valve (MV) can be found isolated or in association with another congenital cardiac malformation. Amongst all of the possible causes of congenital mitral stenosis (MS), parachute MV (PMV) is a very infrequent one (incidence of 0.17%). This anomaly is often associated with another obstructive lesion in the left heart - Shone Complex (SC).
Clinical case: Woman, 56 years old, obese. Complaints of palpitations and fatigue for small / medium efforts with 1.5 months of evolution. History of peripheral venous insufficiency and pulmonary thromboembolism (secondary to oral contraceptives). Admitted to our department due to onset of acute Heart Failure (HF), with progression to cardiogenic shock with severe biventricular dysfunction (Ejection Fraction (EF): 10-15%), and atrial flutter (HR 178 bpm). Inotropic, vasopressor and ventilatory support during the first 72 hours of hospitalization.
After clinical stabilization, we performed a new echocardiography that revealed reversal of biventricular dysfunction (EF 58%), the presence of MV with reduced opening (1.3 cm2 of functional area) and insertion of both primary tendinous chordae in the posterior papillary muscle. We assumed the diagnosis of PMV and, therefore, we opted for a conservative approach, with regular follow-up in our cardiology department.
1-year follow-up without intercurrences. During the follow-up, we performed a transoesophageal echocardiography to better characterize the MV and identify possible associated lesions, that showed the presence of moderate MS (area of 1.2 cm2) and mild mitral regurgitation and a fibrous membrane immediately above the MV ring. Mild tricuspid regurgitation with moderate pulmonary hypertension (PSAP 52 mmHg). We assumed the presence of two elements of the SC (PMV and supravalvular ring).
Recently, she underwent effort echocardiography that revealed mean gradient of 12mmHg and PSAP of 80mmHg. Consequently, valvular intervention was proposed.
Conclusion: The SC, whether in its complete or incomplete form, is a rare and underdiagnosed entity. Despite its low mortality in adulthood, it is associated with significant morbidity related to arrhythmias, HF and the need for valvular intervention. The recognition of this entity and associated complications is thus essential for a correct clinical orientation.

Comorbidities and cardiomyopathies: how to manage?

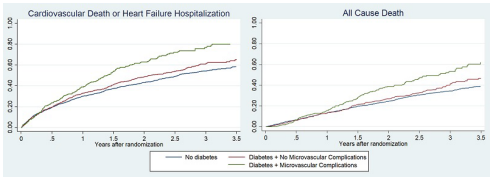
Microvascular complications in diabetes patients with heart failure and reduced ejection fraction

1387

S L Kristensen[1]; R Roerth[2]; PS Jhund[2]; L Shen[2]; M Lee[2]; MC Petrie[2]; L Kober[1]; J Mcmurray[2]
[1]*Rigshospitalet - Copenhagen University Hospital, Cardiology, Copenhagen, Denmark*; [2]*Cardiovascular Research Centre of Glasgow, Cardiology, Glasgow, United Kingdom*

On behalf of: BEST investigators

Background: The role of microvascular complications in the risk conferred by diabetes in heart failure with reduced ejection fraction (HFrEF) is unknown.
Methods: We studied 2707 HFrEF patients in the Beta-blocker Evaluation of Survival Trial (BEST), stratified into 3 groups: no diabetes and diabetes without or with microvascular complications (neuropathy, nephropathy or retinopathy). The risks of the composite of cardiovascular death or heart failure hospitalization, and all-cause death, were studied using Cox regression analyses adjusted for other prognostic variables.
Results: 964 patients had diabetes, of which 313 (32%) had microvascular complications. Patients with microvascular complications had more severe symptoms (New York Heart Association functional class IV 12% vs. 9% diabetes with no complications and 7% no diabetes), and worse quality of life (Minnesota living with HF median score 60 vs. 54 and 51 points). In patients with diabetes and complications, the rate of the composite outcome was 45 per 100 person-years of follow-up (compared with 34 and 29 in those with diabetes and no microvascular complications and participants without diabetes, respectively). Compared to patients without diabetes, the adjusted hazard ratio (HR) for the composite outcome was 1.44 (95% CI 1.22-1.70) and 1.18 (1.03-1.35) for patients with diabetes with and without complications, respectively. The risk of all-cause mortality was similarly elevated: adjusted HR 1.42 (95% CI 1.16-1.74) and 1.20 (1.01-1.42), respectively (Figure 1). Each type of microvascular complication was associated with a similar increment in risk and patients with more than one complication had an even greater elevation in risk.
Interpretation: In HFrEF, diabetes with microvascular complications is associated with worse symptoms and outcomes, than diabetes without microvascular complications. Prevention of microvascular complications has the potential to improve HFrEF outcomes.



Outcomes according to diabetes status

The importance of measuring fractional flow reserve to improve the efficiency of endovascular treatment on left main bifurcation lesions

1388

D A Daniil Maximkin[1]; Z KH Shugushev[1]; AG Chepurnoy[1]; OO Safonova[1]; AG Faibushevich[1]
[1]*Peoples Friendship University of Russia (RPFU), Moscow, Russian Federation*

Aim: to increase the effectiveness of endovascular treatment in patients with LM bifurcation lesions.
Methods: 157 patients were enrolled in the study. Inclusion criteria: true bifurcation stenosis of the LMCA according to QSA and IVUS; total risk according SYNTAX score < 32. All patients initially performed 'Provisional T' stenting of the LMCA (1stent strategy). After the procedure, a fractional flow reserve (FFR) was measured in the side branch of bifurcation (LCx or LAD)/ The main cohort of patients (n = 88) were divided into 2 groups. Group I (n = 44) included patients with FFR SB '+', and group II (n = 44) - FFR SB '-'. In the Ist group, after FFR measurement, all patients underwent complete bifurcational stenting (revers-crush, revers-culott), and in group II, implantation of the 2d stent was not performed. In retrospectively, the third (III) control group was formed (n = 69), where the 'Provisional T' stenting of the LMCA was performed without a control FFR measurement. Drug-eluting stents were implanted in all patients. At the end of the stenting procedure, all patients underwent IVUS for evaluating the optimal stent implantation. Long-term results after 48 months were followed in all patients. Primary endpoints: frequency of MACE (death, MI, repeated interventions). (death, MI, revascularizations). Secondary endpoints: frequency of restenosis and late stent thrombosis according to QSA and IVUS.
Results: survival of patients from Group I and II in the long-term period was 100%, and in the third group - 97.1% (p>0.05). Nonfatal MI was observed in 2 patients (2.9%) from group III (p < 0.05), in the Ist and IId group of cases MI was not recorded. The frequency of restenosis of and target lesion revascularization (TLR) according to QSA and IVUS was observed in 1 patient (2.3%) in group I and in 5 patients (7.2%) in group III (p < 0.05). Frequency of the target vessel revascularization (TVR) occurred in I and II group in 2.3% of patients, and in group III - in 2.9% (p>0.05). The total frequency of MACE in groups I, II and III was 4.5; 2.3 and 15.4%, respectively (p < 0.05).
Conclusion: measurement of FFR in the lateral branch of the left main bifurcation after performed PTS significantly improves the prognosis of patients with lesions of the LCA trunk and improves the efficacy and safety of PCI.

Characterization of plasmacytoid and myeloid dendritic cells in acute human and experimental myocarditis

1390

R Pistulli[1]; E Andreas[2]; S Koenig[3]; S Drobnik[4]; D Kretzschmar[1]; M Lichtenauer[5]; B Heidecker[6]; M Franz[1]; G Mall[4]; A Yilmaz[7]; P C Schulze[1]
[1]*University Hospital of Jena, Internal Medicine I, Dept. of Cardiology, Jena, Germany*; [2]*University Hospital of Jena, Department of Anesthesiology, Jena, Germany*; [3]*Heart Center of Leipzig, Cardiac Electrophysiology, Leipzig, Germany*; [4]*University Hospital of Jena, Department of Forensic Science, Jena, Germany*; [5]*Paracelsus Private Medical University, Cardiology, Salzburg, Austria*; [6]*University Heart Center, Cardiology, Zurich, Switzerland*; [7]*Elisabeth-Hospital, Clinic of Internal Medicine II, schmalkalden, Germany*

AIMS: Dendritic cells (DCs) are central mediators of adaptive immunity but their role in human myocardial inflammatory disease is still unknown. We hypothesized that plasmacytoid (p) and myeloid (m) DCs are involved in the mechanisms of myocarditis and analyzed these two main subtypes in human myocarditis subjects as well as in a murine model of experimental autoimmune myocarditis (EAM).
Methods: Circulating DCs were analyzed by flow cytometry (FACS) in patients with acute myocarditis (n = 33), dilated cardiomyopathy (DCM, n = 33) and controls (n = 33) at initial diagnosis and at follow-up at 6 and 12 months. Myocardial biopsies of acute myocarditis patients (n = 18) were immunostained for the presence of DCs and compared to non-diseased controls (n = 5). In a mouse model of acute myocarditis induced through synthetic cardiac myosine injection, effects of DC inhibition through MCS-18 treatment and placebo were tested. Histology, immunohistochemistry and echocardiography were performed at 21 days (peak myocarditis) and 28 days (recovery phase) following EAM induction.
Results: Circulatory pDCs and mDCs were significantly reduced in myocarditis patients (p < 0.01 for both), increased at 6 months follow-up, yet remained reduced compared to controls (pDCs p = 0.015, mDCs p = 0.002). Circulatory DCs of DCM patients were initially indifferent, but gradually decreased during follow-up, reaching significant reduction at 6 (mDCs, p 0.03) or at 12 months (pDCs, p < 0.01) follow-up. Human myocarditis biopsies showed accumulation of pDCs (2-fold CD304+ / 3-fold CD123+, all p < 0.01) compared to controls. Myocardial pDCs and mDCs accumulated in EAM (p for both < 0.0001). MCS-18 Inhibition reduction pDC levels (p = 0.009), reduced myocardial inflammation (myocarditis score reduction from 2.6 to 1.8, p = 0.026) and improved ejection fraction (p = 0.03) at peak myocarditis.
Conclusions: Circulating DCs are reduced in human myocarditis and accumulate in the inflamed myocardium. MCS-18 inhibits DCs in EAM leading to amelioration of inflammation and LV remodeling during the acute phase of myocarditis. Our data

further elucidate the role of DCs and their specific subsets in acute inflammatory cardiomyopathies.

1392

Waist-hip ratio and mortality in heart failure; contradicting the obesity paradox

K W Koen Streng[1]; AA Voors[1]; JL Hillege[1]; SA Anker[2]; JG Cleland[3]; K Dickstein[4]; G Filippatos[5]; M Metra[6]; LL Ng[7]; P Ponikowski[8]; DJ Van Veldhuisen[1]; F Zannad[9]; K Damman[1]; P Van Der Meer[1]; CC Lang[10]
[1]University Medical Center Groningen, Groningen, Netherlands; *[2]German Center for Cardiovascular Research, Berlin, Germany*; *[3]Imperial College London, National Heart & Lung Institute, Royal Brompton and Harefield Hospitals, London, United Kingdom*; *[4]Stavanger University Hospital, Stavanger, Norway*; *[5]National & Kapodistrian University of Athens, School of Medicine, Department of Cardiology, Heart Failure Unit, Athens, Greece*; *[6]University of Brescia, Brescia, Italy*; *[7]NIHR Biomedical Research Unit in Cardiovascular Disease, Leicester, United Kingdom*; *[8]Wroclaw Medical University, Department of Heart Diseases, Wroclaw, Poland*; *[9]University of Lorraine, Nancy, France*; *[10]University of Dundee, School of Medicine Centre for Cardiovascular and Lung Biology, Division of Medical Sciences, Dundee, United Kingdom*

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Background: A higher body mass index (BMI) is associated with better survival in heart failure (HF) patients, also known as the obesity paradox. However, BMI does not account for body composition. We therefore analysed the association between abdominal fat, measured via waist-hip ratio (WHR), BMI and all-cause mortality in patients with heart failure.
Methods: For this analysis 1738 patients from The BIOlogy Study to TAilored Treatment in Chronic Heart Failure (BIOSTAT-CHF) study were included. Patients without waist and hip measurements were excluded. WHR was defined as waist circumference/hip circumference, divided into tertiles and split for sex. A linear regression of principal components from an extensive panel of biomarkers was performed to provide insight in the pathophysiology behind a higher WHR.
Results: In total, 1479 patients with were included, of which 33% were female and mean age was 75 ± 11 years. A higher WHR was independently associated with a higher BMI, a higher prevalence of diabetes and higher functional NYHA class. There was a significant interaction between sex and WHR on its association with mortality ($P < 0.001$). In women, a higher WHR was associated with a higher mortality risk (HR 2.01; 95% confidence interval (CI) 1.33-3.02, $P = 0.001$), whereas no significant association was found in men (HR 1.21, 95% CI 0.87-1.69, $P = 0.262$). We found a strong association between a higher WHR and elevated markers of inflammation and MAPK cascade in women, while in men these associations were less profound.
Conclusions: A higher WHR was associated with a higher risk of death in female, but not in male heart failure patients. These findings challenge the obesity paradox, and suggest that fat deposition is pathophysiologically harmful and may be a target for therapy in female patients with heart failure.

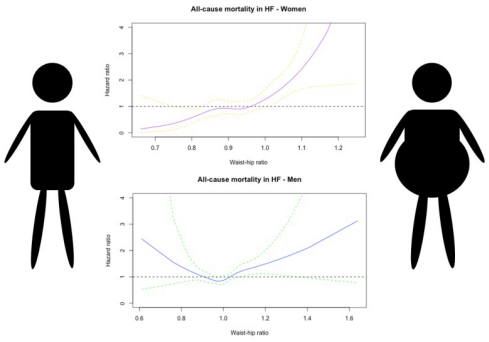

Figure 1; WHR and all-cause mortality

1395

Inotersen improves quality of life, polyneuropathy, and cardiomyopathy in patients with hereditary transthyretin amyloidosis: results of the phase 3 study NEURO-TTR

C Whelan[1]; B Drachman[2]; S Heitner[3]; M Maurer[4]; T Damy[5]; D Judge[6]; B Monia[7]; S Hughes[7]; J Kwoh[7]; B Jung[7]; E Ackermann[7]; M Benson[8]
[1]University College London-National Amyloidosis Centre, London, United Kingdom; *[2]University of Pennsylvania, Philadelphia, United States of America*; *[3]Oregon Health & Science University, Portland, United States of America*; *[4]Columbia University Medical Center, New York, United States of America*; *[5]Centre Hospitalier Universitaire Henri-Mondor, Creteil, France*; *[6]Medical University of South Carolina, Charleston, United States of America*; *[7]Ionis Pharmaceuticals, Carlsbad, United States of America*; *[8]Indiana University School of Medicine, Indianapolis, United States of America*

Funding Acknowledgements: This study was sponsored by Ionis Pharmaceuticals (Carlsbad, CA, USA).

INTRODUCTION: Hereditary transthyretin (TTR) amyloidosis (hATTR) is a rare, progressive, and fatal disease caused by misfolded TTR that builds up as amyloid in major organ systems, especially cardiac tissue and nerves, causing cardiomyopathy (CM) and polyneuropathy (PN), respectively. hATTR causes significant morbidity and a progressive decline in patient quality of life.
Purpose: To evaluate the efficacy and safety of inotersen, an antisense oligonucleotide inhibitor of TTR protein production, in patients with hATTR with CM and PN.
Methods: NEURO-TTR (NCT01737398) is a global, randomised, double-blind, placebo-controlled phase 3 study. Adults (n = 172) with hATTR-PN (stage 1 or 2) with or without CM were randomly assigned 2:1 and received 300-mg weekly subcutaneous inotersen or placebo for 15 months. CM was defined as diagnosis of hATTR-CM or = 1.3 cm interventricular septum thickness (IVS; by echocardiography) at baseline. Primary endpoints were change from baseline to week 66 in the modified Neuropathy Impairment Score+7 (mNIS+7) and Norfolk Quality of Life−Diabetic Neuropathy (Norfolk QOL-DN) total score. Exploratory outcomes included measures of CM, including IVS, left ventricle mass (LVM), and posterior wall thickness (PWT).
Results: At baseline, 69% of patients were male, mean age was 59 years (range, 27-81 years), and 63% (108/172) had CM. Of patients given placebo and inotersen, 55% (33/60) and 67% (75/112), respectively, had CM. Inotersen treatment compared with placebo resulted in significant improvement from baseline to week 66 in mNIS+7 ($P < 0.0001$) and Norfolk QOL-DN total score ($P = 0.0006$) in all patients, irrespective of CM status. The subset of patients with CM also demonstrated significant improvement from baseline to week 66 in mNIS+7 ($P < 0.001$) and Norfolk QOL-DN total score ($P = 0.036$) with inotersen treatment compared with placebo. Patients with significant CM at baseline (IVS = 1.5 cm) treated with inotersen compared with placebo also showed significant benefit in IVS ($P = 0.0150$), LVM ($P = 0.0288$), and PWT ($P = 0.0425$). Most adverse events were mild or moderate. Key safety findings of thrombocytopenia and renal events were easily managed and monitored with routine testing.
Conclusion: Inotersen demonstrated significant benefits in quality of life and prevention of cardiac and neurological disease progression in patients with hATTR with CM and PN.

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The Left atrial strain provide improved diagnostics for elevated filling pressures at rest and/or during exercise in heart failure patients

A Manouras[1]; A Lundberg[1]; M Back[1]; LA Lund[1]; A Nagy[2]
[1]Karolinska Institute, Institute of Medicine Solna, Stockholm, Sweden; *[2]Semmelweis University, Heart and Vascular Center, Budapest, Hungary*

Funding Acknowledgements: Heart Lung Fond

Background/Introduction: The non-invasive assessment of left ventricular diastolic function and filling pressures is an important clinical question. Particularly challenging is the diagnosis of those patients whose left atrial pressure (LAP) is within normal range at rest, but increases pathologically on exertion. Current recommendations on diastolic assessment are complex, have limited diagnostic accuracy and provide no guidance for that latter scenario.
Purpose: As recent data suggests that the LA constitutes an important pathophysiological substrate of diastolic heart failure we hypothesized that mechanical alteration in LA function, as expressed by reduced LA strain (LA-GS), might contribute in identification of elevated LAP and thus sought to investigate this question.
Methods: 220 patients referred for right heart catheterization (RHC) to Karolinska University Hospital for HF assessment were enrolled prospectively. Simultaneous echocardiographic examination and RHC at rest and during exercise was performed. Patients with precapillary pulmonary hypertension, constrictive pericarditis and significant valvular disease were excluded
Results: In total 164 patients were included. 56% of the patients had preserved EF. At rest, the pulmonary arterial wedge pressure (PAWP) was elevated in 97 patients and further 34 patients with normal resting PAWP values demonstrated abnormal PAWP elevation during exercise. LA-GS measurements was feasible in 97% of the patients. LA-GS showed the strongest correlation with resting PAWP (r=- 0.64 for preserved EF, and -0.46 for reduced EF, $p < 0.001$ in both cases) compared to the individual indices (E/E', LAVi, TR-Vmax) incorporated in the currently recommended diagnostic EACVI algorithm. The diagnostic performance of LA-GS for detecting elevated resting PAWP was good (AUC:0.87 and 0.74 in patients with preserved and HFrEF, respectively). More importantly, resting LA-GS values performed even better for identifying patients with pathological PAWP either at rest or on stress (AUC:0.90 and 0.80, respectively). On the other hand, the currently proposed EACVI algorithm

demonstrated a modest diagnostic ability limited in patients with preserved EF (AUC = 0.69 at rest and 0.67 for detecting patients with pathological PAWP either at rest or on exertion). Conclusion(s) - Resting LA-GS provides superior diagnostic discrimination between normal and elevated PAWP values at rest as compared to EACVI algorithm. More importantly, resting LA-GS demonstrates augmented diagnostic ability for patients with pathological elevation of PAWP during exertion.

1397

Exercise hemodynamic profile of patients with heart failure with preserved versus mid-range ejection fraction

AJ Andreas Joachim Rieth[1]; MJ Richter[2]; K Tello[2]; W Seeger[2]; V Mitrovic[1]; C Hamm[2]

[1]Kerckhoff Heart Center, Bad Nauheim, Germany; *[2]Justus-Liebig University of Giessen, Giessen, Germany*

Background: According to the 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure, the term "HFpEF" (heart failure with preserved ejection fraction) is reserved for patients with left ventricular ejection fraction (LVEF) = 50%, and the new term "HFmrEF" denotes those with LVEF 40-49%. Possible differences in exercise hemodynamic profile between these two entities are unknown to date.
Methods: Results of exercise right-heart catheterization performed from 2009 to 2017 were screened for patients with HFpEF or HFmrEF, and 233 patients were determined to be suitable for further analysis. Differences between hemodynamic variables in the two groups were analyzed, and the ratio of tricuspid annular plane systolic excursion (TAPSE) to pulmonary artery systolic pressure estimated by Doppler echocardiography (PASP) compared for the two groups. Each group was then subdivided according to whether the TAPSE/PASP ratio was greater than or less than the median, and the hemodynamic variables were compared in the resulting four groups.
Results: The cohort of 180 patients with HFpEF and 53 with HFmrEF had the following baseline characteristics: 53% men, median age 73 years (IQR 67-77), median NTproBNP 1132 pg/ml (IQR 570-2255), 27% in NYHA class II and 69% in class III, and 66% with atrial fibrillation. Key resting hemodynamic parameters, expressed as mean mmHg (SD) or l/min/m2 (SD) for cardiac index (CI), were: mean right atrial pressure 7.55 (4.29) in HFpEF and 7.4 (5.15) in HFmrEF; mean pulmonary artery pressure (mPAP) 25.71 (7.60) in HFpEF and 25.98 (11.43) in HFmrEF; mean pulmonary artery wedge pressure (PAWP) 16.02 (5.44) in HFpEF and 15.85 (7.50) in HFmrEF; CI 2.54 (0.63) in HFpEF and 2.44 (0.60) in HFmrEF. Multiple hemodynamic exercise parameters showed no significant differences between the two groups at comparable workload, maximum heart rate, and final mixed venous oxygen saturation. However, the TAPSE/PASP ratio was significantly different (p = 0.001) between HFpEF and HFmrEF patients. Subgrouping according to median TAPSE/PASP ratio showed significant differences between the four groups: the increase in cardiac output during exercise (p = 0.001), maximum total pulmonary resistance (p = 0.000), maximum pulmonary artery compliance (p = 0.000), and maximum transpulmonary gradient (p = 0.003), whereas the rise in PAWP was not different.
Conclusions: Standard hemodynamic parameters at rest and during exercise did not differ significantly between patients with HFpEF and HFmrEF. Instead, partitioning of the two entities using an echocardiographic parameter of the right ventricular-pulmonary circulation unit showed marked differences in the exercise hemodynamic profile between the different subgroups. Thus, LVEF may be not the appropriate parameter to stratify heart failure patients with an EF >40%, but parameters of the right ventricular-pulmonary circulation unit, including exercise hemodynamics, may be helpful for profiling.

1398

Imaging phenotypes of left-dominant arrhytmogenic cardiomyopathy and dilated cardiomyopathy - a comparative magnetic resonance study

R Rocio Eiros[1]; JB Augusto[2]; T Treibel[3]; G Captur[3]; MM Akhtar[3]; A Protonotarios[3]; T Gkosios[3]; K Savvatis[3]; S Mohiddin[3]; J Moon[3]; LR Lopes[3]

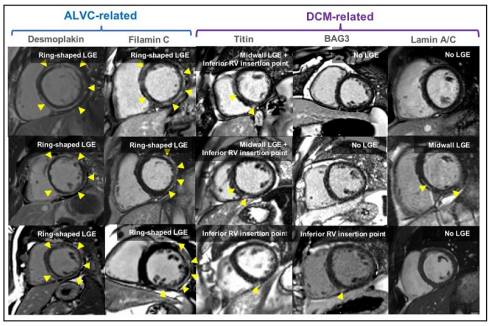
[1]University Clinic of Navarra, Cardiology, Navarra, Spain; *[2]Hospital Prof. Doutor Fernando Fonseca, Lisboa, Portugal*; *[3]Barts Health NHS Trust, London, United Kingdom*

Background: Emerging data have illustrated the diversity of genetic causes of arrhythmogenic cardiomyopathy (AC) with dominant LV involvement (ALVC).The relation between genotype and clinical phenotype is scarce and there are no systematic studies examining imaging phenotypes using cardiac magnetic resonance (CMR).
Objective: To identify phenotypic traits that distinguish ALVC from other genetic causes of dilated cardiomyopathy(DCM).
Methods: CMR data acquired for 30 patients (pts) with confirmed ALVC /DCM associated mutations in desmoplakin (DSP), filamin C (FLNC), lamin A/C (LMNA), titin (TTN) and BAG3 were retrospectively re-analysed and compared on the basis of different individual genes and when grouped as ALVC (DSP / FLNC) vs DCM (others).
Results: Causal genes included DSP (n = 11), FLNC (n = 4), lamin A/C (n = 6), BAG3 (n = 4), titin (n = 5). A comparison of clinical and imaging features is presented in Table 1. Figure 1 shows a comparison of late gadolinium enhancement patterns between different genes.
Conclusions: Patients with genetic causes of ALVC have a higher burden of myocardial scar, in a more often sub-epicardial and ring-shaped pattern, in contrast with a more discrete midwall septal late gadolinium enhancement in other genetic causes of DCM. Other imaging parameters, including LV and RV sizes and function were similar.

Comparision of CMR characteristics

	DSP-FLNC (n = 15)	Non-DSP-FLNC (n = 15)	P Value
Age, years	44.5± 17.2	44.2± 13.3	0.972
Male gender,n (%)	7 (46.7)	11 (73.3)	0.136
LV EDV_i,ml/m^2	105.1± 32.3	97.6 ± 20.6	0.463
LV SV_i,ml/m^2	49.5 ± 10.6	48.5 ± 13.3	0.816
LV Mass index, g/m^2	59.7 ± 10.9	60.4 ± 16.3	0.883
LV EF, %	48.1 ± 13	49.2 ± 7.5	0.784
RV EDV_i,ml/m^2	90.1 ± 19.0	81.1 ± 25.7	0.284
TAPSE,mm	21 ± 4.6	21.6 ± 6.8	0.827
RV EF, %	52.6 ± 16.3	56.4 ± 5.7	0.405
LGE 5SD, g	14.2 (7.8-18.9)	1.12 (0-34)	<0.001
LGE over median 4.5g, n (%)	13 (86.7)	2 (13.3)	<0.001
LGE as % of mass	13.2 (9.9-19.5)	0.7 (0-2.3)	<0.001
LGE over median 5.2%,n (%)	13 (86.7)	2 (13.3%9	<0.001
Subepicardial LGE,n (%)	13 (86.7)	2 (13.3)	0.001
Ring-shaped LGE, n (%)*	11 (73.3)	0	<0.001

* > 3 contiguous subepicardial segments in the same slice.



CMR LGE patterns according to genes

1389

Pretreatment with P2Y12 Receptor Antagonists in ST-Elevation Myocardial Infarction: A Report from the Swedish Coronary Angiography and Angioplasty Registry

E Elmir Omerovic[1]

[1]Sahlgrenska University Hospital, Gothenburg, Sweden

Background: Prehospital administration of P2Y12 receptor antagonists to patients with ST-elevation myocardial infarction (STEMI) is supported by guidelines and is a common practice despite the lack of definite evidence for its benefit.
Methods: Using data from the Swedish Coronary Angiography and Angioplasty Registry on procedures between 2005 and 2016 we stratified all patients who underwent primary PCI due to STEMI in Sweden by whether or not they were pretreated with P2Y12 receptor antagonists. We investigated associations between P2Y12 pretreatment and the risk of adverse outcomes with propensity-scores adjusted mixed-effects logistic regression, which accounted for clustering of patients within hospitals. The primary endpoint was all-cause death within 30 days. Secondary endpoints were IRA (infarct-related artery) occlusion, 30-day stent thrombosis, in-hospital bleeding, neurological complications and cardiogenic shock.
Results: In total, 44,804 patients were included. They were treated with clopidogrel (N = 26,136, 58.3%), ticagrelor (N = 15,792, 35.3%), or prasugrel (N = 2,352, 5.3%);

37,840 (84.5%) were pretreated, and 30,387 (67.8%) had IRA occlusion. At 30 days, there were 2,488 (5.6%) deaths and 267 (0.6%) stent thromboses. Pretreatment was not associated with better survival (OR 0.1.07; 95% CI 0.94-1.22; P = 0.313) at 30 days, reduced IRA occlusion (OR 1.01; 95% CI 0.95-1.08; P = 0.635), or decreased stent thrombosis (OR 0.99; 95% CI 0.69-1.41; P = 0.941), or higher risk of in-hospital bleeding (OR 1.04; 95% CI 0.89-1.23; P = 0.604), or neurological complications (OR 0.66; 95% CI 0.38-1.30; P = 0.129). We found no difference in risk of cardiogenic shock between the groups (OR 0.91; 95% CI 0.78 - 1.07; P = 0.264)
Conclusion: Pretreatment of STEMI patients with P2Y12 receptor antagonists was not associated with improved clinical outcomes.

1391

Ticagelor is not superior to clopidogrel in patients with acute coronary syndrome: A report from SCAAR

E Elmir Omerovic[1]
[1]*Sahlgrenska University Hospital, Gothenburg, Sweden*

Background: The PLATO trial has shown that ticagrelor compared to clopidogrel improves survival and decreases risk for stent thrombosis in patients with acute coronary syndrome. The aim of this study was to investigate whether treatment with ticagrelor is superior to clopidogrel in patients with acute coronary syndrome in "real-world".
Methods: We used data from the SCAAR registry (Swedish Coronary Angiography and Angioplasty Registry) for the PCI procedures performed in Västra Götaland County in Sweden. The database contains information about all PCI procedures performed at five hospitals (˜20% of all SCAAR data). All consecutive procedures between 2005 and 2015 for UA/NSTEMI and STEMI were included. We used multilevel modeling based on complete−case mixed-effects logistic regression to adjust for hierarchical database due to clustering of observations. The following variables were used for adjustment of risk estimates: age; gender; hypertension; hyperlipidemia; smoking status; diabetes; calendar year; indication for PCI; prior MI, CABG and/or PCI; cardiogenic shock; severity of coronary artery disease; number of implanted stents; completeness of revascularization; type of stent. The primary combined endpoint was death or stent thrombosis at 30 days. The secondary end points were death at 30-days, death at one-year and cardogenic shock.
Results: The total of 12,168 patients were included in the study of which 2,929 (19%) were treated with ticagrelor. 44% had STEMI. There were 555 events at 30-days of which 53 (9.5%) were stent thromboses. 844 patients were dead at one-year. Treatment with ticagrelor was not associated with lower risk for primary endpoint (OR 0.97; 95% CI 0.66 - 1.43; P = 0.887). Estimated risk of death at 30-days (OR 1.02; 95% CI 0.59 - 1.76; P = 0.937) and one-year (OR 1.01; 95% CI 0.68 - 1.47; P = 0.992) was not different between the groups. We found no difference in risk of cardiogenic shock between the groups (OR 1.32; 95% CI 0.75 - 1.23; P = 0.330)
Conclusions: In this observational study, treatment with ticagrelor was not superior to clopidogrel in patients with acute coronary syndrome treated with PCI.

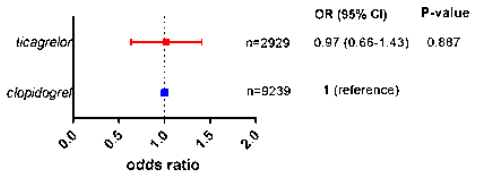


Fig. 1 Odds ratio for death or stent thrombosis at 30 days.

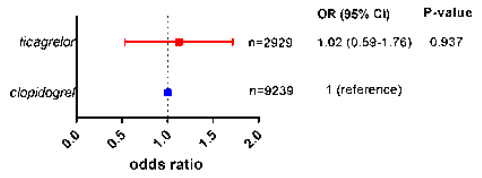


Fig. 2 Odds ratio for mortality at 30 days.

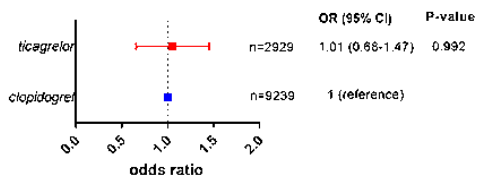


Fig. 3 Odds ratio for mortality at one year.

Forrest plots

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Dilated cardiomyopathy with midrange ejection fraction at diagnosis: characterization and natural history

P Gentile[1]; M Merlo[1]; A Cannata'[1]; M Gobbo[1]; M Marco Mase[1]; D Zaffalon[1]; M Gigli[1]; G Barbati[2]; F Ramani[1]; D Stolfo[1]; B Pinamonti[1]; G Sinagra[1]
[1]*Ospedale Cattinara, Cardiovascular Department, Trieste, Italy*; [2]*University of Trieste, Biostatistics Unit, Department of Medical Sciences, Trieste, Italy*

Background: Few data on the characteristics and outcomes of mid-range EF (mrEF) patients are available, mostly in the specific group of dilated cardiomyopathy (DCM).
Purpose: To define characteristics, evolution and prognosis of DCM patients with mrEF at diagnosis.
Methods: DCM patients were analyzed. mrEF and reduced EF (rEF) were defined in presence of baseline left ventricular EF between 40 and 49% and < 40% respectively. The study end-points were all-cause mortality or heart transplantation (D/HT) and sudden cardiac death or malignant ventricular arrhythmias (SD/MVA). EF worsening below 40% during follow-up was also considered.
Results: Among 812 DCM enrolled patients, 175 (22%) presented mid-range EF at baseline. Compared with rEF group, mrEF patients had smaller left ventricular end-diastolic volume, lower rates of left bundle branch block, right ventricular dysfunction, moderate−severe mitral regurgitation and restrictive filling pattern. During a mean follow−up of 135 ± 87 months, mrEF group presented a lower rate of D/HT (9.1% vs. 36%, $p < 0.001$) and SD/MVA (4.5% vs.15.2%, $p < 0.001$). Finally, 29 out of 175 mrEF patients (17%) evolved to rEF at a mean follow−up of 64 ± 40 months, showing a subsequent worsening of long−term prognosis. A restrictive filling pattern emerged as the strongest predictor of rEF development at multivariate analysis. Conclusions. mrEF identified a consistent subgroup of DCMs diagnosed in an earlier stage and presenting an apparent better long-term evolution. However, 17% of those patients evolved into rEF despite medical therapy. Baseline restrictive filling pattern was found to be independently associated with subsequent evolution in rEF.

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Thromboembolic events in left ventricular non-compactation cardiomyopathy, are there any predictors?

N Nuno Craveiro[1]; H Antunes[2]; N Marques[3]; L Reis[4]; R Santos[5]; AR Almeida[6]; O Azevedo[7]
[1]*Hospital of Santarem, Cardiology, Santarem, Portugal*; [2]*Hospital Sao Teotonio, Viseu, Portugal*; [3]*Algarve Biomedical Center, Centro hospitalar do Algarve, Cardiology, Faro, Portugal*; [4]*University Hospitals of Coimbra, Coimbra, Portugal*; [5]*Hospital Espirito Santo de Evora, Evora, Portugal*; [6]*Hospital Centre do Tamega e Sousa, Penafiel, Portugal*; [7]*Hospital Guimaraes, Guimaraes, Portugal*

On behalf of: SUNSHINE

Introduction: Patients with left ventricular non-compaction cardiomyopathy (LVNC) have a higher prevalence of heart failure, ventricular arrhythmias and thromboembolic events leading to increased mortality and morbidity.
Aim: To identify predictors of thromboembolic events in patients with LVNC.
Methods: One-hundred-eleven-patients (N = 111) diagnosed with LVNC were included from a Portuguese multicenter study involving 12 hospital centers. We evaluated demographic, clinical, electrocardiographic, echocardiographic and cardiac magnetic resonance, and follow-up data. We determined the factors and conducted a multivariate analysis to establish the independent predictors that were associated with the occurrence of thromboembolic events in these patients.
Results: A thromboembolic event occurred in 10 patients (9%). In our study the factors associated with a thromboembolic event were male gender (90% p = 0,042), presence of diastolic dysfunction as evaluated by deceleration time (200 ± 81 ms vs 191 ± 44 ms, p = 0,001) and left atrium volume (40,58 ± 16,6 ml/m2 vs 30,4 ± 11,7 ml/m2 p = 0,036), as well as older age of diagnosis (60,4 ± 13,9 years vs 45,13 ± 17,7 years p = 0,010) and the presence of sustained ventricular tachycardia in Holter monitoring (p = 0,03). After multivariable analysis the only independent predictor of thromboembolic event was the presence of sustained ventricular tachycardia in Holter monitoring (Beta = 0,334; p = 0.016).
Conclusion: Thromboembolic events are frequently associated with LVNC. In our population the incidence of thromboembolism was 9%. The presence of sustained ventricular tachycardia in Holter monitoring was an independent predictor of events in our study.

1399

De novo mutation rate in patients with hypertrophic cardiomyopathy and left ventricular non-compaction.

E Elena V Zaklyazminskaya[1]; M Polyak[1]; A Bukaeva[1]; G Radzhabova[1]; S Dzemeshkevich[1]

[1]B.V. Petrovsky Russian Scientific Center of Surgery of the Russian Academy of Medical Sciences, Moscow, Russian Federation

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Introduction: Recent advances in genetic technologies provide a new insight into molecular pathogenesis of the left ventricular hypertrophy and/or non-compaction. Clinical appearance of the single mutation can vary significantly in different families and even within the same affected pedigree. Genotype-phenotype correlation is poorly understood despite extensive study worldwide.

Materials and methods: Cohort of patients. From 2009-2015 150 probands with hypertrophic cardiomyopathy (HCM) and 60 probands with LVNC had underwent genetic screening.

Genetic analysis. Study was performed in accordance with the Helsinki declaration and the local ethics committee. Genetic screening of the targeted 10 genes (MYBPC3, TAZ, TPM1, LDB3, MYL2, ACTC1, MYL3, MYH7, TNNI3, and TNNT2) was performed by next generation sequencing followed by Sanger re-sequencing. Cascade familial screening was performed when available. De novo mutational status was counted only if genetic testing reveal absence of the genetic variant in both parents.

Results: "Damaging" or "probably damaging" genetic variants were found in 39 HCM index cases (26%) what is less than expected. The vast majority of mutations were found in the MYH7 and MyBPC3 gene what fits with worldwide mutation rates. De novo origin was confirmed for 4 mutations (10% of all genotype-positive cases, and 2.6% in the whole HCM cohort). Three mutations had raised de novo in the MYH7 gene, and 1 probably damaging de novo variant was found in the TPM1 gene. Single de novo genetic variant in the MYH7 gene was found in the patient with familial HCM in addition to the known mutation in the MyBPC3 gene inherited from the affected mother. This patient had severe clinical phenotype and underwent reconstructive extended myectomy and ICD implantation at the age of 15 y.o.

"Damaging" or "probably damaging" genetic variants were found in 14 LVNC index cases (23%). Mutations in the MYH7 gene were also the most common finding. De novo status was confirmed for 4 mutations in the MYH7 gene (29% of all genotype-positive cases, and 6.6% in the whole LVNC cohort).

All carriers of de novo mutations had significantly younger age of clinical manifestation within own group.

Totally 18 mutations in the MYH7 gene were detected in this study in the whole cohort of patients (HCM and LVNC), and five of them had raised de novo.

Conclusion: Mutations de novo are responsible for a significant portion of the LVNC, and are less common but not negligible in HCM patients. Severe clinical phenotype within "mildly" affected family might be explained by additional de novo mutation (at least in some families). The MYH7 gene is an important source of de novo mutations maintaining the high prevalence of HCM and LVNC in population.

Study limitation.

We were unable to track mutation origin in half of the cases because of incomplete data from the families. So the real prevalence of de novo mutations might be underestimated.

Moderated Posters - Basic Science

1400

Alpha1-adrenergic receptor agonists activate Akt signalling via insulin family receptors

A Angela Clerk[1]; KA Rostron[1]; DN Meijles[2]; S Shaw[1]; JJ Cull[1]; SJ Fuller[1]; PH Sugden[1]
[1]*University of Reading, Reading, United Kingdom*; [2]*St George's University of London, London, United Kingdom*

Funding Acknowledgements: British Heart Foundation

Background: Akt signalling (first delineated in the context of insulin receptor signalling) is cardioprotective. Akt is potently activated by insulin or insulin-like growth factor 1 (IGF1), acting through insulin or IGF1 receptors (IRs or IGF1Rs). Other receptors including a1-adrenergic receptors (a1ARs) activate Akt, but the mechanism of activation is not clear.
Purpose: Our hypothesis is that a1-ARs activate Akt via insulin family receptors (InsFRs). Our aim was to establish if this is the case, and if linsitinib [a highly selective inhibitor of insulin family receptors (InsFRs) developed for cancer] affects the functional consequences of a1-AR agonists on the heart.
Methods: Rat neonatal cardiomyocytes were exposed to or adult rat hearts perfused with a1AR agonists [50 nM A61603; 100 μM phenylephrine (PE)] in the absence/presence of 10 μM linsitinib. Effects on signalling were assessed by immunoblotting with antibodies to phosphorylated (activated) kinases. Protein synthesis was assessed by incorporation of 3H-Phe. Cardiac function in perfused hearts was measured using a Millar catheter. Effects of linsitinib (2 mg/kg/d) on cardiac function/hypertrophy induced by PE (40 mg/kg/d, 4 d) in mice (male C57Bl6; 10 wks) in vivo were by determined. Echocardiography was used to assess cardiac function. M-mode images were used for analysis of cardiac dimensions. Pulsed wave doppler was used to assess aortic and pulmonary flow.
Results: In addition to IRs/IGF1Rs, our data indicate a third InsFR is expressed in heart, the insulin receptor-related receptor (IRR). IRRs are alkali-sensitive and required for pH regulation in kidney. Alkaline pH (pH 9.0) activated IRRs and Akt, and was associated with increased protein synthesis in perfused hearts. IRRs were activated in a complex with IR/IGF1Rs. a1ARs activated Akt in cardiomyocytes and perfused hearts and increased protein synthesis. Activation of Akt and the increase in protein synthesis induced by alkaline pH or a1AR agonists was inhibited by linsitinib. Thus, a1ARs signal selectively via InsFRs to Akt and protein synthesis. Functionally, in perfused hearts, linsitinib enhanced the increase in developed pressure induced by A61603 and, in vivo, linsitinib enhanced PE-induced left ventricular (LV) hypertrophy with increased LV wall thickness and decreased internal diameter. Aortic (but not pulmonary) flow was compromised in the presence of PE/linsitinib. Therefore, there appear to be opposing effects of a1-AR signalling via InsFRs to cardiomyocyte vs cardiac hypertrophy.
Conclusions: Our data demonstrate a novel signalling paradigm in which a1-ARs signal through InsFRs in cardiomyocytes to activate Akt and increase protein synthesis although, functionally, the InsFR signal appears to mitigate some of the hypertrophic effects of a1-AR signalling in the whole heart. The data have implications for development of novel therapeutic targets for heart failure and potential cardiotoxic effects of cancer therapies.

1401

Kruppel-like factors regulation in a zebrafish heart failure model

A Salgado-Somoza[1]; I Ernens[1]; A Lumley[1]; L Zhang[1]; Y Devaux[1]
[1]*Luxembourg Institute of Health, CVRU, Strassen, Luxembourg*

On behalf of: Cardiolinc Network (www.cardiolinc.org)
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Background: According to recent estimations, heart failure (HF) is projected to rise by almost 50% by 2030. New investigation is needed to improve the current therapies in order to palliate this "epidemic". Animal models provide a valuable source of information about the mechanisms leading to disease. Beneficial remodelling in HF can be studied in zebrafish, an animal which is able to regenerate its heart after injury. Transcriptomic studies helped to decipher the mechanisms contributing to cardiac regeneration. Several families of transcription factors, such as Kruppel-like factors (KLF), are known to be associated with heart development and pathology and may play a role in cardiac regeneration. The study of these transcription factors may open new therapeutic avenues of HF.
Purpose: To characterize the regulation of KLF family members during HF development and regression in the zebrafish heart.
Methods. A HF development-regression model was developed in zebrafish using phenylhydrazine (PHZ) treatment for 5 weeks (HF development) followed by a regeneration period of 2 weeks (HF regression). Whole-genome microarray analysis was performed in heart samples at different time-points during HF development (3 and 5 weeks after PHZ treatment initiation) and during HF regression (2 and 9 days after PHZ treatment discontinuation). Gene regulation patterns were characterized using bioinformatics and validated by quantitative PCR.

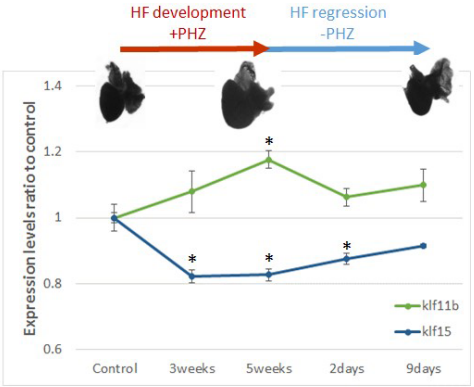

Figure: Expression of klf11b and klf15 during heart failure (HF) development and regression. Values are from microarrays normalized to control. PHZ: phenylhydrazine. * adjusted p <0.01.

Results: Microarray data analysis identified 1469 genes differentially expressed between control and PHZ-treated fish, either during HF development (1382 genes) or during HF regression (486 genes). Six KLF family members were regulated during HF development and regression: klf2a/b, klf4, klf7, klf11b and klf15. Klf2a/b, klf4, klf7 and klf15 are transcriptional activators and showed a downregulation during HF development. In addition, klf15 expression returned to baseline levels at the end of the regression period (Figure). Conversely, klf11b is known to work as a transcriptional repressor and showed an increase during HF development and a return to baseline levels during HF regression (Figure). Quantitative PCR confirmed that klf15 was significantly downregulated (3-fold, $p < 0.001$) whilst klf11b showed an increase (5-fold, $p = 0.008$) at the end of the HF development period. Furthermore, expression levels of both KLF were back to baseline at the end of the HF regression period.
Conclusion: The KLF family of transcription factors is regulated during HF development and regression in zebrafish. Whether these factors are functionally involved in these processes and constitute relevant therapeutic targets remains to be established.

1402

Improved diastolic stiffness through restored endothelial function and titin phosphorylation with chronic stimulation of soluble guanylyl cyclase in heart failure with preserved ejection fraction

A Kovacs[1]; A Gevaert[2]; A Leloup[2]; P Fransen[2]; G Fulop[3]; M Herwig[1]; D Kolijn[1]; M Breitkreuz[1]; P Sandner[4]; S Van Linthout[5]; Z Papp[3]; C Tschope[5]; G De Keulenaer[2]; W Linke[6]; N Hamdani[1]

[1]Ruhr University Bochum (RUB), Department of Cardiovascular Physiology, Bochum, Germany; *[2]University of Antwerp, Department of Pharmaceutical Sciences, Laboratory of Physiopharmacology, Antwerp, Belgium*; *[3]University of Debrecen, Faculty of Medicine, Department of Cardiology, Division of Clinical Physiology, Debrecen, Hungary*; *[4]Bayer AG, Drug Discovery Cardiology, Wuppertal, Germany*; *[5]Charité - Universitätsmedizin Berlin, Department of Medicine and Cardiology (CVK), Berlin, Germany*; *[6]University of Münster, University Hospital Münster, Institute of Physiology II, Münster, Germany*

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Background: Heart failure (HF) with preserved ejection fraction (pEF) is characterized by diastolic dysfunction, increased myocardial stiffness and high oxidative stress. Here we investigated the role of enhancing the nitric oxide/soluble guanylyl cyclase/cyclic guanosine monophosphate/protein kinase G (NO/sGC/cGMP/PKG) signalling pathway in the modulation of diastolic function in a HFpEF model.
Purpose: What is the effect of sGC stimulation on 1) oxidative stress, 2) endothelial function, 3) left ventricular (LV) relaxation and filling, 4) collagen content and 5) cardiomyocyte titin-based stiffness.
Methods: Chronic sGC stimulation was studied on 15-week-old male Dahl/Salt Sensitive rats. Age-matched male SS-13BN rats served as controls (CTRL). Rats were randomized in 8 groups (n = 8-12/group): HFpEF; CTRL; and both HFpEF and CTRL treated with 0.25, 0.75 and 1.5 mg/kg/day BAY 41-8543 via drinking water for 4 weeks.
Results: LV diastolic dysfunction was found in HFpEF animals vs. CTRL (E/A: 1.17 ± 0.04 vs. 1.81 ± 0.11; IVRT: 35.4 ± 1.8 ms vs. 28.0 ± 0.9 ms; Tau: 11.8 ± 0.6 ms vs. 9.7 ± 0.4 ms, respectively), and improved upon treatment with 1.5 mg/kg (1.59 ± 0.06; 26.6 ± 1.2 ms; 9.3 ± 0.4 ms, respectively). High LV end-diastolic pressure in HFpEF rats vs. CTRL (11.9 ± 2.9 mmHg vs. 4.2 ± 0.6 mmHg, respectively) and an upwards and leftwards shift of LV end-diastolic pressure-volume relationship - as indicative of diastolic dysfunction - were improved upon treatment with 1.5 mg/kg (4.4 ± 0.6 mmHg). Arterial elastance was increased in HFpEF rats, and reduced upon treatment with 1.5 mg/kg. This result is in accordance with ex vivo vascular experiments showing arterial stiffening and endothelial dysfunction in the HFpEF group, which was corrected after 1.5 mg/kg treatment. Cardiac fibrosis and collagen gene expression were reduced in HFpEF rats after 1.5 mg/kg treatment. High oxidative stress level and inflammation were reduced after 1.5 mg/kg treatment, which corrected the low NO level observed in HFpEF rats. In addition, increased expression level of sGC in the heart after 1.5 mg/kg treatment was observed using immunohistochemistry. This improvement resulted in increased cGMP concentration and PKG activity in HFpEF rats after 0.25, 0.75 and 1.5 mg/kg treatments. Total and PKG-mediated site-specific Ser-4080 hypophosphorylation of titin in HFpEF animals (relative to CTRL:41% and 33%, respectively) were greatly improved by 1.5 mg/kg treatment (182% and 210%, respectively). Accordingly, the HFpEF group showed increased cardiomyocyte stiffness, which was reduced upon 0.25, 0.75 and 1.5 mg/kg treatments. Conclusion: Chronic stimulation of the NO/sGC/cGMP/PKG signalling pathway decreased LV passive stiffness and improved global LV performance via reduced oxidative stress and fibrosis, and restored endothelial function and titin phosphorylation. Our data suggest that chronic stimulation of sGC may be a promising treatment option for HFpEF patients.

1403

A comparative study of LCZ696, valsartan and resveratrol for the treatment of acute cardiac remodeling and dysfunction in myocardial infarction induced rats

P Pema Raj[1]; L Yu[2]; M Parikh[1]; J Wigle[1]; T Netticadan[1]; S Zieroth[1]

[1]University of Manitoba, Winnipeg, Canada; *[2] Canadian Centre for Agri-Food Research in Health and Medicine, Winnipeg, Canada*

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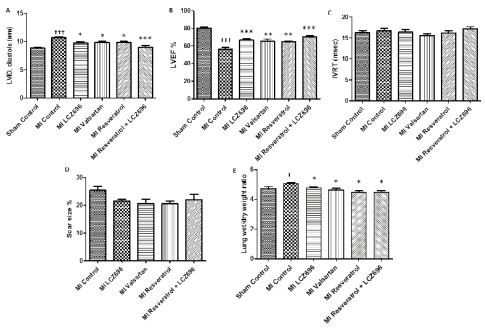
Background: The PARADIGM-HF trial demonstrated the first-in-class angiotensin receptor blocker–neprilysin inhibitor, LCZ696, is superior to enalapril in reducing the risk of death and hospitalization in symptomatic heart failure (HF) with reduced ejection fraction patients. Resveratrol is a promising cardioprotective plant bio-active. Our previous work demonstrated that resveratrol was comparable to perindopril in improving cardiac function and remodeling linked to HF in myocardial infarction (MI) induced rats. In the context of the above new clinical HF trial data, we developed a pre-clinical study comparing the standalone and combinatorial efficacy of LCZ696 with resveratrol in the setting of MI in a rat model.
Purpose: To evaluate the efficacy of LCZ696 as standalone and in combination treatment with resveratrol in MI rats.
Methods: The left anterior descending coronary artery was occluded to mimic MI in male Sprague Dawley rats. Sham operated rats served as controls. Sham and MI study groups received either, vehicle alone, LCZ696 alone (68mg/kg), valsartan alone (31mg/kg), resveratrol alone (2.5mg/kg) or LCZ696+resveratrol combination(68+2.5 mg/kg) daily for 8 weeks. Echocardiography was performed at 8 weeks. Left ventricular ejection fraction (LVEF), isovolumic relaxation time (IVRT) and LV internal dimension (LVID) were measured using EchoPAC. Percentage of scar and lung wet/dry weight ratio were determined. The study was approved by animal ethics board.
Results: Treatment with LCZ696, valsartan, resveratrol and LCZ696+resveratrol significantly prevented LV dilation in MI rats compared to MI control rats (Fig. 1 A: LVID diastole: 10.66 ± 0.18 vs 9.78 ± 0.20, 9.85 ± 0.23, 9.82 ± 0.21 ($p < 0.05$) and 9.01 ± 0.31 ($p < 0.001$). LVEF was significantly lower in MI control rats compared to sham control rats (Fig. 1 B: 56.60 ± 1.70 vs 80.33 ± 1.41 ($p < 0.001$)). LCZ696, valsartan, resveratrol, and LCZ696+resveratrol significantly improved LVEF in MI rats compared to MI control rats (56.60 ± 1.70 vs 66.82 ± 1.43 ($p < 0.001$), 65.45 ± 2.70, 64.82 ± 1.02 ($p < 0.01$), and 70.30 ± 1.63 ($p < 0.001$)). LCZ696+resveratrol treatment showed a trend towards an incremental benefit, but it was not statistically significant. IVRT and scar size were comparable between the groups (Fig. 1 C and D). MI control rats had significantly increased lung wet/dry weight ratio compared to sham control rats (Fig. 1 E: 5.07 ± 0.07 vs 4.73 ± 0.12 ($p < 0.05$)). LCZ696, valsartan, resveratrol and LCZ696+resveratrol significantly lowered lung wet/dry weight ratio in MI rats compared to MI control rats (5.07 ± 0.07 vs 4.77 ± 0.82, 4.62 ± 0.12 ($p < 0.05$), 4.47 ± 0.09, ($p < 0.01$) and 4.48 ± 0.10 ($p < 0.001$)).
Conclusion: Standalone treatment with LCZ696, resveratrol or valsartan significantly prevented cardiac remodeling and dysfunction in MI rats. Combination treatment with LCZ696 and resveratrol was also cardioprotective. LCZ696 and resveratrol may be further explored for their efficacy in the prevention of HF post-MI in future clinical trials.



Echocardiography ((A) LVID, (B) LVEF, (C) IVRT), scar size (D) and lung wet/dry weight ratio (E) data at 8 weeks. All values are expressed as mean±SEM. Sample size n 9 11. ***p<0.001, *p<0.05 vs Sham Control; ###p<0.001, ##p<0.01 and #p<0.05 vs MI Control.

Figure 1

1404

Omecamtive mecarbil causes alternating excitation-contraction coupling at high pacing frequencies

B Balazs Horvath[1]; R Veress[1]; D Baranyai[1]; GA Fulop[2]; A Kovacs[2]; T Csipo[2]; Z Papp[2]; A Toth[2]; A Olah[3]; T Radovits[3]; PP Nanasi[1]

[1]University of Debrecen, Department of Physiology, Debrecen, Hungary; *[2]University of Debrecen, Division of Clinical Physiology, Department of Cardiology, Debrecen, Hungary*; *[3]Semmelweis University, Heart and Vascular Centre, Budapest, Hungary*

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Rationale: Omecamtiv mecarbil (OM) is a myosin activator agent developed for the treatment of heart failure. OM was reported to improve left ventricular (LV) systolic function by increasing ejection fraction and systolic ejection time, but little is known about the effect of heart rate on the action of OM.
On the cellular level the present study was designed to investigate the frequency-dependent effects of OM on the elements of excitation-contraction coupling of the LV: action potential (AP) morphology, intracellular calcium transients (CaT), and unloaded cell shortening were investigated in canine cardiomyocytes. To test the in vivo effects of OM on LV function at high heart rates, rats were chosen as experimental models, having resting heart rates around 350-450 beats per minute.
Methods: During our in vitro experiments, effects of 1 μM OM were tested on isolated canine LV cardiomyocytes at pacing frequencies of 1-5 Hz. APs were recorded through an intracellular microelectrode, cell length was monitored by an optical

edge detector and CaTs were visualized using the fluorescent calcium-sensitive dye, Fura-2. In vivo effects of OM on LV function of Wistar-Kyoto rats were assessed by echocardiography and continuous LV pressure and volume monitoring. OM was administered through a jugular venous canule in increasing doses between 200-1200 μg/kg.
Results: 1 μM OM did not change the overall AP configuration or the average CaT. OM however significantly reduced both diastolic and systolic cell lengths, increased fractional cell shortening and increased the overall time of contraction. Accordingly, OM improved LV systolic function (increased ejection fraction and dP/dtmax), but impaired diastolic function (decreased E/A ratio and increased isovolumetric relaxation time).
With increasing stimulation frequency, alternating APs, CaTs and cell shortening could be seen in 1 μM OM. Such behavior could not be observed in the absence of OM at any stimulation rates, or even in the presence of OM at low pacing rates (1 Hz and 2 Hz). In line with these observations, 1200 μg/kg OM evoked alternating LV contractions in the majority of cases: every effective contraction was followed by an ineffective one. This could be seen both on echocardiography and on pressure-volume records.
Conclusion: Our results suggest that supratherapeutic concentrations of OM may impair the overall LV function especially in tachycardic patients.

1405
Colchicine improves experimental murine Coxsackievirus B3-induced myocarditis involving the NLRP3 inflammasome

S Sophie Van Linthout[1]; K Pappritz[1]; M Sosnowski[1]; M El-Shafeey[1]; C Tschoepe[1]
[1]*Berlin-Brandenburg Center for Regenerative Therapies, Berlin, Germany*

Background: We recently demonstrated the relevance of the pattern recognition receptor Nucleotide-binding oligomerization domain-containing protein 2 (NOD2) and downstream NLRP3 inflammasome in Coxsackievirus (CVB3)-induced myocarditis. The anti-inflammatory drug Colchicine, which is traditionally used to treat gout, exerts its effects among others via reducing NLRP3 activity, and has been shown to improve several cardiac diseases including pericarditis.
Purpose: The aim of the present study was to evaluate the potential of Colchicine to improve experimental CVB3-induced myocarditis.
Methods and Results: Supplementation of 100 ng/ml Colchicine to CVB3-infected HL-1 cardiomyocytes decreased the CVB3-induced NLRP3 activity, as obviated by 1.3-fold ($p < 0.005$), 1.2-fold ($p = 0.001$), and 2.0-fold ($p < 0.0001$) lower ASC-, caspase 1-, and IL-1ß-expressing cells in CVB3+Colchicine versus CVB3-infected HL-1, respectively. In addition, Colchicine reduced the expression of the Coxsackie- and adenovirus receptor and the percentage (%) of CVB3-induced apoptotic cells by 1.7-fold ($p < 0.0005$) and 1.4-fold ($p < 0.0001$), respectively, as assessed by flow cytometry. In vivo, 5 μmol Colchicine/kg body weight per os, 1 day post CVB3 infection in C57BL/6j mice, improved left ventricular (LV) function. This was paralleled by a 1.8-fold ($p < 0.05$) reduction in LV CD68 presence, and a 1.4-fold ($p < 0.05$), 2.1-fold ($p < 0.05$), 1.7-fold ($p < 0.05$), and 4.4-fold ($p < 0.01$) decrease in LV Ly6C, TNF-a, caspase-1, and CVB3 mRNA expression versus CVB3 mice, respectively. Whereas LV NOD2, NLRP3 and ASC expression was unaltered in CVB3+Colchicine versus CVB3 mice, the % of splenic NOD2- and ASC-expressing F4/80 macrophages was 1.5-fold ($p < 0.0001$) and 1.7-fold ($p < 0.05$) lower in CVB3+Colchicine versus CVB3 mice, respectively. In addition, Colchicine decreased the CVB3-induced % of splenic pro-inflammatory Ly6Chigh monocytes and the proliferation (division index) of CD68 cells by 1.3-fold ($p < 0.0001$) and 1.3-fold ($p < 0.0001$), respectively.
Conclusion: Colchicine improves experimental murine CVB3-induced myocarditis in C57BL/6j mice involving reduction of NLRP3 activity in the spleen.

1406
Deleting cardiac GRK5 catalytic activity impairs basal cardiac function without affecting myocardial growth

A Cannavo[1]; A Elia[2]; C De Lucia[1]; D Liccardo[2]; N Ferrara[2]; N Paolocci[3]; G Rengo[2]; WJ Koch[1]
[1]*Temple University School of Medicine, Center for Translational Medicine, Philadelphia, United States of America*; [2]*Federico II University of Naples, Translational Medical Sciences, Naples, Italy*; [3]*Johns Hopkins University of Baltimore, Baltimore, United States of America*

Introduction: G protein-coupled receptor (GPCR) kinase 5 (GRK5) is a multifunctional protein. When at the plasma membrane, GRK5 exerts "canonical" effects regulating some GPCRs, such as ß-ARs, and their downstream signaling. Conversely, when in the cytosol or in the nucleus, it interacts with non-GPCRs related proteins. Interestingly, due to these multiple activities GRK5 is considered either a protective and noxious molecule. In this context, previous studies have demonstrated that cytosolic GRK5 can directly regulate p53, leading to apoptosis inhibition in several cell types, including cancer cells. While, when localized in the nucleus GRK5 can trigger pro-hypertrophic signaling in cardiomyocytes, inducing cardiac dysfunction. Surprisingly, the role played by the catalytic activity of the enzyme has not been addressed yet. Thus, it is unclear whether, and what GRK5 effects can be attributed to its catalytic domain.
Purpose: To determine whether deleting cardiac GRK5 catalytic activity impacts basal cardiac function and the heart's ability to respond to chronic stress.
Methods: Using the CRISPR/Cas9 system, a new knock-in mouse line with lysine (K) 215 replaced by arginine (R) in the GRK5 protein (K215R mice) was generated. This intervention abolishes GRK5 catalytic activity. K215R mice underwent chronic pressure overload (via transverse aortic constriction, TAC), to induce heart failure (HF) onset and progression.
Results: Compared to age-matched littermates, nine weeks-old, unstressed K215R mice exhibited larger LV chamber dimensions (LVID) and increased heart rate. Mutant mice showed higher extent of basal apoptotic rates, but no signs of maladaptive hypertrophy or fibrosis. However, TAC induced a faster progression towards HF in GRK5-K215R mice, along with markedly worsened LV function deterioration and chamber remodeling. Molecularly, after K215R mice displayed basal down-regulation of EGFR protective signaling, concomitant with a rise in p53 expression. Conclusion: Alterations in basal GRK5 catalytic activity impairs basal LV function and accelerates HF progression in mice with pressure overload due to repressed pro-survival signaling pathways. Our study suggests that rescuing GRK5 catalytic activity is a promising new avenue to prevent or reverse HF progression.

1407
Role of the cardiotrophin-1/Galectin-3 axis in myocardial fibrosis. From mechanistic insights to clinical implications.

A Gonzalez Miqueo[1]; E Martinez-Martinez[2]; C Brugnolaro[3]; J Ibarrola[2]; S Ravassa[1]; M Buonafine[4]; B Lopez[1]; A Fernandez-Celis[2]; R Querejeta[5]; E Santamaria[6]; J Fernandez-Irigoyen[6]; G Rabago[7]; F Jaisser[4]; J Diez[1]; N Lopez-Andres[2]
[1]*CIMA, University of Navarra, Program of Cardiovascular Diseases & CIBERCV, Carlos III Institute of Health, Pamplona, Spain*; [2]*Miguel Servet Foundation, Cardiovascular Translational Research, Navarrabiomed, Complejo Hospitalario de Navarra, IdiSNA, Pamplona, Spain*; [3]*CIMA, University of Navarra, Program of Cardiovascular Diseases, Pamplona, Spain*; [4]*The Cordeliers Research Center, INSERM UMRS 1138 Team 1, University Pierre and Marie Curie, Paris, France*; [5]*Donostia University Hospital, Department of Cardiology, Biodonostia, Basque Country University, San Sebastian, Spain*; [6]*Miguel Servet Foundation, Proteomics Unit, Navarrabiomed, IdiSNA, Proteored-ISCIII, Pamplona, Spain*; [7]*University of Navarra Clinic, Department of Cardiology and Cardiac Surgery, Pamplona, Spain*

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Purpose: Myocardial fibrosis is a main contributor to the development of heart failure (HF). Cardiotrophin-1 (CT-1) and galectin-3 (Gal-3) are increased in HF and associated with myocardial fibrosis. The aim of this study is to analyze whether CT-1 regulates Gal-3, and to evaluate their potential clinical impact.
Methods: Quantitative proteomics was used in human cardiac fibroblasts (HCFs) treated with CT-1. Male Wistar rats and B6CBAF1 mice were treated with CT-1 (20 μg/kg/day) for 6 and 2 weeks, respectively. Half of the mice received the Gal-3 inhibitor, modified citrus pectin (100 mg/kg/day). Dahl salt-sensitive hypertensive rats were used as a model of HF with preserved ejection fraction (HFpEF). Finally, CT-1 and Gal-3 levels were measured in plasma and myocardial biopsies from patients with HF of hypertensive etiology.
Results: Proteomic analysis revealed that Gal-3 was up-regulated by CT-1 in HCFs in parallel with other profibrotic and proinflammatory markers such as collagen type I, fibronectin, a-smooth muscle actin, vimentin, osteopontin, TGF-ß, CTGF, IL-6 and IL-1ß. CT-1 up-regulation of Gal-3 was mediated through the stimulation of ERK 1/2 and Stat-3 pathways. Rats and mice treated with CT-1 presented higher cardiac Gal-3 levels as well as perivascular fibrosis. In addition, CT-1 increased the expression of collagen type I, a-smooth muscle actin, vimentin, TGF-ß and CTGF. In CT-1-treated rats, direct correlations were found between cardiac CT-1 and Gal-3 levels, as well as between Gal-3 and perivascular fibrosis. Gal-3 genetic disruption in HCFs and pharmacological Gal-3 inhibition in mice prevented the profibrotic and proinflammatory effects of CT-1. Rats with HFpEF showed increased cardiac CT-1 and Gal-3 expression together with cardiac fibrosis. Cardiac CT-1 protein was directly associated with Gal-3 mRNA. Additionally, there was a direct correlation of CT-1 protein and Gal-3 with perivascular fibrosis. In a small cohort of 24 HF patients, myocardial CT-1 and Gal-3 were increased and directly correlated. Likewise, plasma CT-1 and Gal-3 levels were also increased and directly correlated in an independent cohort of 234 HF patients. Elevated serum CT-1 or Gal-3 levels were both significantly associated with cardiovascular death in the large cohort of HF patients. Interestingly, patients with both CT-1 and Gal-3 elevated presented a 4-fold higher risk of cardiovascular death than patients with normal values for

both parameters, after adjustment for clinically relevant risk factors and confounding factors.
Conclusions: Our data suggest that CT-1 up-regulates Gal-3 which, in turn, mediates the proinflammatory and profibrotic myocardial effects of CT-1. The elevation of both molecules in blood from HF patients identifies a subgroup of patients with high cardiovascular mortality. The CT-1/Gal-3 axis emerges as a candidate target for treating myocardial fibrosis in HF.

1408

A Kinase Interacting Protein 1 (AKIP1) regulates cardiomyocyte elongation and promotes physiological cardiac remodeling by activating the AKT/CEBP-b/CITED4 pathway

K T Kirsten Nijholt[1]; HG Booij[1]; RA De Boer[1]; SU Oberdorf[1]; M Pavez[1]; WH Van Gilst[1]; HHW Sillje[1]; BD Westenbrink[1]
[1]*University Medical Center Groningen, Experimental Cardiology, Groningen, Netherlands*

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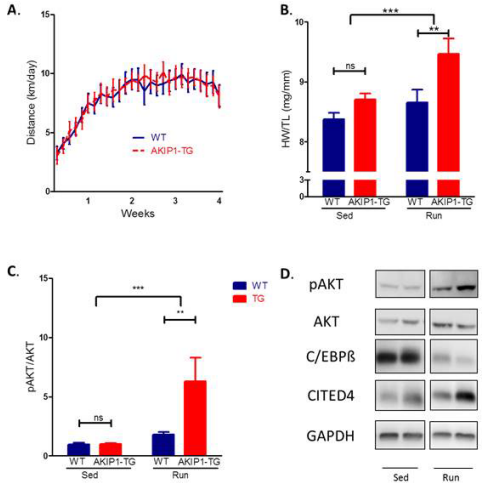
INTRODUCTION: A Kinase Interacting Protein 1 (AKIP1) has been proposed to serve as a nodal point for physiological cardiomyocyte hypertrophy based on studies in cultured cardiomyocytes. Whether AKIP1 regulates the cardiac adaption to physiological stress in vivo is unknown.
Purpose: To determine the effect of cardiomyocyte-specific overexpression of AKIP1 on the cardiac response to voluntary wheel running (VWR).
Methods: Adult male mice (8-12 weeks) with cardiomyocyte specific overexpression of AKIP1 (AKIP1-TG) or their wild type (WT) littermates were caged individually with or without the unlimited access to a running wheel (N = 9-20 / group). Exercise performance, heart weight/tibia length (HW/TL) , cardiac MRI, cardiac histology, and left ventricular (LV) biochemistry were evaluated. Groups were compared by Two-way ANOVA.
Results: Cardiac mass and function were comparable between sedentary WT and AKIP1-TG mice and the average running speed and distance were similar among genotypes. Cardiac hypertrophy induced by VWR was markedly augmented in AKIP1-TG vs WT mice as evidence by 57 % higher increase in HW/TL and a 27 % greater increase in LV- mass on MRI. The estimated cardiomyocyte volume was also increased by 27% in AKIP1-TG vs WT mice, which was predominately determined by an increase in cardiomyocyte length (61.94 ± 5.35 μm vs 99.48 ± 2.18 μm; $p < 0.05$). The augmentation of cardiac hypertrophy induced by VWR in AKIP1-TG mice was associated with a 6-fold increase in the phosphorylation of AKT, downregulation of C/EBPß and the subsequent upregulation of CITED4 mRNA and protein levels in LV lysates.
Conclusion: In conclusion, AKIP1 promotes cardiomyocyte elongation and physiological cardiac remodeling through activation of the AKT/C-EBPß/CITED4 pathway. These findings suggests that AKIP1 may serve as a nodal point for beneficial reprogramming of hypertrophic heart disease.



1409

Atrial natriuretic peptide hypersecretion contributes to systemic insulin resistance in pressure overload heart failure

F Gao[1]; X Qin[1]; J Xu[1]; X Xing Zhang[1]
[1]*Fourth Military Medical University, Xi'an, China People's Republic of*

Funding Acknowledgements: This study was supported by the grants from National Natural Science Foundation of China (No. 31500928, No. 81670253)

Background: Emerging evidence has shown that heart failure (HF) may increase the risk of systemic insulin resistance (IR), resulting in a deleterious vicious cycle of cardiac dysfunction and worsening of clinical outcomes in HF patients. However, the underlying mechanism is still elusive.
Purpose: This study aims to investigate the role of HF-induced natriuretic peptides in systemic IR and the underlying mechanism.
Methods: To delineate the relationship between natriuretic peptide (NP) and IR in the context of HF, 136 HF patients and 20 age-matched healthy subjects were included in this study. We evaluated serum NP levels and systemic insulin sensitivity (HOMA-IR). A mouse model of pressure overload-induced HF and atrial natriuretic peptide (ANP) knockout mice were used to examine the role of ANP in systemic IR in HF.
Results: We found that systemic IR was prevalent in HF patients compared with age-matched healthy subjects as evidenced by HOMA-IR. A Spearman's rank correlation analysis showed that serum ANP had the highest association with systemic IR in hypertensive HF patients ($r = 0.429$, $p < 0.001$). The association between ANP and IR was further evaluated with laboratory studies of gain- and loss-of-function in mice. ANP infusion to C57BL/6J mice decreased insulin sensitivity, whereas ANP knockout mice exhibited increased insulin sensitivity. Moreover, using a mouse model of transverse aortic constriction-induced HF, impaired insulin sensitivity as well as increased serum ANP were observed in HF mice, while blocking ANP signaling with either a pharmacological inhibitor (isatin, the inhibitor of ANP receptor) or genetic manipulation (ANP knockout mice) showed ameliorated HF-induced systemic IR. Mechanistically, ANP impaired insulin-stimulated glucose uptake as evidenced by blunted insulin-stimulated Akt phosphorylation and GLUT4 translocation in skeletal-muscle C2C12 cells.
Conclusion: These results suggest that ANP suppresses skeletal muscle glucose uptake, which contributes to systemic IR in pressure overload-induced HF.

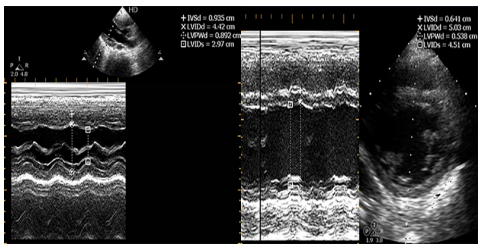
Clinical Case Corner 4 - The great fire: inflammation of the heart and beyond

1410

A case of lupus myocarditis presenting as acute cardiogenic shock

A Elsayed[1]; M Ali Dawood[1]; M Hassan Abada[2]; A Beltagy[3]
[1]*Alexandria University, cardiology and angiology department, Alexandria, Egypt*;
[2]*Alexandria University, Critical care medicine department, Alexandria, Egypt*;
[3]*Alexandria University, Rheumatology and Clinical Immunology Department, Alexandria, Egypt*

Introduction: Systemic lupus erythematosus (SLE) is an autoimmune disorder. Cardiac involvement may be in the form of pericarditis or myocarditis. In our case report we are reviewing the management of a case of lupus myocarditis presenting with acute cardiogenic shock.
Case report: A 20-year-old female previously diagnosed lupus nephritis class V with maintenance treatment of mycophenolate mofetil (MMF), hydroxychloroquine and low dose prednisolone presented with dyspnea. On clinical examination she was hypotensive, tachycardic, tachypneic with audible pulmonary rales, she also was oliguric and hypoxic on room air. She was mechanically ventilated and Norepinephrine infusion was added with up-titration to 10μg/Kg/min but no improvement. Chest x-ray revealed pulmonary congestion and left pleural effusion. Echocardiography revealed dilated left ventricle (LV) dimensions (end diastolic dimension(EDD)/end systolic dimension (ESD); 52/46 mm) with global severe hypokinesia sparing the apex and reduced LV systolic function (Ejection fraction (EF); 30%).
Laboratory findings were; Anemia (Hemoglobin; 8.7g/dl), Hypoalbuminemia (serum Albumin; 1.7g/dl), (Erythrocytes sedimentation rate; 44mm/h), positive cardiac enzymes (Troponin I; 25 ng/mL, normal; less than 0.01 ng/mL), consumed complement (C3-C4), positive anti-nucleic acid (ANA) and anti-dsDNA. We could make a diagnosis of acute lupus myocarditis based on the previous results Dopamine infusion and intravenous methylprednisolone (500mg/day) for 5 days were added with marvelous response. Urine output and vital signs improved within 2 days, so Dopamine and norepinephrine infusions were weaned and anti-failure measures were initiated including intravenous furosemide, spironolactone (50mg/day) and angiotensin converting enzyme inhibitors.
After 5 days of initial management an echocardiography was done revealed dramatic improvement of the LV systolic function (EDD/ESD; 44/29mm) and (EF; 55%).
Conclusion: SLE is a common multisystem autoimmune disorder with female to male ratio 9:1. Cardiac affection of SLE can be in the form of pericarditis, myocarditis, coronary arteritis and premature coronary atherosclerosis. Echocardiography helps in diagnosis of SLE-related pericardial effusion, myocardial affection, valvular involvement, and cavity thrombus formation. Other imaging modalities can be used such as cardiac computed tomography (CT) and cardiac magnetic resonance (CMR). Management of lupus myocarditis relies on previous case reports in literature due to rarity of clinical evidence.
Although our case was on immunosuppressive medications she developed lupus myocarditis and this considered inadequate control of activity. Our case responded marvelously to high dose steroids and was shifted to monthly cyclophosphamide pulse therapy. Also, medical management of heart failure including angiotensin-converting enzyme inhibitors, beta-blockers and diuresis was a cornerstone.



Echo showing EF before & after treatment

1411

Case of massive thromboembolism in a patient with necrotic vasculitis and inherited thrombophilia

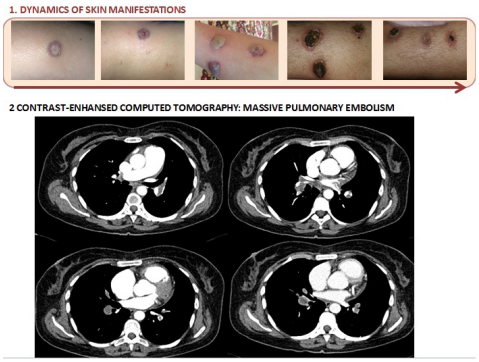
S Martirosyan[1]; H Kosmachova[1]; T Matushina[1]
[1]*Cuban Regional Clinical Hospital No 1, Krasnodar, Russian Federation*

Introduction: a 43-year-old women with preliminary diagnosis of right-heart infective endocarditis was delivered to our clinic to resolve the issue of surgery.

Clinical characteristics

	BP, mmHg	HR, bpm	SatQ2,%	D-Dimer, ng/ml	NTproBNP, pg/ml	HB, g/l	WBC
D1	100/80	140	82	3406	7318	92	10,6
D22	110/70	100	96	456	597	107	7,8

D1 - admission date, D29 - discharge date



Presenting condition: pale skin with multiple rounded wounds in the scarring stage on the legs, progressive dyspnea with wet wheezes, SpO2 82-84%, arterial BP 100/80 mmHg.
Anamnesis: patient with no history of heart or vascular diseases. Rounded bullous rashes on legs with hyperemia and edema appeared 2 months earlier. Progressive dyspnea appeared 2 weeks ago. In regional hospital was suspected right-heart infective endocarditis and the patient was sent to our clinic for surgery
Gynecological anamnesis: pregnancy - 9 miscarriage - 6
Identification of the problem: D-Dimer 3406 (N = 243) NTproBNP - 7318 (N = 110)
On ECG: sinus tachycardia HR140 Esco: MV - mid reg TV - med reg LA 22 mm LV 33 mm RA 50x55 mm RV 43 mm EF 38% Systolic Pulmonary artery pressure >100 mmHg NO EVIDENCE OF ENDOCARDITIS
Contrast-enhanced computed tomography of the chest: massive pulmonary embolism
Ultrasound of lower limbs: bilateral thrombosis of superficial femoral veins
Anticoagulation (enoxaparin 1 mg/kg each 12 h -> rivaroxaban 15 mg each 12 h) therapy, CPAP-BIPAP ventilation has been started. The patient's condition was stabilized in 2 weeks .
Questions and problems:
1. Was the diagnosis of right-heart infective endocarditis competent? Did this patient need the surgery? There were no any reasons for acquiring an infectious process on the tricuspid valve, so no need for surgery
2. What is the cause of massive thromboembolic events?
Considering gynecological anamnesis, in order to find the answer to this question, we conducted a genetic test for susceptibility to thrombophilia. The mutation in folate metabolism was found. So we added to the treatment folic acid.

3. What were the causes and nature of skin rashes?
We performed a biopsy of the skin flap with histological examination. The cutaneous form of necrotic leg ulcerative vasculitis was revealed.
This patient was discharged in a satisfactory condition with positive clinical dynamics.
Conclusions: the correct interpretation of heart failure symptoms and searching for etiological and pathogenic triggers of cardiac decompensation is the only way to successful treatment.

1412
Giant cell myocarditis: a giant challenge

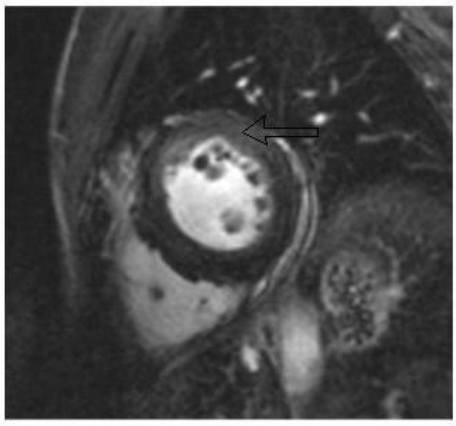
A Addas[1]; M Kuehl[2]; K Jawad[1]; S Feder[1]; J Jozwiak-Nozdrzykowska[3]; J Fischer[1]; M Nozdrzykowski[1]; A Al-Naamani[1]; M Sandri[3]; P Lurz[3]; A Arya[2]; A Meyer[1]; S Lehmann[1]; J Garbade[1]; M Borger[1]
[1]Heart Center of Leipzig, Department of cardiac surgery , Leipzig, Germany; [2]Heart Center of Leipzig, Department of Electrophysiology, Leipzig, Germany; [3]Heart Center of Leipzig, Department of cardiology, Leipzig, Germany

A 51-year-old man with no previous medical history presented with an episode of pre-syncope, orthopnea and paroxysmal nocturnal dyspnea. Echocardiography showed severely impaired left ventricular systolic function with global hypokinesia (LVEDd 59mm, LVEF: 30%), mildly reduced right ventricular systolic function, and moderate mitral and tricuspid valve regurgitation. An initial cardiac MRI scan showed signs of acute myocarditis. Coronary angiography excluded coronary artery disease. After initial stabilisation and initiation of heart failure drugs, the patient was discharged home. Two weeks later the patient was readmitted to our hospital with worsening heart failure. An endomyocardial biopsy was performed and demonstrated histological features consistent with giant cell myocarditis. Immunosuppressive therapy with Cyclosporin, Steroids and monoclonal antibodies (Rituximab) was immediately initiated. After further two weeks an intermittent AV-Block III° required the implantation of a permanent dual chamber defibrillator. A repeat cardiac MRI scan showed progressive worsening of both ventricular systolic function and still signs of active myocarditis. Beginning end-organ involvement required the initiation with Milrinon (0,5 μg/kg/min). A right heart catheterization whilst on inotropic support demonstrated a severely reduced cardiac index of 1.5 [l/min/m^2] and the patient was therefore listed for urgent heart transplantation. During the next weeks the patient suffered from recurrent sustained VT's refractory to medical therapy, DC cardioversions or overdrive pacing and therefore underwent radiofrequency ablation of the ventricular arrhythmia. Over the next weeks, the inotropic requirements increased and signs of end-organ failure and cardiogenic shock developed (INTERMACS 1). Therefore it was necessary to implant a left ventricular assist device (HeartMate III). Despite this mechanical support the patient developed progressive right heart failure, which made the implantation of an extracorporeal right ventricular assist device (Levitronix) necessary. Under the support of both devices, the patient's clinical condition stabilized, and the renal and hepatic functions improved. The further clinical course was complicated by a spontaneous haemothorax under therapeutic anticoagulation, requiring a thoracotomy. Finally, the patient underwent orthotropic heart transplantation approximately 6 months after the initial presentation and the patient was discharged home in a very good clinical condition.
Conclusion: Giant cell myocarditis can cause rapid deteriorating heart failure. For a successful management the complete armamentarium of modern heart failure therapy might become necessary. Early transfer to a specialized heart centre is the key to survival.

1413
Cardiogenic shock as first manifestation of multiple sclerosis relapse

B Barbara Hudournik[1]; G Voga[1]; N Glavnik Poznic[2]
[1]General Hopsital Celje, Medical intensive care unit, Celje, Slovenia; [2]General Hopsital Celje, Department of cardiology, Celje, Slovenia

Introduction: Multiple sclerosis (MS) is the leading cause of neurological disability in young adults. Most patients with cardiovascular involvement present with signs of autonomic dysfunction. Compromised systolic function is seldom described. We present a case of young female admitted due to cardiogenic shock, which preceded signs of MS relapse.
Case presentation: 33-year old woman with known MS experienced headache, vertigo and nausea while on the swing on a picnic. Upon arrival to the emergency room she was hypotensive and severely respiratory distressed due to pulmonary oedema. Neurological status was correct. Cardiac ultrasound (US) demonstrated severe systolic dysfunction of both ventricles. She was intubated and mechanically ventilated. Hemodynamic monitoring by transpulmonary thermodilution revealed low cardiac index (CI), low global end diastolic volume index and high extra-vascular lung water. High dose noradrenaline and dobutamine were started simultaneously with low dose of levosimendan. Despite extensive support she remained hemodynamically unstable. Intra-aortic balloon pump was inserted, which resulted in only slight increase of CI. We considered the possibility of relapse of MS to be the cause of refractory cardiogenic shock. Five hours after ICU admission she received first dose of methylprednisolone (1g/day). Approximately six hours afterwards CI improved significantly. After second dose the methylprednisolone was changed to human immunoglobulin (0,4 g/kg/day) due to evolving infection. Two days later we were able to wean the patient from inotropes, vasopressors and mechanical circulatory and respiratory support. Coronary angiography and serologic tests for cardiotropic viruses revealed no pathology. Magnetic resonance imaging (MRI) showed some myocardial oedema, described as residual after stress cardiomyopathy or myocarditis. MRI of the brain revealed significant dissemination of demyelinating lesions. Neurologic evaluation demonstrated severe gait disorder, which persisted after six months. At the same time US and MRI revealed complete restoration of cardiac function and morphology. Discussion Several case reports of acute cardiac failure in patients with MS relapse have been described in literature. Clinical trials evaluating cardiac function in patients with MS frequently showed reduced systolic function of left or both ventricles in otherwise hemodynamically stable patients. Different theories have been proposed as possible mechanism, but we still lack robust evidence. Common feature of all described cases is severe impairment of systolic function, which responds to treatment of MS relapse. Although it is impossible to exclude spontaneous and relatively rapid recovery typical for stress-induced cardiomyopathy of any cause, we believe in the light of available evidence that these patients should receive high dose corticosteroids in the absence of contraindication and in conjunction with supportive treatment.



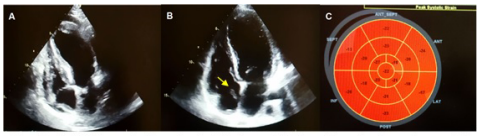
Cardiac MRI:Anterolateral wall oedema

1414
When an exhausted heart holds on for two: a remarkable case of fulminant myocarditis

L Luis Graca Santos[1]; F Montenegro Sa[1]; C Ruivo[1]; R Ribeiro Carvalho[1]; J Correia[1]; J Guardado[1]; S Pernencar[1]; J Morais[1]
[1]Hospital Santo Andre, Cardiology, Leiria, Portugal

We present the case of a 27-year-old black woman, 7 weeks pregnant, who was brought to the Emergency Room following a syncopal episode. She complained of a 4-day course influenza-like syndrome associated to epigastric discomfort, fatigue and dyspnea. The patient had no relevant medical history, denying drug abuse, and was taking iodine and folic acid. At admission, she was conscious and oriented, with sinus tachycardia, hypotension (90/50mmHg), fever (38,8°C), and polypnea with peripheral oxygen saturation of 95%. Cardiopulmonar auscultation was normal. The electrocardiogram revealed concave and diffuse ST segment elevation. Blood tests showed elevated C-reactive protein (15.7mg/L, normal (N) <5.0), CK-mb (87U/L, N = 5.0-24.0) and troponin I (4.37ng/mL, N <0.04). Transthoracic echocardiogram (TTE) revealed biventricular systolic dysfunction (left ventricular ejection fraction (LVEF) of 28%; systolic excursion of the tricuspid ring (TAPSE) of 13mm) and mild to moderate circumferential pericardial effusion (Panel 1.A)
The presumptive diagnosis of acute myocarditis was established and the patient admitted to the Cardiac Intensive Care Unit. Few hours later, she developed cardiogenic shock with need for high doses of dobutamine and noradrenaline. Due to refractoriness to aminergic support, the patient was transferred the next day to the nearest cardiac surgery department anticipating the need for mechanical ventricular assistance. The following days, her haemodynamic state gradually improved and

amines were totally suspended on the 7th day, initiating bisoprolol and spironolactone at low doses. The patient chose not to interrupt the pregnancy. On the 8th day, TTE revealed normalization of biventricular systolic function and important reduction of the pericardial effusion presenting, however, signs of thrombus in the right atrium (RA) adherent to the central venous catheter (Panel 1.B). Subcutaneous enoxaparin 1.5mg/Kg/day was started. She returned to the cardiology ward on the 13th day, clinically stable and asymptomatic, and was discharged two days later only on enoxaparin. The pre discharge TTE showed good biventricular function (LVEF 60% with global longitudinal strain -21.1% (Panel 1.C), TAPSE 24mm), residual pericardial effusion and >50% reduction of the RA thrombus size.
During follow-up, the patient remained asymptomatic presenting with optimal functional class. TTE performed a month after discharge showed no signs of thrombus in the RA. She was closely followed by an experienced obstetrician. The pregnancy and delivery were uneventful and the baby was born apparently healthy.
The present case of a young pregnant woman developing fulminant myocarditis represents a challenging case of acute heart failure not only due to its rarity and high mortality but also because the patient's decision not to interrupt pregnancy has conditioned the medical management, however, with no apparent impact on maternal and fetal prognosis.



Panel 1. **(A)** Mild to moderate pericardial effusion on initial transthoracic echocardiogram; **(B)** Filiform mobile echogenic structure in the right atrium suggestive of thrombus (yellow arrow); **(C)** Longitudinal global strain the day before discharge (mean value -21,1%)

Serial transthoracic echocardiograms

1415
Mid-ventricular Takotsubo cardiomyopathy caused by myasthenic crisis

T Furlan[1]; S Poznic[1]; D Kosuta[1]; B Leskovar[1]
[1]*Trbovlje General Hospital, Department of Internal Medicine, Trbovlje, Slovenia*

Introduction: Myasthenic crisis is an autoimmune condition, characterized by muscle weakness that leads to respiratory failure. Takotsubo cardiomyopathy is a syndrome, characterized by profound but reversible left ventricular dysfunction in the absence of coronary artery disease.
Case report: We describe a case report of a 66-year-old man with arterial hypertension, COPD and myasthenia gravis treated with pyridostigmine who developed Takotsubo cardiomyopathy and concomitant myasthenic crisis that were triggered by a physically and emotionally stressful event. On admission, he presented with mid-sternal chest pain and severe shortness of breath leading to respiratory failure requiring intubation. Electrocardiogram showed ST elevation in lateral leads and echocardiography showed diffuse hypokinesia. His troponin level was elevated, while cardiac catheterization revealed no significant coronary artery disease. Left ventriculogram showed mid-ventricular akinesia with reduced overall left ventricular systolic function suggestive of Takotsubo stress cardiomyopathy. He transiently required intra-aortic balloon pump, but his condition improved quickly and was extubated on the second day. Plasmapheresis or immunoglobulin therapy were not required. Control echocardiogram seven days after acute presentation showed complete resolution of cardiac function with normal left ventricular chamber size, normal ejection fraction and no regional wall motion abnormalities.
Discussion: There are only a few case reports describing causative associations between myasthenic crisis and Takotsubo cardiomyopathy. In our case it seems that a severe physical and emotional stress triggered both myasthenic crisis and Takotsubo cardiomyopathy. Takotsubo cardiomyopathy is a clinical syndrome characterized by transient left ventricular systolic dysfunction, mimicking myocardial infarction. It is most commonly presented as apical ballooning on left ventriculogram, but our patient had a less common variant with ventricular hypokinesis restricted to the mid-ventricle and relative sparing of the apex (mid-ventricular type). It is generally a transient disorder that is managed with supportive therapy. Myasthenic crisis is a life-threatening condition with respiratory failure due to weakness of respiratory muscles. It can be precipitated by various factors, most often concurrent infection but physical and emotional stress have also been described as a trigger. General measures are supportive therapy and intravenous immunoglobulins and plasma exchange as primary pharmacologic therapies. In our case, we observed quick resolution of symptoms with supportive measures only.
Conclusions: Takotsubo cardiomyopathy can be a rare presentation of myasthenic crisis, both can be precipitated by physical or emotional stress and managed with supportive therapy only.

1416
A rare case of leptospira myocarditis

CT Ng[1]; CY Khoo[1]; L Chan[1]; D Sim[1]; LY Teo[1]
[1]*National Heart Centre Singapore (NHCS), Singapore, Singapore*

Introduction: A 60-year-old Chinese male visiting from Australia presented with syncope, cough, fever and myalgia. Past medical history included AF and hypertension. He reported contact with pond water 2 weeks ago. Vitals were stable. Labs were unremarkable except for raised troponin of 3680ng/L and transaminases. The infectious disease physician empirically started antibiotics (ceftriazone & doxycycline) after septic workup. Paired convalescent leptospiral IgM was positive, confirming acute leptospirosis.
Management: Initial transthoracic echocardiogram (TTE) showed depressed left ventricular ejection fraction (LVEF) of 42%. Overnight, he had alternating bundle branch blocks. He subsequently VT, which was terminated by lignocaine and amiodarone. Urgent coronary angiogram showed minor coronary artery disease.
On day 3, Veno-Arterial Extracorporeal membrane oxygenation (VA-ECMO) circuit was inserted for refractory cardiogenic shock despite dual inotropes. There was no pulse pressure and cardiac rhythm while on ECMO. Repeat TTE showed severely depressed LVEF of 10%. Renal replacement therapy (RRT) was initiated in view of acute renal impairment. Endomyocardial biopsy was also done on day 3.
The patient was started on pulsed methylprednisolone 1g daily for 3 days. His blood pressure and ventricular arrhythmias improved with pulsed steroids. ECMO was successfully explanted after 10 days of support. TTE performed at 3 weeks showed normalisation of the LVEF to 65%.
Etiology: Given the presentation of viral-like symptoms with rapid onset of cardiogenic shock and malignant arrhythmias, our initial diagnosis was acute viral myocarditis. Comprehensive hunt for the etiology was started after considering the travel history and exposure to pond water. Endomyocardial biopsy was consistent with myocarditis, and the positive paired convalescent leptospiral IgM pointed to leptospirosis as the most likely cause.
Diagnosing leptospira myocarditis requires high clinical suspicion as it could present with only conduction abnormalities. Our patient had malignant arrhythmias with episodes of VT, VF and AF.
Treatment: Acute fulminant leptospira myocarditis is associated with a high mortality rate. Timely recognition and initiation of antimicrobial therapy is pivotal. Management of hemodynamic instability associated with leptospira myocarditis is supportive. VA-ECMO therapy was used as a bridge to recovery. Our patient responded favourably to steroids. To our knowledge, this is the first successful reported case of fulminant leptospira myocarditis managed by using VA-ECMO and pulsed steroids.
Conclusion: Although uncommon, fulminant leptospira myocarditis should be considered in patients with risk factors. Endomyocardial biopsy and early initiation of appropriate antimicrobials and supportive treatment such as VA-ECMO support can improve survival. More studies would be required to confirm the efficacy of pulsed steroids in this group of patients.

1417
Severe cardiac dysfunction in a patient with acute myocardial infarction and multiple sclerosis-more than a coincidence?

AM Chitroceanu[1]; N Patrascu[2]; VD Vintila[2]; D Vinereanu[2]
[1]*University Emergency Hospital of Bucharest, Cardiology, Bucharest, Romania*;
[2]*University of Bucharest Carol Davila, Bucharest, Romania*

Intriduction: The increased risk of mortality in patients with multiple sclerosis (MS) may be explained by a higher cardiovascular risk and occurrence of cardiovascular disease. Although recent evidence shows controversial results, cardiac dysfunction (CD) might not be so exceptional and could be secondary to disease treatment. Herein, we wanted to draw attention to a rare togetherness by reporting a case of acute myocardial infarction in a patient with MS and interferon induced thyroiditis, in which CD seems to be prior to the acute coronary event.
Case report: A 49 year-old man presented with new onset chest pain 6 hours prior to arrival without signs of heart failure. Acute antero-lateral ST-elevation myocardial infarction, Killip I class was diagnosed. He was diagnosed for 9 years with multiple sclerosis in treatment with interferon beta-1a, without any relapse-remitting episode during this time. He admitted to smoke (40PY) and had a previous history of diabetes and interferon induced autoimmune thyroiditis. Coronary angiogram revealed only one-vessel disease with partially occlusive thrombus in proximal left anterior descending artery (LAD), TIMI 0 flow. Primary percutaneous coronary intervention was performed with successful stenting, without procedural complications, TIMI 3 flow. Transthoracic echocardiogram detected markedly reduced left ventricular (LV) ejection fraction (25%), mild mitral regurgitation, global hypokinesia with apical and inferior akinesia and increased LV sphericity. We confirmed hypothyroidism and severe dyslipidemia. Additionally to standard cardiac management, we postponed the nextscheduled interferon dose taking into consideration its immunomodulatory effects that could interfere with cardiac remodelling.
Questions, problems. In our case, echocardiogram revealed increased LV sphericity, important LV remodelling, severe global dysfunction and extensive impaired

wall motion which exceeded the LAD topography, otherwise rapidly reperfused. This finding suggests a pre-existing cardiac dysfunction which could be explained in the context of MS or, even if controversial, by its treatment. Main possible mechanisms are oxidative stress with endothelial dysfunction, inflammatory status with subclinical myocarditis, myocyte structure alteration, vascular microthrombosis, and perfusion abnormalities; also, associated secondary hypothyroidism. Moreover, cardiovascular risk factors (hypertension, diabetes, and smoking) which our patient with MS leads to an excess of cardiovascular disease.
Conclusions.To sum up, in the setting of a chronic neurological disease in which the treatment has multiple secondary effects, an acute coronary syndrome in a young patient with cardiovascular risk factors can unmask a pre-existing subclinical CD. Scarce data existing about CD in SM, we consider mandatory a rigorous imagistic follow-up plan (cardiological and neurological).

1418

Safe use of percutaneous right ventricular assist device for prevention of acute right ventricular failure during pericardiectomy for constrictive pericarditis

R Rastko Rakocevic[1]; H Singh[2]; M Shah[3]; A Lucev[3]; B Kim[2]; R Berkowitz[2]; M Anderson[4]; K Satya[2]
[1]New Jersey Medical School, Internal Medicine, Newark, United States of America; *[2]Hackensack University Medical Center , Cardiology, Hackensack, United States of America*; *[3]New Jersey Medical School, Cardiology, Newark, United States of America*; *[4]Hackensack University Medical Center , Cardiothoracic Surgery, Hackensack, United States of America*

Constrictive pericarditis (CP) causes restriction of diastolic heart filling and heart failure. Pericardiectomy is standard of treatment for CP. However, myocardial atrophy in prolonged constriction and rapid increase in venous return after pericardial decompression leads to 'low output syndrome' and right ventricular (RV) failure. Recent studies showed that percutaneous right ventricular assist device (pRVAD) is effective solution for treatment of acute RV failure. Thus, we report a first case of successful use of pRVAD for prevention of acute RV failure peri- pericardiectomy for CP.
A 57-year-old male with paroxysmal atrial fibrillation (AF) on apixaban, and CP, was transferred to our hospital for CP surgery. He had four-year history of shortness of breath (SOB), lower extremity (LE) edema, weakness and chest discomfort with establish diagnosis of CP by cardiac catheterization (CATH) in 9/2015. Physical exam was noted for JVD, regular heart rhythm, bibasilar lung crackles, abdominal distension and bilateral LE edema. Interferon-gamma release assay and A1AT were negative. Drained pleural fluid was serous without malignant cells and negative for ADA. EKG, chest XR and transthoracic echocardiography (TTE) showed typical changes for CP. Chest CT showed pericardial calcification along anterior aspect of RV and right atrium (RA) and along the inferior aspect of LV. Bilateral CATH was characteristic for CP with coronary artery changes unchanged from the CATH in 2015. pRVAD and pulmonary artery catheter were placed preoperatively. During pericardiectomy pRVAD was on RCFV 6 mode. Pre, during and after procedure transesophageal echocardiography (TEE) was obtained. During surgery, total anterior pericardiectomy was undertaken from phrenic to phrenic with excellent removal results over anterior and diaphragmatic RV surface and entire RA. The LV was not involved. Pericardial pathology result showed fibrosis with calcification. Bilateral pleural drains and mediastinal drains were placed and surgical field was closed in the usual manner. Postsurgical TEE revealed preservation of ventricular function with no new wall motion abnormalities. Eight hours after the surgery, monitored intracardiac pressures were satisfactory, with CVP of 15 mmHg, and hence pRVAD and pulmonary artery catheter were removed. Patient was discharged on sixth postoperative day.
This case demonstrates safe and effective use of pRVAD as a preventive measure in patients with anticipating acute RV failure, such as in patients with CP requiring pericardiectomy.

1419

Takayasu arteritis associated with chronic reduced heart failure. Study of a case.

EJJ Eduardo Julian Jose Chuquiure[1]; C Silva-Ruz[1]; G Gabriela Mendez[2]; M Chuquiure-Gil[3]; K Jacobo-Garcia[1]; R Hernandez-Isidro[1]; E Morales-Hinojosa[1]; O Fiscal-Lopez[1]
[1]Instituto Nacional de Cardiologia "Ignacio chavez", Mexico City, Mexico; *[2]Universidad del estado de México, Medicina, ciudad neza, Mexico*; *[3]Instituto Tecnologico de Estudios Superiores de Monterrey, Escuela de Medicina, Monterrey, Mexico*

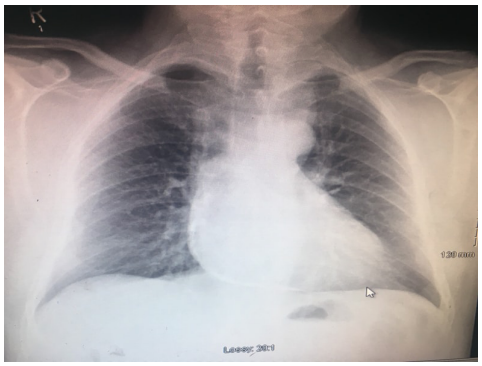
Female 29 years old.
At 7 years, the patient presented intense thoracic-abdominal pain, lasting more than 6 hours, associated with dizziness. He received symptomatic treatment.
At 15 years, she showed a two-week evolution with progressive dyspnea to small efforts, orthopnea, fever, and abdominal epigastric pain with vomit, dry cough in accesses. Irregular, characteristically nocturnal palpitations, Hypertension. ECHO LVEF: 25%. Treatment: Oral Carvedilol and Diltiazem.
At 18, she had dyspnea at rest, hydric retention. Cardiomegaly was detected.
At 28 Caesarean by pregnancy of 36 weeks.
Physical examination:
Murmur in the neck and left supraclavicular area, Blood pressure is not felt in both arms, imperceptible radial pulses, pedial pulses very reduced, both legs claudication (since four years). Abdominal murmur (left flank). Mitral and tricuspid regurgitation.
Labs and Imaging
Negative Viral and Chagas serological test. NT-pro-BNP 2240 pg/dL.
Endomyocardial biopsy: Increase in the size of myocytes and their nuclei, hyperchromatic and atypical, minimal endocardial fibrosis.
MRI: Total obliteration of the left common carotid artery, as well as ipsilateral subclavian artery. External carotid occlusion, infrarenal abdominal aorta severe stenosis. Left common iliac arterywith major stenosis.
PET/CT: Hyper-uptake at brachiocephalic trunk suggesting activity. Takayasu type V (Numano).
ECHO: Four cavities dilation, LV generalized hypokinesia, LVEF 24% TAPSE 11 mm. systolic dysfunction. Mitral and tricuspid regurgitation.
Conclusions: There are few reported cases of myocardial damage associated with acute arteritis. The present case exemplifies the association between Takayasu's Arteritis with HFrEF of long evolution as an etiological feature.

1420

A tight squeeze: constrictive pericarditis in the presence of myelodysplastic syndrome-a case report

F Fionnuala Kennedy[1]; C Kennedy[1]; A Flynn[1]
[1]HSE West, Cardiology, Galway, Ireland

Introduction: Constrictive pericarditis (CP) is a form of diastolic heart failure caused by an inelastic pericardium inhibiting ventricular filling. It must be considered in all cases of unexplained heart failure (HF). Pericardectomy is the only definitive treatment. This case highlights the importance of considering this rare cause of HF and highlights the challenge a dual diagnosis of Myelodysplastic Syndrome (MDS) presents.
A 67 y/o haulage business owner presented to the emergency department in December 2016 with exertional dyspnea, orthopnea and paroxysmal nocturnal dyspnoea for the past six weeks. He had noticed a gradual decrease in his exercise tolerance and general fatigue for the previous six months. Clinical examination revealed a raised jugular venous pressure, bilateral pitting oedema to the mid-calf and bi-basal inspiratory crackles.
His past medical history included hypertension and obesity. He was undergoing investigation for pancytopenia at the time of presentation for a subsequent diagnosis of MDS.
Historical data from old records revealed a pericardial ring on a chest X-ray from 2014. A repeat chest X-Ray done on this admission showed progression of this calcification. There was also evidence of venous pulmonary congestion.
An echocardiogram gave further supportive evidence showing a ventricular septal shift on respiration and hepatic vein flow reversal during expiration on doppler imaging. His ejection fraction was low-normal at 50-55%. Right heart catheterisation confirmed the diagnosis of CP with a Right Ventricular Diastolic Pressure of 29mmHg and Left Ventricular Diastolic Pressure of 24 mmHg. The End Diastolic Pressures in the Right and Left Ventricle were 34mmHg and 35 mmHg respectively. He was discharged on 40mg of Furosemide but re-presented twice with acute decompensated heart failure and was ultimately referred for pericardectomy. Of course other causes of HFpEF were considered, including hypertensive heart disease, hypertrophic cardiomyopathy and infiltrative disorders including hemochromatosis and amyloid. The calcification on X-Ray and echocardiogram findings, however, were most suggestive of constriction. After this diagnosis was made the biggest challenge facing us was managing his perioperative risk given his thrombocytopaenia, which increased his overall mortality significantly. CP still poses a diagnostic challenge today. This case highlights the typical clinical, radiological and echocardiographic features of this condition. In a large proportion of patients with surgically confirmed CP, the non-invasive imaging techniques, including chest x-ray, echocardiogram, computed tomography and magnetic resonance imaging, lack characteristic features; this makes CP a very difficult diagnosis to make in the early stages. Despite this, it must remain an important consideration in the differential of diastolic heart failure, a condition which has similarly poor 5 year mortality as HFrEF.



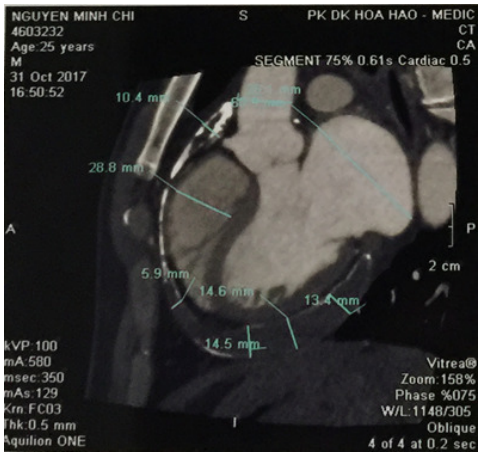
admission chest x ray

1421

A case of severe calcific chronic constrictive tuberculous pericarditis

H Thai Hao Phan[1]
[1]*Pham Ngoc Thach University of Medicine, Cardiology, Ho Chi Minh, Vietnam*

Introduction: Chronic constrictive pericarditis is a chronic inflammatory process that involves both fibrous and serous layers of the pericardium in which fibrous thickening of the pericardium occur. Many etiological factors have been identified. Among them infection, idiopathic chronic pericarditis, post cardiac surgery, mediastinal radiotherapy are important. But pericarditis caused by Mycobacterium tuberculosis is the most common cause in endemic area. We reported a case of severe calcific chronic constrictive tuberculous pericarditis.



cardiac MSCT

Case Report: A 25-year-old Vietnamese, nonsmoker, nonalcoholic, non-diabetic, normotensive salesman from a province near our city presented with dyspnea on exertion, ankle edema, puffiness of face and abdominal distension, nonproductive cough, weight loss about 14kg for two months and a half. Night sweat, slight evening fever for about a week. General examination revealed generalized pitting edema, swelling of face, elevated jugular venous pressure, Kussmaul's sign. Physical examination revealed a pericardial knock over the left sternal border, distended abdomen, liver 3 cm from right costal margin. Patient was previously healthy, referring no prior cardiac surgery, chest radiotheray or tuberculosis. His family were normal.

Results: CRP: 25.44mg/l (<5mg/l). NT-proBNP: 592pg/ml (<75y: = 125pg/ml; = 75y: = 450pg/ml). TSH: 4.76 µIU/ml (0.32-5 µIU/ml), anti ds-DNA was negative. Chest X-ray: frontal and lateral views showed calcified pericardium, cardiac shadow was within normal limits. Abdomen Ultrasonography: mild ascites and congestive hepatomegaly. Echocardiography: pericardial thickened (5mm), moderate pericardial effusion (12mm), left atrium enlargement (LA = 48mm), EF: 55%. Cardiac MSCT: Left and right atrium enlargement. Total thickened and calcified pericardium. Normal coronary arteries. After 42 days of admission, surgical procedure pericardiectomy was done. Histopathological report of removed pericardium consistent with tuberculous pericarditis. After operation patient's postoperative course was uneventful with improvement of heart function.

Discussion: This case we diagnosed of constrictive pericarditis is based on 2015 ESC Guidelines for the diagnosis and management of pericardial diseases consist of the association of signs and symptoms of right heart failure and impaired diastolic filling due to pericardial constriction by one or more imaging methods including: Chest X-ray, Echocardiography, CT. Cause of this constrictive pericarditis was tuberculous pericarditis confirmed by histopathological report.

Conclusion: Constrictive pericarditis, a disease with particularly high morbidity and mortality, remains a challenging clinical diagnosis, and one that is frequently overlooked. The commonest aetiologies are idiopathic pericarditis, prior cardiac surgery and chest radiotherapy in the developed world and Tuberculosis pericarditis in the developing world.

1422

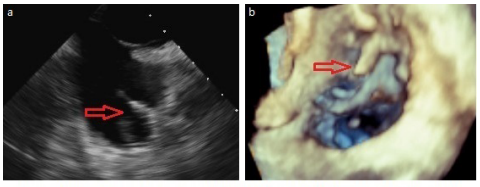
The "irritable pericardium": a rare cause of heart failure

E Piccinelli[1]; A Maloberti[1]; F Musca[1]; L D'angelo[1]; P Vallerio[1]; R Pirola[1]; N Morici[2]; A Sacco[2]; G Viola[2]; G Magenta[3]; F Oliva[2]; M Lunati[3]; A Moreo[1]; C Giannattasio[1]
[1]*Niguarda Ca' Granda Hospital, Cardiology IV Unit, Milan, Italy*; [2]*Niguarda Ca' Granda Hospital, Cardiology I Unit, Milan, Italy*; [3]*Niguarda Ca' Granda Hospital, Cardiology III Unit, Milan, Italy*

A 73 year old woman with worsening dyspnea, orthopnea and bilateral ankle swelling was referred to our hospital emergency department. Those symptoms were present for some weeks but exacerbate in the days before the admission.

She had a previous history of Hashimoto thyroiditis and leukocytosis of unknown origin. A bicameral pacemaker was implanted 40 days before the actual presentation for brady-tachy syndrome.

At admission, physical examination revealed rhythmic and paraphonic heart sounds with bilateral basal pulmonary crackles. She was hemodynamically stable with a blood pressure of 135/65 mmHg, a heart rate of 64 bpm and arterial oxygen saturation was 97% while she was breathing ambient air. A Chest x-ray showed cardiomegaly in the absence of pleural effusion or pulmonary thickening. Electrocardiogram revealed low voltages of the QRS complex while laboratory exams showed only anemia (haemoglobin 10 g/dL), leukocytosis (leukocytes 12.000/L) and renal insufficiency (creatinine 1.5 mg/dL), all stable in comparison with previous data.



Pacemaker's atrial lead in deep contact with the right atrial appendage chronically rubs and irritates the visceral pericardium (a. 2D TEE; b. 3D TEE).

Transthoracic echocardiography (TTE) revealed the presence of diffuse pericardial effusion (maximum thickness 60 mm) with signs of initial diastolic collapse of the right atrial and ventricular walls. The patient was urgently subjected to pericardiocentesis with drainage of 1200 cc of citrine liquid. The cytological examination showed an inflammatory nature of the drained fluid.

Two days later, the subsequent chest-abdominal Computed Tomography (CT) scan excluded the presence of cancer while detecting the persistence of the pericardial effusion (thickness 30 mm) with evident contrast enhancement of the pericardial layers.

A transesophageal echocardiography (TEE) confirmed the circumferential distribution of the pericardial effusion and established that the pacemaker's atrial lead was in deep contact with the right atrial appendage wall and was near to cross it. This data was also confirmed by 3D TEE.

We concluded that the etiopathogenesis of the tamponant pericardial effusion appeared to be a mechanical/irritative mechanism of the distal end of the pacemaker leads on the visceral pericardium. So a procedure of both leads removal was performed, with modest resistance in extraction of the right atrial lead.

After PM removal, ECG monitoring revealed episodes of marked sinus bradycardia and 2nd degree sinoatrial block and a bicameral pacemaker urgent reimplantation was done. At discharge, TEE showed almost complete resolution of the pericardial effusion.

This case shows an infrequent cause of a cardiac tamponade that need to be considered in clinical practice, i.e. the continuous mechanical-irritating stimulation of a badly inserted pacemaker lead even after weeks from implantation. Moreover, it is confirmed the importance of echocardiography in the first approach to the patient

in order to understand the cause of signs and symptoms of heart failure and then in establishing exactly the etiopathogenesis.

1423

Early transition to myocardial recovery in a case of cardiogenic shock and possible myocarditis

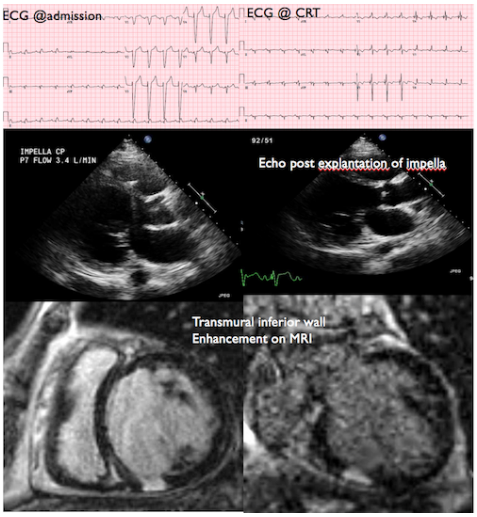
P P Poorna Pushkala Natarajan[1]; M T Slawsky[1]; G Valania[1]; E Y Lau[1]; J Hernandez-Montfort[1]

[1]Baystate Medical Center, Cardiology - Advanced heart disease, Springfield, United States of America

Myocarditis is inflammation of the heart muscle and can lead to dilated cardiomyopathy (DCM) in up to 30% of patients. Inflammatory dilated cardiomyopathy (DCMi) is characterized by inflammation of the heart muscle in addition to dilation and impaired contraction that is not explained by abnormal loading conditions or coronary artery disease. In patients with unexplained heart failure, 9-10% of cases was reported to be due to inflammatory cardiomyopathy. DCMi is a major cause of DCM and leads to sudden cardiac death in younger patients. Long-term prognosis of DCMi is unclear, suggesting the need for markers to assess the clinical course and to identify patients at increased risk for adverse events.

A 48 year old male with history of uncontrolled diabetes, obesity, obstructive sleep apnea not on treatment, post traumatic stress disorder was transferred with progressively worsening shortness of breath over 1 month, new onset left bundle branch block on ECG and an echocardiogram showing biventricular dilatation and systolic dysfunction with an ejection fraction < 20 %. There was no family history of congestive heart failure and no ingestion of toxic substances. A right heart catheterization showed hemodynamics of left more than right elevated filling pressures with PAPi (Pulmonary artery pulsatility index) >1.0 despite a right atrial pressure of 20 cm and cardiac index of 1.4 L/min/m2. An intraaortic balloon pump (IABP) was placed. However his mental status deteriorated and respiratory distress ensued requiring mechanical ventilation. Left coronary circulation was without obstructive coronary artery disease. Since IABP alone was insufficient, a decision was made to place an Impella CP. Hemodynamics post Impella implantation improved, however with evidence of left ventricle to paortic uncoupling with a cardiac output of 3.8 L/min at maximal flow. Course was complicated by hemolysis and hence transitioned to Impella 5.0. In the interim, he developed thrombocytopenia and fever. Group A beta hemolytic streptococcus was isolated from sputum. After 10 days, he was able to be weaned off the Impella. Neurohormonal initiation was delayed due to acute tubular necrosis from cardiorenal syndrome. He underwent cardiac resynchronization therapy (CRT). Cardiac MRI showed severely dilated and thinned out LV with global hypokinesis and transmural enhancement in the inferior wall after gadolinium suggestive of small infarct vs myocarditis.

Our patient had a subacute presentation, with cardiogenic shock in the setting of an inflammatory response from streptococcal pneumonia. Underlying preexisting cardiomyopathy is not ruled out. His recovery reiterated that timely use of appropriate mechanical support device, guideline directed medical therapy, and CRT can help recover cardiac function in situations where there is a reversible cause of cardiogenic shock.



echo and CMR -cardiogenic shock

Clinical Case Session 2

1466

A reversible cause of heart failure: a vascular dilemma

H Miranda[1]; C Sousa[1]; G Sobrinho[2]; J Gouveia[3]
[1]*Centro Hospitalar Barreiro Montijo, Cardiology, Barreiro, Portugal*; [2]*Centro Hospitalar Lisboa Norte, Vascular Surgery, Lisboa, Portugal*; [3]*Centro Hospitalar Lisboa Norte, Intensive Care Unit, Lisboa, Portugal*

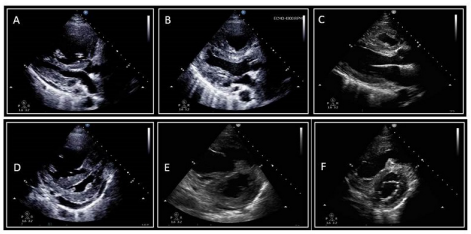
Case Report: Man, 65 years old. History of hypertension, permanent atrial fibrillation and nonmalignant intestinal polyposis. Admitted to our department due to functional incapacity for moderate efforts, abdominal volume increase and progressive lower limb edema (2 months of evolution).
The physical examination showed a non-painful hepatomegaly and edema in the lower limbs, while the auscultation revealed a cardiac ejection murmur, more audible in the precordium, and the presence of continuous murmur on the right flank.
Marked elevation of NT-proBNP (4012 pg / ml) with estimated creatinine clearance of 72 ml / min. The echocardiogram revealed a dilated left ventricle with an estimated ejection fraction of 40% and biauricular dilatation. Dilated right ventricle with decreased systolic function (TAPSE - 13mm; RV S '- 9cm / s). Moderate tricuspid regurgitation associated with tricuspid ring dilatation.
Medical therapy was optimized and a coronary angiography (which revealed occlusion of the medial anterior descending artery) and a hemodynamic study (cardiac index of 6.83 l/min/m2; pulmonary arteriolar resistance of 1.1 Uwood; PSAP 72 mmHg) were requested.
A contrast injection at the level of the abdominal aorta was performed. It showed a high-caliber, high-flow communication between this vessel and the inferior vena cava, rising the hypothesis of a high-throughput fistula.
Given this diagnostic hypothesis, an abdominal angiography was performed and the presence of a high-throughput arteriovenous fistula was confirmed.
In this context, the patient was presented to our vascular surgery team and underwent surgical intervention.
Evaluation at the 1st and 3rd month after surgery revealed progressive functional (patient currently in class I of the NYHA scale) and echocardiographic improvement (Ejection Fraction 51% and PSAP 34mmHg).
Conclusion: One possible cause of reversible heart failure is the presence of a high-throughput arteriovenous fistula. From a clinical point of view, its presentation is similar to other causes and, as such, a high degree of suspicion is needed. On the other hand, its recognition is crucial since its treatment allows the reversibility of a dramatic clinical situation.

1467

Heritable pulmonary arterial hypertension with cardiogenic shock: venous-arterial extracorporeal membrane oxygenation (VA ECMO) as a bridge to bilateral lung transplantation

H Husnat Ahmed[1]; EP Kew[1]; S Lim[1]
[1]*University Hospital Birmingham, Cardiology, Birmingham, United Kingdom*

A 23 year-old man with end stage hereditable pulmonary arterial hypertension was assessed at our centre in August 2017 for lung transplantation. He was taking triple vasodilator therapy (Ambrisentan, Tadalafil and intravenous Iloprost).
His Echo showed severe right ventricular (RV) hypertrophy and dilatation with severely impaired systolic function. LV function was borderline reduced. Cardiac MRI confirmed the echo findings and showed no RV late gadolinium enhancement. Right heart catheter study showed mean right atrial (RA) pressure of 15 mmHg, mean pulmonary arterial pressure (PAP) of 85 mmHg, transpulmonary gradient (TPG) of 62 mmHg, cardiac index of 1.4 L/min/m2 and pulmonary vascular resistance (PVR) of 23 Woods unit. He was listed for routine bilateral lung transplantation.
He later presented to the hospital with worsening right heart failure. Repeat ECHO confirmed previously documented severe RV impairment with compression of left ventricular (LV) cavity. He was admitted to intensive care unit for invasive monitoring and commenced on Milrinone and vasopressin to support his low cardiac output state and lung transplant waiting list priority was changed from routine to urgent.
Despite above measures, he developed multi-organ failure. Venous-arterial extracorporeal membrane oxygenation (VA ECMO) support was started as a bridging strategy to lung transplantation as well as to restore perfusion to his end-organs with subsequent satisfactory haemodynamic and biochemical improvement. TOE at this point showed some improvement in RV function. After 4 days he received successful bilateral lung transplantation. TOE on day-3 post-op showed good RV function, so VA ECMO was weaned off and explanted. His post-operative recovery course was uneventful.
Discussion: 1)Given the severe pulmonary hypertension and associated RV dysfunction, our options were to offer him heart-lung transplant or bilateral lung transplant but the evidence is unclear as to which option is more superior. A recent observational study suggests both options achieved good long term survival rates. Based on the improvement seen in RV function following VA ECMO, we felt that there was enough RV contractile reserve to warrant a double lung transplantation rather than heart-lung transplantation.
2)There are a few bridging strategies to lung transplantation for pulmonary hypertension: VA ECMO, temporary right ventricular assist device (RVAD), lung assist device (LAD) and atrial septostomy. We opted for VA ECMO for a combination of factors including our institutional experience and the less invasive nature of VA ECMO.
Conclusion: We report a successful case of bilateral lung transplantation in the context of severe pulmonary hypertension and significant RV dysfunction. VA ECMO is a viable bridging strategy. It also allowed us to assess RV contractile reserve prior to transplantation and strengthened our decision on bilateral lung transplantation instead of heart- lung transplantation.



Long Axis ECHO images. A: Pre-transplant ; B: Pre-transplant on ECMO; C: Post-transplant
Corresponding Short Axis images. D: Pre-transplant; E: Pre-transplant on ECMO; F: Post transplant

1468

Reversal of heart failure and pulmonary hypertension by arteriovenous fistula ligation in patient with arteriovenous fistula toxicity

B Burabha Pussadhamma[1]
[1]*Srinagarind hospital, Khon Kaen University, Khonkaen, Thailand*

A 57-year-old man with history of end-stage renal disease and needed hemodialysis via arteriovenous fistula (AVF) (1997), percutaneous coronary intervention (PCI) to left anterior descending artery (LAD) (2002), kidney transplantation (KT) (2009), and arterial hypertension, presented by intractable heart failure for 2 months (Feb 2014). Initial physical examination revealed BP of 148/84 mmHg, HR of 88 bpm in sinus rhythm, puffy eyelids, jugular vein engorgement, normal heart sound without heart murmur, bilateral pulmonary crackle, pitting edema 3+ of both legs, and residual functioning AVF at left arm (figure 1), which was left unused since his successful KT. Transthoracic echocardiography (TTE) demonstrated right ventricular dilatation (figure 2), with D-shape of left ventricle and pulmonary hypertension (PH), with tricuspid regurgitation maximal velocity (TRVmax) of 3.1 m/s, and estimated right ventricular systolic pressure (RVSP) of 55 mmHg. Right heart catheterization (RHC) was further performed and confirmed the evidence of combined pre- and post-capillary PH, with mean right atrial pressure of 24 mmHg, mean pulmonary artery pressure of 59 mmHg, left ventricular end-diastolic pressure (LVEDP) of 24 mmHg, transpulmonary gradient of 35 mmHg, cardiac output (CO) of 6.3 L/min, cardiac index of 3.8 L/min/m2, and pulmonary vascular resistance (PVR) of 5.5 Wood units. The CO dropped to 5.1 L/min after occlusion of left arm AVF. Thyroid function test was normal. The diagnosis was heart failure and PH. Although the ultrasound Doppler of AVF showed no evidence of highly abnormal flow, but due to the high cardiac output detected from RHC, the AVF toxicity was then the most likely etiology. Diuretics was administered to control congestion whereas pulmonary arterial hypertension (PAH) specific drug was not given due to worrying about high LVEDP and

lacking definite evidence of benefit of PAH-specific drug use in combined pre- and post-capillary PH. AVF ligation was successfully underwent on May 2014. After the procedure, the AVF was totally absence (figure 3), and he regained his normal functional capacity with no recurrent heart failure. Oral diuretics was uneventfully discontinued and follow-up TTE on Sep 2016 showed a complete recovery of right ventricular dilatation and PH (figure 4), with TRVmax of 2.2 m/s, and estimated RVSP of 22 mmHg.

Conclusions: Long-standing high flow from AVF could lead to heart failure and PH in susceptible patient. AVF ligation, a correction of primary pathology, is an effective method that could reverse both heart failure and PH.

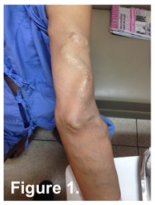
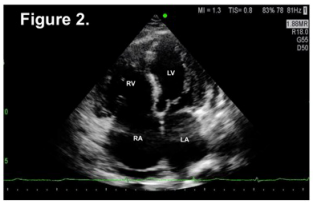


Figure 1.



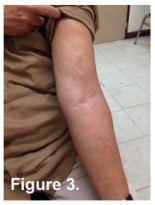
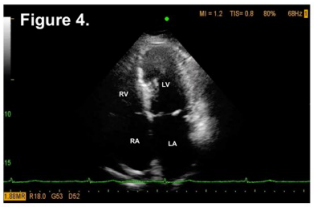


Figure 3.



1469

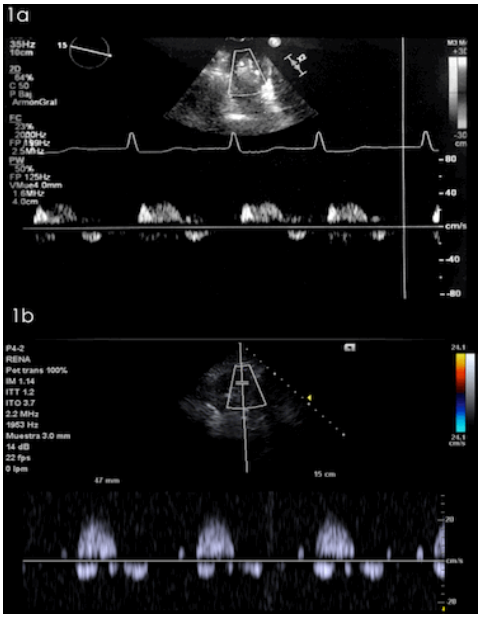
Intrarenal venous flow patterns in acute heart failure: an insight into intrarenal hemodynamics

R De La Espriella Juan[1]; J Gonzalez[1]; M Amiguet[1]; G Minana[1]; E Santas[1]; J Nunez[1]

[1]*University Hospital Clinic of Valencia, Cardiology Department , Valencia, Spain*

We report a case of an 81-year-old woman with heart failure with preserved ejection fraction and type 2 cardiorenal syndrome that presented with increased dyspnea, abdominal discomfort and 1.5 kg gain. The patient had been strictly followed-up for recurrent episodes of congestion and diuretic resistance that required intravenous diuretics repeatedly over the last two-years. The echocardiography showed a normally functioning prosthetic mechanical mitral valve, a dilated right ventricle with preserved systolic function and double tricuspid lesion: moderate-severe regurgitation and moderate stenosis. The laboratory analysis showed an NT-proBNP of 3205 pg/ml, CA-125 68 U/ml (prior determination within normal range) and serum creatinine of 1.9 mg/dL with estimated GFR 27 ml/min/1.73m2 (previously she had an estimated GFR of 39 ml/min/1.73m2). Vital signs at presentation: heart rate 69 bpm, arterial blood pressure 87/56 mmHg. The physical examination revealed abdominal distention, positive hepatojugular reflux but no peripheral edema nor signs of pulmonary congestion. Her pre-admission daily diuretic regimen was: furosemide 160 mg/d, chlorthalidone 25 mg/d, acetazolamide 125 mg/d, spironolactone 12.5 mg/d. We performed an intrarenal doppler ultrasonography using color Doppler images to determine interlobar vessels, and pulsed Doppler waveforms to record interlobar arteries and veins simultaneously. A monophasic intrarenal venous flow pattern (figure 1a) was obtained. Question: Which is the best treatment strategy to improve her clinical status? 1) intravenous diuretic intensification; 2) oral diuretic intensification; 3) intermittent inotropic therapy; 4) reduce the diuretic therapy.

Answers and Discussion: given the clinical presentation, the change in CA125 serum levels and the venous flow pattern obtained in intrarenal ultrasonography, we considered that the renal function deterioration was related to an increased in renal venous pressure. With this in mind, we administered 250 mg of intravenous furosemide diluted in 1.4% hypertonic saline solution over 3 hours. At 48 hours visit, we performed an additional intrarenal ultrasonography, and we observed a biphasic venous flow pattern (figure 1b). In parallel to those findings, there was an improvement in patient clinical status (resolution of abdominal heaviness) and renal function (GFR of 38 ml/min/1.73m2). Low intrarenal venous impedance index calculated from the renal venous waveforms has been classically linked with elevated renal interstitial pressure caused by renal obstruction. However, recent evidence suggests the potential application of this imaging modality as a surrogate of intrarenal hemodynamics in heart failure. We hypothesized that intrarenal venous flow pattern and its reversibility in response to diuretic therapy could help us to identify a potential phenotype of patients with "congestive kidney failure."



1470

An atypical case of cardiac tamponade: what should be the best approach?

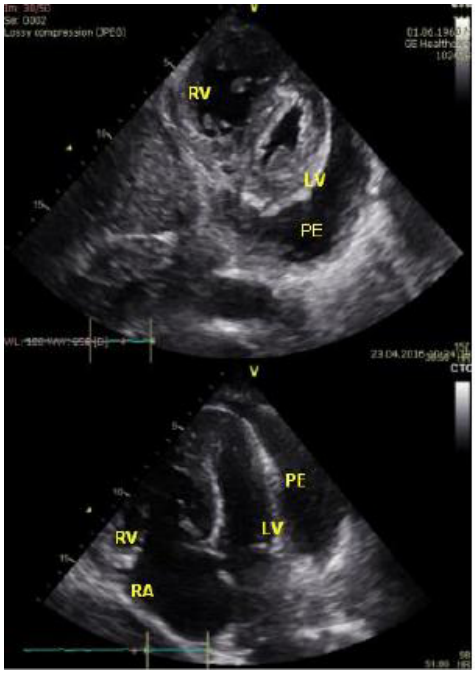
D Deniz Cadil[1]; M Stoian[1]; S Iancovici[1]; M Dorobantu[1]

[1]*Emergency Clinical Hospital Floreasca, Cardiology, Bucharest, Romania*

Systemic sclerosis (SSc) is an autoimmune disorder in which symptomatic pericarditis occurs in 7 to 20% of patients, making it the connective tissue disorder with the most cases of pericardial involvement.

A 55-year old male patient diagnosed with SSc in 2014, with pulmonary fibrosis and chronic cor pulmonale, was referred for progressive dyspnea in the last 3 months, aggravated in the last 3 days. On admission, the patient had hemodynamic compromise with a BP of 85/60 mmHg, intense dyspnea and anasarca. The ECG showed sinus tachycardia and low voltage QRS complexes. The transthoracic echocardiogram (ETT) revealed a moderate pericardial effusion (20 mm) located posterior and lateral to the left ventricle, with extremely dilated right cavities, with right ventricular dysfunction and severe pulmonary artery hypertension. The left cavities were compressed between the pericardial effusion and the right ones. There was a respiratory variation of the mitral and tricuspid inflow, with 25% relative decrease in inspiratory flow across the mitral valve and 50% relative augmentation in inspiratory flow across the tricuspid valve. The patient underwent a thoracoscopic pericardial fenestration and 200 ml of pericardial fluid were extracted. The afterwards ETT showed no pericardial effusion and an improvement in left cavities' function. Hours after the procedure the patient developed hemodynamic instability followed by cardiogenic shock that lead to cardiac arrest and death.

There are few cases of cardiac tamponade and SSc cited in literature, most of which had a poor outcome due to severe pulmonary hypertension, renal or heart failure, with infrequent exceptions. The questions that arise are firstly the aetiology - whether it is a primary pericardial involvement of SSc or, most probably, secondary to severe PAH that lead to right ventricular failure. The pathology findings support this theory, as the analysis of pericardial fragments showed a normal hystological structure and a minimal vascular congestion. Secondly, it is an atypical case of cardiac tamponade with the absence of right cavities' collapse and pulsus paradoxus and the presence of isolated left ventricle compression. In this situation there is an interventricular asynchrony that impairs the preload of the LV and leads to further decreases in cardiac output. The therapeutic challenge consists of deciding whether to drain the effusion or to stabilise the right heart function with vasoactive therapy (bosentan, sildenafil). Literature data is limited and controversial, while cardiac tamponade is a clear indication for drainage. In conclusion, pericardial tamponade is exceptional in SSc patients and the management of such clinical cases is still a challenge and also a controversy. The treatment of choice remains pericardiocentesis, while further studies are required in order to determine whether stabilisation of severe PAH and cautious drainage afterwards can be a more effective approach.



Cardiac tamponade and severe PAH

1471

Combination cisplatin and 5-fluorouracil-induced takotsubo cardiomyopathy in oropharyngeal cancer: a case report

N Nkem Okonkwo[1]; A Barron[1]
[1]*Harefield Hospital, London, United Kingdom*

Introduction: Takotsubo Cardiomyopathy (TC) is a rare yet increasingly reported syndrome described as a sudden yet temporary weakness or 'stunning' to the myocardium. There remains much intrigue in the correlation between cancer, chemotherapy and takotsubo syndrome especially in this era whereby as cardiologists we are faced with growing referrals of patients who have suffered cardiotoxic side effects from these agents.
Case presentation: We describe the case of a 52-year-old patient with T2 N2c M0 squamous cell carcinoma of the oropharynx who presented with acute heart failure, acute kidney injury and transaminitis requiring Intensive Care Unit admission within hours of receiving her first course of infusional 5-fluorouracil (5-FU) and Cisplatin. Her history included an upper GI bleed and non-alcoholic fatty liver disease, but no history of cardiac disease while being a lifelong non-smoker and was abstinent from alcohol. Additionally, there was no history of emotional or psychological factors at play that could have contributed to the patient's presentation. Within 72 hours of chemotherapeutic treatment, she developed sudden onset dyspnoea with associated chest pain. ECG displayed sinus tachycardia with lateral T-wave flattening. Subsequent CT pulmonary angiogram showed bilateral parenchymal changes and associated moderate volume bilateral pleural effusions, suggestive of fluid overload but no pulmonary embolus. An echocardiogram performed at initial presentation showed left ventricular ejection fraction of 15%. She was initially diuresed with intravenous furosemide but her worsening clinical state necessitated escalation to haemofiltration following the development of a severe AKI and symptomatic uraemia. The differential diagnoses suggested at this juncture included acute coronary vasospasm, inflammatory myocarditis or chemotherapy-induced cardiomyopathy. Consequent coronary angiogram reported unobstructed coronary arteries. A follow-up MRI scan 10 days after admission showed a return of normal LV function consistent with stress cardiomyopathy. Subsequent 5-FU treatment was discontinued and the patient went on to receive radiotherapy and cetuximab as second-line chemotherapy.
Conclusion: 5-FU is the most common chemotherapy molecule associated with TC in the literature. Cisplatin and other platinum agents have been implicated in TC both in combination with 5-FU and in isolation. A multispecialty approach is required when managing such a significant clinical phenomenon such that oncologists and cardiologists alike must remain aware of the varied cardiotoxic consequences of these frequently administered chemotherapy agents. Furthermore, clinicians may be able to stratify those patients at risk of stress cardiomyopathy, which may prompt seeking alternative agents and avoid rechallenging with the same drug

Patient management - From oral treatment to transplant

1536

Structured follow-up program of patients with heart failure: impact on quality of life and prognosis.

J Ribeiro Agostinho[1]; J Rigueira[1]; A Nunes-Ferreira[1]; R Santos[1]; I Aguiar-Ricardo[1]; I Goncalves[1]; T Guimaraes[1]; R Pires[2]; F Veiga[1]; M Mendes Pedro[1]; FJ Pinto[1]; D Brito[1]

[1]Cardiology Department, Santa Maria Hospital, CHLN, CCUL, Lisbon University, Lisbon, Portugal; *[2]Faculty of Psychology, CINEICC, University of Coimbra, Coimbra, Portugal*

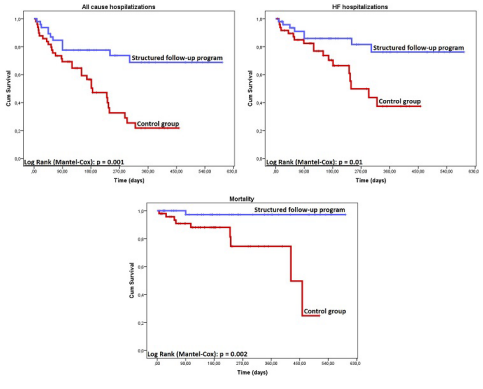
On behalf of: RICA-HFTeam

Introduction: Patients with heart failure (HF) benefit from regular clinical follow-up in order to maintain therapeutic optimization and to identify early signs of decompensation, thereby reducing readmission rates and improving prognosis. However, the magnitude of this potential benefit is seldom objectified.

Objective: To evaluate the actual impact of the implementation of a structured follow-up program in pts with HF, regarding quality of life (QoL) and hospitalization and mortality rates.

Methods: Nested-case control study, with prospective data registry of 50 consecutive pts discharged after hospitalization for acute HF (AHF). This population (study group) was followed (HF team) at 10 days, 3, 6 and 12 months after discharge, with predefined procedures (by protocol), including clinical evaluation, therapeutic optimization (according to ESC guidelines), laboratorial, electrocardiographic and echocardiographic evaluations, and QoL assessment [Kansas City Cardiomyopathy Questionnaire (KCCQ)]. The control group consisted of 100 pts hospitalized for AHF and regularly followed after discharged but prior to the implementation of the protocol. Cox Regression, Kaplan-Meier survival analysis and Wilcoxon test were the statistical methods used.

Results: The study group (mean age: 67.1 ± 11 years, 75.5% males) had a mean left ventricular ejection fraction (LVEF) of 27.6 ± 10.3% (85.7% with LVEF < 40%) at discharge. Sixteen pts (31%) were discharged in NYHA I functional class, 63.3% in class II and 6.1% in class III. Demographics and all functional cardiac variables were similar in the two. Mean follow-up time was 8.2 ± 5.3 months in the study group, and 8 ± 4.7 months in the control group (p = NS).



In the study group, there was a significant improvement in LVEF (p < 0.001), NYHA functional class (p = 0.001), and in all the parameters assessed by the KCCQ, namely in symptoms (p < 0.001) and overall QoL (p < 0.001). There was also an effective optimization of treatment during follow up, including the up-titration of recommended drugs: compared to the doses of pharmacological therapies previously used before the index-admission for AHF, a significant increase in doses of angiotensin converting enzyme inhibitor/angiotensin II receptor antagonists (p < 0.001), beta-blockers (p < 0.001) and mineralocorticoids receptor antagonists (p < 0.001), was achieved during follow up.

In comparison with the results observed in the control group, the group included in the structured follow-up program showed a significant reduction in all cause readmissions (24.5% vs 61.2%, p = 0.001), HF readmissions (16.3% vs 36.7%, p = 0.001) and total mortality (2% vs 18.4%, p = 0.001) during follow up. Conclusion: A structured follow-up program of HF patients allowed a significant reduction in readmission and mortality rates in the medium term, and was associated with a significant improvement in functional class, quality of life, and LVEF. These results support the imperative need to establish such programs.

1537

Impact of physicians' adherence to guideline-recommended therapy on heart failure re-hospitalizations: data from the Optimize Heart Failure Care Program

Y M Lopatin[1]; A Grebennikova[1]; H Sisakian[2]; H Hayrapetyan[3]; Z Pagava[4]; T Abdullaev[5]; G Dadashova[6]; S Berkinbayev[7]; A Rakisheva[7]; A Chesnikova[8]; E Tarlovskaya[9]; Z Kipiani[10]; N Koziolova[11]; V Tseluyko[12]; L Voronkov[13]

[1]Volgograd State Medical University, Volgograd Regional Cardiology Centre, Volgograd, Russian Federation; *[2]Yerevan State Medical University Hospital 1: University Cardiology Clinic, Yerevan, Armenia*; *[3]Erebouni Medical Center, Yerevan, Armenia*; *[4]Centre of Vascular and Heart Diseases, Tbilisi, Georgia Republic of*; *[5]Specialized Cardiology Center of the Republic of Uzbekistan, Tashkent, Uzbekistan*; *[6]Scientific Research Institute of Cardiology, Baku, Azerbaijan*; *[7]Scientific Research Institute of Cardiology and Internal Diseases, Almaty, Kazakhstan*; *[8]State Medical University of Rostov-on-Don, Rostov-on-Don, Russian Federation*; *[9]Nizhny Novgorod State Medical Academy, Nizhny Novgorod, Russian Federation*; *[10]"New Hospital", Tbilisi, Georgia Republic of*; *[11]Perm State Medical Academy, Perm, Russian Federation*; *[12]Kharkiv National Academy of Postgraduate Education, Kharkiv, Ukraine*; *[13]NSC Institute of Cardiology M.D. Strazhesko, Kiev, Ukraine*

Background: In spite of the evidence that good adherence to guidelines can improve clinical outcomes many studies demonstrate suboptimal implementation of guideline-based heart failure (HF) treatment into real clinical practice. The aim of our study was to evaluate the impact of physicians' adherence to guideline-recommended therapy on the rate of HF re-hospitalizations at 12-months of follow-up.

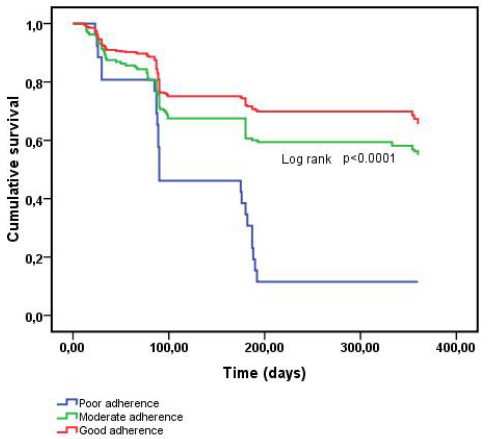
Methods: This study was part of an international multicenter Optimize Heart Failure Care Program and included 740 patients hospitalized due to worsening HF (mean age 61.9 ± 11.8 years, 70% male, 77.7% with sinus rhythm, NYHA II-IV, mean 2.7 ± 0.6, mean LVEF 35.1 ± 9.9%). To assess physicians' adherence to the medications recommended by the 2016 ESC HF guidelines, a five-class guideline adherence score for angiotensin converting enzyme inhibitors (ACEIs), beta-blockers (BBs), angiotensin receptor blockers (ARBs), mineralocorticoid receptor antagonists (MRAs), and ivabradine was used.

The score was calculated for each patient by summing the points: 0 for non-prescription of medication in the absence of contraindications and one point each for the use of ACEIs/ARBs, BBs, MRAs and ivabradine. Three types of adherence were defined: good adherence (use of all guideline-recommended medications; score = 1); moderate adherence (use of >50% recommended medications; score >0.5- <1); poor adherence (use of 50% recommended medications; score = 0.5). To analyze the adherence to the recommended doses of HF medications the score was calculated for each patient by summing the points: 0 for non-prescription of medication, 0.5 points for use of <50% of target doses and 1 point for the each prescribed medication at = 50% target dose.

Results: The score of adherence to guideline-recommended medications was good in 80%, moderate in 16%, and poor in 4% of HF patients. However, at discharge from hospital, the proportion of patients at target doses and = 50% of target doses was low (17.7% and 47% for ACEIs/ARBs, 15% and 42% for BBs, 14% and 35% for ivabradine, respectively). 70% of HF patients were at recommended doses of MRAs. The score of adherence to the recommended doses of HF medications was good in 35%, moderate in 63%, and poor in 2% of HF patients without a tendency for improvement during 12 months of follow-up. Poor adherence to guideline-recommended HF medications and to the recommended doses was associated with significantly higher HF hospitalization rates (HR 1.46, 95% CI, 1.18-1.76, p = 0.0001 and HR 1.46, 95% CI, 1.18-1.76, p = 0.0001, respectively) (Figure).

Conclusion. Regardless of the prevalence of good scores of physicians' adherence to guideline-recommended HF medications, in most cases the doses of these agents continue to be suboptimal. Poor adherence to guideline-recommended

therapy is associated with a higher rate of HF re-hospitalizations. New educational initiatives improving physicians' adherence to guidelines are required.



Event-free curves for HF hospitalization

1538

Perceptions of heart failure treatment decision-making and side effects of heart failure treatment by patients and cardiologists: a multinational survey in the real-world cardiology setting

B Balas[1]; S Bruce Wirta[2]; CC Proenca[3]; H Bailey[4]; Z Phillips[4]; S Cotton[4]; J Jackson[4]

[1]Novartis Pharma AG, Basel, Switzerland; *[2]Novartis Sweden AB, Stockholm, Sweden*; *[3]Wellmera AG, Basel, Switzerland*; *[4]Adelphi Real World, Bollington, United Kingdom*

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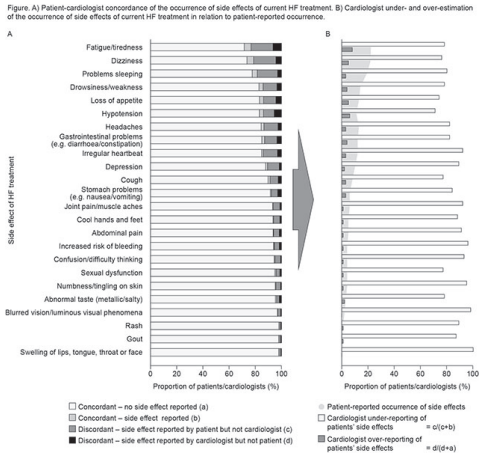
Background and Purpose: This study aimed to explore how often patients with heart failure (HF) are consulted regarding their treatment decisions and also the extent to which side effects experienced by patients as a result of their HF treatment regimen are recognized by their cardiologists.

Methods: A cross-sectional survey of cardiologists and their consulting patients with HF was conducted in 10 countries (Argentina, Brazil, China, Colombia, France, Japan, Mexico, Russia, Saudi Arabia and Turkey). Patient record forms (PRFs) were completed by cardiologists for consecutively consulting patients with HF, who were then invited to complete a patient self-completion questionnaire (PSC). Only responses from PRFs with an associated PSC were analyzed. Patients and cardiologists reported the degree of patient input into treatment decisions and the side effects experienced as a result of the patient's current HF treatment regimen; these were compared, and concordance calculated. Responses were also analyzed by taking the patient perspective and evaluating how often a patient-reported side effect was not recognized in the PRF (cardiologist under-reporting) and vice versa (cardiologist over-reporting).

Results: Almost one third (30%) of patients were not consulted on their choice of therapy. For 65% of patients, a discussion occurred with the cardiologist having the final call, while for 6% of patients a discussion occurred but the patient had the final call. A high level of concordance (74%) between matched cardiologist and patient pairs (n = 2228) was observed for the degree of patient input into treatment decisions. Concordance was also high between matched cardiologist and patient pairs (n = 2385) for the occurrence of side effects, ranging from 77% (fatigue/tiredness) to 98% (gout, rash and swelling of lips, tongue, throat or face) (Figure). Individual side effects were reported by 1-22% of patients (Figure). Cardiologists more often under- than over-reported the occurrence of side effects of treatment reported by patients (Figure).

Conclusions: Shared decision-making is the pinnacle of patient-centred care whereby the physician educates the patient about treatment options, possible outcomes and side effects, in order to reach an informed treatment decision. This process could be considered fundamental to an overall improvement of patient care. In this study, we observed that almost one third of patients were not at all involved in decisions about their HF treatment, and, when they were, the ultimate decision was not made in partnership between the patient and cardiologist. Side effects experienced by patients as a result of their HF treatment regimen were more frequently under-reported than over-reported by their cardiologists. Improved communication between patients and cardiologists is essential to optimize treatment decision-making and to increase awareness of, and concordance with, the occurrence of treatment side effects.



1539

The effect of home-based cardiac rehabilitation following coronary artery bypass graft surgery in a low income country: A controlled trial

J Jamal Uddin[1]

[1]Ibrahim Cardiac Hospital & Research Institute, Dhaka, Bangladesh

Background: CVD is the leading cause of mortality and morbidity in Lower and low to middle income countries, including Bangladesh. To date no controlled trials of cardiac rehabilitation (CR) have been conducted in low or low to middle income countries (LLMICs).

Methods: A quasi-randomised controlled trial comparing home-based CR plus usual care (CR group) to usual care alone (UC group) for patients following coronary artery bypass graft (CABG) surgery. CR consisted of an initial CR class, an educational booklet with details of a home-based exercise programme, and monthly telephone calls from a CR team member over a 12-month period. The outcomes of maximal oxygen uptake (VO2max), coronary risk factors, health-related quality of life, and mental health status were collected at baseline between at 3 and 6 months follow-up. Differences in outcomes between groups were compared in patients with complete outcome data.

Results: A total of 142 participants participated in the trial; 71 patients in each group. At 12-months follow-up, 61 (86%) patients in the CR group and 40 (56%) in the UC group provided complete outcome data.VO2maxwas higher in CR compared to UC group (mean difference: 7 ml/kg/min, 95% CI: 2 to 11, P = 0.005).In addition, greater improvements in health-related quality of life, and coronary heart disease (CHD) risk factors were seen for CR group compared to UC group.

Conclusions: In the context of a low-income country, the addition of a home-based CR programme supported by telephone calls following CABG surgery has been shown to provide important patient benefits compared to usual care alone.

1539 Between group difference in baseline and

Risk factors	CR group, (n = 61)	UC group, (n = 40)								
Baseline Mean (SD)	6-months follow-up Mean (SD)	Within group Mean change (95% CI)	p-value	Baseline Mean (SD)	6-months follow-up Mean (SD)	With group mean change (95% CI)	p-value	Between group; mean difference& (95% CI)	P-Value	
BMI (kg/m^2)	25.54 (2.53)	24.63 (2.26)	.91 (0.07 to 1.75)	0.03	24.77 (2.86)	24.47(2.6 to 8.00)	0.29 (-0.94 to 1.53)	0.63	-0.61 (-1.07 to -0.16)	0.008
SBP (mm Hg)	122.95 (13.02)	114.42 (6.71)	8.52 (4.93 to 12.11)	<0.001	126.75 (15.56)	116.87 (10.23)	9.87 (4.08 to 15.66)	0.001	1.35 (-4.21 to 6.90)	o.63
DBP(mm Hg)	77.45 (8.38)	74.01 (5.68)	3.44 (0.86 to 6.02)	0.009	79.75 (7.64)	76.62 (6.34)	3.12 (-0.009 to 6.25)	0.05	-0.31 (-0.39 to 3.33)	0.86
Total cholesterol (mg/dl)	179.98 (53.17)	112.29 (36.40)	67.68 (50.95 to 84.42)	<0.001	175.27 (55.96)	160.57 (53.35)	14.70 (-9.63 to 39.03)	0.23	-52.98 (-80.41 to 25.55)	<.001
LDL-cholesterol (mg/dl)	131.44 (54.46)	87.14 (23.17)	44.30 (28.83 to 59.76)	<0.001	123.14 (56.38)	119.05 (40.31)	4.09 (-17.43 to 25.61)	0.70	-40.21 (-60.26 to 20.15)	<0.001
Triglycerides (mg/dl)	180.42 (114.36)	108.85 (48.83)	71.57 (39.02 to 104.12)	<0.001	179.92 (75.94)	161.37 (64.72)	18.55 (-12.53 to 49.63)	0.23	-53.02 (-86.24 to -19.80)	0.002
HDL-cholesterol (mg/dl)	30.80 (6.50)	35.34 (4.79)	-4.54 (-6.56 to -2.51)	<0.001	29.40 (6.53)	30.80 (4.94)	-1.00 (-3.77 to 1.77)	0.47	3.54 (0.81 to 6.26)	0.01
HbA1c(mg/ml)	7.46 (2.07)	6.28 (0.92)	1.18 (0.58 to 1.77)	<0.001	7.11 (1.5)	6.42 (1.03)	0.68 (0.11 to 1.26)	0.019	-0.49 (-1.14 to 0.16)	0.14

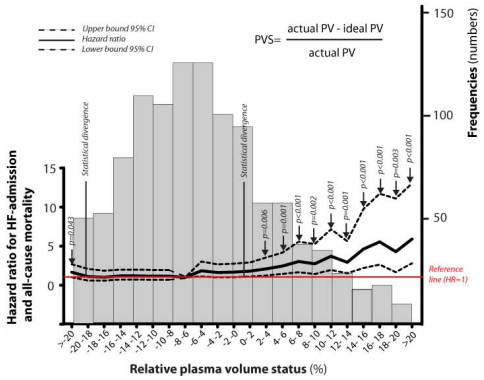
Between group difference in baseline and 6-month follow-up clinical risk factors

1540

The optimal plasma volume status in heart failure in relation to clinical outcome

P Pieter Martens[1]; P Nijst[1]; M Dupont[1]; W Mullens[1]
[1]*Hospital Oost-Limburg (ZOL), Cardiology, Genk, Belgium*

Background: Progressive plasma volume (PV) expansion is a hallmark of chronic heart failure (HF), ultimately contributing to decompensated heart failure. Monitoring PV might offer prognostic information and might be a target for tailored therapy.
Methods: The correlation between technetium-(99Tc)-labeled red blood cell measured PV and calculated PV was first determined in a validation cohort. The relationship between PV-status (PVS; a marker how much actual PV deviated from the ideal PV; for formula see figure) and outcome was analyzed using cox-proportional modeling in a prospective CHF-population (the outcome cohort).
Results: Thirty-one HF-patients were included in the validation cohort. Calculated PV correlated well with technetium-(99Tc)-measured PV (r = 0.714; p = 0.001). A total of 1173-patients (HFrEF n = 872, HFmrEF n = 229, HFpEF n = 72) were prospectively included in the outcome cohort. The mean PVS in the outcome cohort was -6.7 ± 10%, indicating slight PV-contraction. Mean PVS was similar in HFrEF, HFmrEF and HFpEF (post-hoc ANOVA all p>0.05). A higher PVS was independently associated with an increased risk for heart failure hospitalization and all-cause mortality (HR = 1.017; CI = 1.007-1.028 per 1 % increase in PVS). ROC-curve analysis indicated that an PVS of -6.5% optimally predicted absence of adverse outcome (defined as optimal PVS). Hazard ratio analysis indicated that CHF-patients were less equipped in tolerating PV-expansion in comparison to PV-contraction (see figure). The use of ACE-I/ARBs and MRAs were independently associated with a higher odds for having an optimal PVS in HFrEF and HFmrEF (all p <0.05), but not in HFpEF.
Conclusions: Calculated PV correlates well with measured PV in HF-patients. An increase in PV is independently associated with a higher risk for adverse outcome. The optimal PV in HF is lower than what would be expected based on an ideal prediction formula. Higher dosages of Renin-Angiotensin-Aldosterone blockers are associated with a higher odds for having an optimal PV-status in HFrEF, HFmrEF but not HFpEF.



1541

Empagliflozin improves renal outcomes in patients with or without heart failure at baseline - insights from the EMPA-REG OUTCOME trial

J Javed Butler[1]; F Zannad[2]; D Fitchett[3]; B Zinman[4]; A Koitka-Weber[5]; M Von Eynatten[6]; U Hehnke[6]; J George[6]; M Brueckmann[6]; AK Cheung[7]; C Wanner[8]
[1]*Stony Brook University Medical Center, Medicine, Stony Brook, United States of America*; [2]*Institut Lorrain du Coeur et des Vaisseaux, Nancy, France*; [3]*St Michael's Hospital, University of Toronto, Toronto, Canada*; [4]*Lunenfeld-Tanenbaum Research Institute, Mount Sinai Hospital, University of Toronto, Toronto, Canada*; [5]*Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach, Germany*; [6]*Boehringer Ingelheim Pharma GmbH & Co. KG, Ingelheim, Germany*; [7]*University of Utah, Salt Lake City, United States of America*; [8]*Dept of Medicine, Wuerzburg University Clinic, Wuerzburg, Germany*

Funding Acknowledgements: Boehringer Ingelheim & Eli Lilly and Company Diabetes Alliance

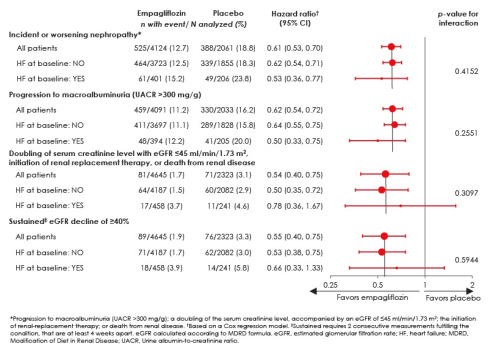
Background: Chronic kidney disease (CKD) is common and portends worse prognosis in patients with heart failure (HF), especially in the presence of type 2 diabetes (T2D). Since pathophysiologically, CKD and HF are linked, progression of CKD and its association with outcomes may not be similar among patients with or without HF. In the EMPA-REG OUTCOME trial (NCT01131676), the SGLT2 inhibitor,

empagliflozin (EMPA) on a background of standard of care significantly reduced the risk of cardiovascular (CV) death by 38% vs placebo (PBO) in patients with T2D and established CV disease (CVD). Empagliflozin also reduced the risk of incident or worsening nephropathy by 39%, and slowed progression of CKD. Here, we report post-hoc kidney outcomes in patients with or without HF at baseline from the EMPA-REG OUTCOME trial.

Methods: Patients were randomized (1:1:1) to EMPA 10 mg, 25 mg or PBO. The composite kidney outcome of incident or worsening nephropathy, defined as progression to macroalbuminuria, doubling of serum creatinine, initiation of renal replacement therapy, or death from renal disease, was analyzed in patients with or without HF at baseline. The incidence of first sustained decline in eGFR from baseline of = 40% was also evaluated. Cox proportional hazards models were used to investigate the consistency of treatment effect across subgroups.

Results: Of 7020 treated patients, 706 (10.1%) had HF at baseline. Overall, the incidence of kidney outcome events was numerically higher in patients with HF than without HF. In the HF group, EMPA reduced the risk of incident or worsening nephropathy by 47% (HR 0.53 [95% CI: 0.36-0.77]) (Figure), consistent with the effects in the overall study population (treatment interaction p-value: 0.42). EMPA reduced progression to macroalbuminuria by 50% (HR 0.50 [0.33-0.75]). The composite of hard renal endpoints (doubling of serum creatinine, initiation of renal replacement therapy, or death from renal disease) was reduced in the overall trial population, and the effect was consistent in the HF subgroup (HR 0.78 [0.36-1.67]) (Figure). The time to first sustained eGFR decline from baseline of = 40% was reduced overall with consistency of effect seen in the HF population (HR 0.66 [0.33-1.33]). All effects in patients with HF were consistent with those in the overall study population (p-values for interaction >0.05).

Conclusions: In the EMPA-REG OUTCOME trial, patients with T2D and concomitant HF at baseline were at high risk of progressive CKD. In this vulnerable population, EMPA reduced the risk of clinically relevant kidney events. The renoprotective effects were observed on a background of standard of care and were consistent with those reported for the overall study population. The potential of empagliflozin to slow CKD progression in patients with HF (with or without diabetes) is being further investigated in ongoing trials in patients with reduced (EMPEROR-Reduced) or preserved ejection fraction (EMPEROR-Preserved).



*Progression to macroalbuminuria (UACR >300 mg/g); a doubling of the serum creatinine level, accompanied by an eGFR of ≤45 ml/min/1.73 m²; the initiation of renal-replacement therapy; or death from renal disease. †Based on a Cox regression model. §Sustained requires 2 consecutive measurements fulfilling the condition, that are at least 4 weeks apart. eGFR calculated according to MDRD formula. eGFR, estimated glomerular filtration rate; HF, heart failure; MDRD, Modification of Diet in Renal Disease; UACR, Urine albumin-to-creatinine ratio.

Renal outcomes by baseline HF

1542

The ketone body 3-hydroxybutyrate increases cardiac output and left ventricular contractile function in heart failure patients with reduced ejection fraction

R Roni Nielsen[1]; N Moller[2]; HE Botker[1]; H Eiskjaer[1]; L Gormsen[3]; H Wiggers[1]
[1]Aarhus University Hospital, Skejby, Department of Cardiology, Aarhus, Denmark; *[2]Aarhus University Hospital, Department of Endocrinology and Metabolism, Aarhus, Denmark*; *[3]Aarhus University Hospital, Department of Nuclear Medicine & PET center, Aarhus, Denmark*

Background: The ketone body 3-hydroxybutyrate (3-OHB) fuels ATP-generation in the heart during prolonged periods of fasting and metabolic stress. Patients with severe heart failure and reduced ejection fraction (HFrEF) have inherently increased utilization of 3-OHB, and it has been hypothesized, that 3-OHB may act as a "super fuel" with beneficial effects on cardiac function in HFrEF patients.

Purpose: To investigate the cardiac and hemodynamic effects of short-term 3-OHB infusion compared to placebo in patients with stable HFrEF. The primary outcome was cardiac output (CO), and secondary outcomes were stroke volume (SV), mixed venous saturation (SVO2), central venous pressure (CVP), left ventricular filling pressure (PCWP), LVEF and strain (GLS).

Methods: We studied 24 stable chronic HFrEF patients (LVEF 36 ± 4%, age 61 ± 11 years) using Swan-Ganz catheterization and echocardiography. Study 1: In a randomized, single blinded cross-over design, 16 patients received 3-OHB (0.18 g/kg/h) or saline (placebo) at an equivalent volume for 3 hours. Study 2: Eight patients were examined in a dose-response study at 3 different rates of 3-OHB infusion for 2 hours consisting of a) saline followed by b) 3-OHB 0.045g/kg/h and c) 3-OHB 0.09g/kg/min.

Results: Study 1: Compared to placebo, 3-OHB infusion increased circulating 3-OHB levels from 0.4 [0.1;0.6]mM to 3.3 [3.1;3.7]mM. (p < 0.001). This was associated with an increase in CO of 42% (p < 0.001, table 1 and figure 1A) mediated by an increase in SV (p < 0.001) and heart rate (p < 0.001). During 3-OHB infusion, SVO2 increased (p < 0.001) whereas CVP (p = 0.04) and PCWP (p = 0.04) decreased while mean arterial (p = 0.47) and pulmonary pressure (p = 0.83) remained unaffected. LVEF (p = 0.001) and GLS (p < 0.001) improved as compared with placebo. Study 2: 3-OHB increased gradually from a: < 0.1mM to b: 0.7 ± 0.1mM and c: 1.6 ± 0.3mM (p < 0.001) with an associated increase in CO (a: 5.0 ± 0.9 vs. b: 5.3 ± 1.0 vs. c: 6.2 ± 1.3 L/min; p < 0.001), which, however, was lower than in the high-dose study 1 (p = 0.007) (figure 1B).

Conclusion: The findings demonstrate dose-dependent beneficial cardiac and hemodynamic effects of 3-OHB in HFrEF patients. Thus, 3-OHB may be used for short-term treatment of heart failure.

Swan-ganz and echo parameters

	Saline (n = 16)	3-OHB (n = 16)	P-value
CO (L/min)	4.8±0.6	6.8±1.0	<0.001
SV (ml)	75±16	95±18	<0.001
SVO2 (%)	72±3	79±4	<0.001
LVEF (%)	35±7	43±9	0.001

Data from the cross-over study during Saline (placebo) and 3-OHB infusion.

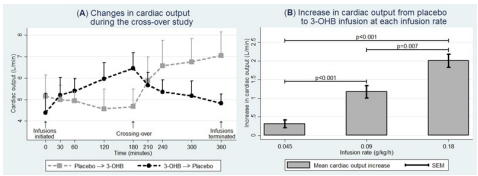


Figure 1: Cardiac output

1543

Are target doses relevant for women with heart failure? - implications for sacubitril-valsartan

HM Helena Norberg[1]; V Pranic[2]; E Bergdahl[2]; K Lindmark[2]
[1]Umea University, Public Health and Clinical Medicine, Pharmacology and Clinical Neuroscience, Umea, Sweden; *[2]Umea University, Public Health and Clinical Medicine, Umea, Sweden*

Funding Acknowledgements: The Heart Foundation of Northern Sweden

Background: In the PARADIGM-HF trial sacubitril-valsartan reduced both heart failure hospitalizations and cardiovascular death by 20% compared to enalapril. The proportion of women in the study was only 21%. Previous work has shown that in a community based heart failure population the proportion of women eligible for sacubitril-valsartan is only 16%. This is surprising since the total heart failure population is evenly distributed.

Purpose: To investigate why so few women are eligible for treatment with sacubitril-valsartan.

Methods: We applied the PARADIGM-HF main inclusion and exclusion criteria to a community based heart failure population in northern Sweden and statistically compared the women and men cohort.

Results: Of the whole heart failure population of 1924 patients, 43% were women. However, in patients with ejection fraction (EF) = 35%, only 28% were women and after applying the PARADIGM-HF main inclusion and exclusion criteria, only 15 women would have been eligible for inclusion in the trial, corresponding to 16% of the eligible patients. The most common reason for not meeting the criteria was failure to reach target dose of ACE inhibitor or ARB. In patients with heart failure and reduced ejection fraction (HFrEF) women were older (81.1 ± 10.6 vs. 74.8 ± 11.5, p < 0.001) had lower body weight (69.4 ± 17.2 vs. 85.3 ± 17.5, p < 0.001), lower estimated glomerular filtration rate (48.5 ± 26.2 vs. 70.1 ± 34.5, p < 0.001), and higher systolic blood pressure (127.4 ± 19.0 vs. 122.5 ± 18.5, p = 0.018). Besides fewer women reached target dose of ACE inhibitor or ARB (26% vs. 43%, p = 0.001), heart failure therapy did not differ between the genders except that women were more often prescribed loop-diuretics and less likely to have an implantable cardioverter defibrillator or cardiac resynchronization therapy defibrillator.

Conclusions: Fewer women suffer from HFrEF and tolerate target doses of ACE inhibitor or ARB, and are consequently less eligible for sacubitril-valsartan compared to men. Women probably tolerate target doses to a lesser degree owing to being older, having lower body weight (less volume of distribution), and lower renal function. Though, we cannot exclude that women are treated differently because of gender bias. This study shows that target doses as entry criteria in clinical trials favors men, which is important to consider in future study design to gain better knowledge of how to offer women with heart failure the best available care. Since current guideline recommended target doses are mainly based on men, we suggest more individualized doses to women with heart failure.

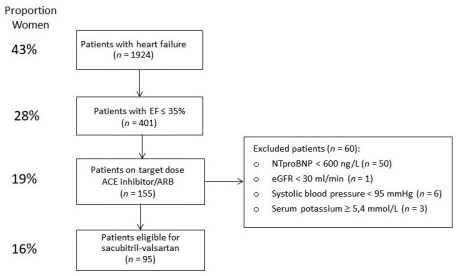


Figure 1 Selection of patients eligible for sacubitril-valsartan in a community based hospital when applying main inclusion and exclusion criteria from the PARADIGM-HF trial. The proportion of women in each selection step is shown on the left.
ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; eGFR, estimated glomerular filtration rate; EF, ejection fraction; NT-proBNP, N-terminal pro-B-type natriuretic peptide; PARADIGM-HF, Prospective Comparison of Angiotensin Receptor-Neprilysin Inhibitor (ARNI) with ACE inhibitor to Determine Impact on Global Mortality and Morbidity in Heart Failure.

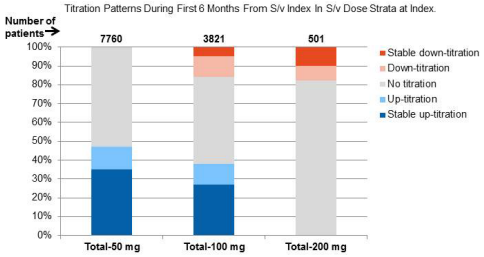
1544

Real-world titration and treatment patterns of sacubitril/valsartan in germany, a retrospective cohort study using a longitudinal pharmacy database

R Wachter[1]; S Klebs[2]; B Balas[3]; CC Proenca[4]; M Dworak[2]; R Schlienger[3]; J Engelhard[5]; T Maier[3]; S Bruce Wirta[6]; K Kostev[5]
[1]Universitätsklinikum Leipzig, Leipzig, Germany; *[2]Novartis Pharma GmbH, Nuremberg, Germany*; *[3]Novartis Pharma AG, Basel, Switzerland*; *[4]Wellmera AG, Basel, Switzerland*; *[5]IQVIA, Frankfurt, Germany*; *[6]Novartis Sweden AB, Stockholm, Sweden*

Funding Acknowledgements: Novartis Pharma AG

Background: The angiotensin receptor neprilysin inhibitor sacubitril/valsartan (s/v) was launched in Germany in January 2016 for the treatment of symptomatic heart failure (HF) with reduced ejection fraction.
Purpose: To characterize real-world titration and treatment patterns of s/v patients in Germany.
Methods: Patients with at least one s/v prescription (Rx) between January 2016 and June 2017 were identified in the German longitudinal pharmacy database (IMS LRx), covering ~60% of all dispensed Rx from statutory insured patients. Prescriber specialty and first recorded s/v dose were analysed (date of first Rx = index date). Titration patterns were defined as "stably up-titrated" (with no subsequent down-titration), "stably down-titrated" (with no subsequent up-titration), and "up-titrated" and "down-titrated" (with a mix of up- and down-titration).
Results: A total of 26,191 patients (= 18 years) fulfilled the inclusion criteria. General practitioners (GPs) accounted for the majority (~80%) of the 127,803 s/v Rx, while cardiologists accounted for ~15% of Rx. Patients with a first s/v Rx by GPs were on average older (mean ± sd 73 ± 12 vs 69 ± 11 years) and more often female (27% vs. 20%) versus those with first s/v Rx from cardiologists. Overall, there was high usage of HF drugs prior to s/v index (angiotensin-converting enzyme inhibitor/angiotensin receptor blocker 92%, beta-blocker 89%, mineralocorticoid receptor antagonist 63%).
Of the 12,082 patients with 12 months pre-index activity (defined by any Rx every 6 months) and a minimum of 6 months follow-up, 64% had a first observed Rx of 50 mg bid, 32% had 100 mg bid and 4% had 200 mg bid. During the first 6 months, 26% of patients with a first cardiologist Rx received the target dose of 200 mg bid, compared to 19% of patients with another specialty at index ($p < 0.001$).
In patients starting on 50 mg bid, 47% were up-titrated, of which 80% maintained a stable dose of either 100 or 200 mg bid. In patients on 100 mg bid at index, 38% were up-titrated, of which 77% maintained the target dose, whereas 5% were stably down-titrated. In patients with target dose at index, 10% were down-titrated to a stable lower dose, and 8% were down-titrated at some point, but then back-titrated to the target dose. The mean (sd) time to first titration was 54 days (44) while the mean time to reach the target dose varied from 79 days (44) to 57 days (47) for patients on 50mg and 100 mg bid at index, respectively ($p < 0.05$). Results were similar across specialty at index.
Conclusion: There were no attempts to up-titrate s/v in the majority of patients, while for patients up-titrated, the overall proportion of stable up-titration was 80%. Overall, only 20% of patients received the target dose of 200 mg bid. Titration took longer than what is recommended in the EU summary of product characteristics. The barriers for up-titration must be further explored and educational efforts to promote up-titration have to be intensified.



Titration Patterns

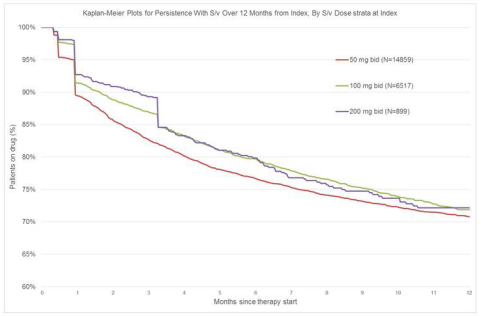
1545

Persistence and compliance amongst sacubitril/valsartan patients in germany, a retrospective cohort study from a longitudinal pharmacy database

S Bruce Wirta[1]; R Wachter[2]; B Balas[3]; S Klebs[4]; AF Fonseca[5]; CC Proenca[5]; M Dworak[4]; R Schlienger[3]; J Engelhard[6]; T Maier[3]; K Kostev[6]
[1]Novartis Sweden AB, Stockholm, Sweden; *[2]Universitätsklinikum Leipzig, Leipzig, Germany*; *[3]Novartis Pharma AG, Basel, Switzerland*; *[4]Novartis Pharma GmbH, Nuremberg, Germany*; *[5]Wellmera AG, Basel, Switzerland*; *[6]IQVIA, Frankfurt, Germany*

Funding Acknowledgements: Novartis Pharma AG

Background: The angiotensin receptor neprilysin inhibitor sacubitril/valsartan (s/v) was launched in Germany in January 2016 for the treatment of symptomatic heart failure (HF) with reduced ejection fraction.
Purpose: To characterize compliance and persistence in s/v patients in real-world clinical practice.
Methods: Patients with at least one s/v prescription (Rx) between January 2016 and June 2017 and 12 months pre-index activity (defined by any Rx every 6 months) were identified in the German longitudinal pharmacy database (IMS LRx), covering approximately 60% of all dispensed Rx from public health insured patients. The date of the first Rx was defined as index. Days' supply was defined as dispensed pack size/2, and discontinuation was defined as no new s/v Rx within 90 days after last days' supply. Compliance was calculated as the proportion of days covered (PDC). Persistence was estimated with Kaplan-Meier (KM) plots, implementing definitions as above, and additionally censoring at end of study period or after a 90 days gap of no activity in the database (any Rx). A multi-variate Cox-regression model was used to assess the association between patient characteristics and persistence.



Kaplan-Meier Plots

Results: A total of 22,275 adult patients (= 18 years) fulfilled the inclusion criteria. S/v persistence at 12 months from index was 71%. Among non-persistent patients, the majority discontinued s/v within the first 90 days. Furthermore, persistence at

12 months was similar across different s/v doses at index, while time to discontinuation was shorter for 50 mg bid at index compared to 100 and 200 mg bid at index. Multivariate analysis revealed that younger age, male sex, a higher index dose of s/v, baseline use of HF therapy, oral diuretics, novel oral anticoagulants and lipid-lowering drugs showed significant associations with higher persistence. Compliance was assessed in a subset of patients with at least 12 months follow-up data, defined as a minimum of one s/v Rx each during 6 months post-index and 7-12 months post-index (N = 8,226). High s/v compliance (PDC >80%) was observed. Compliance increased with the maximum dose reached by 6 months (PDC was 77% for 50 mg bid, 82% for 100 mg bid, and 85% for 200 mg bid). The same trend was observed for strata of s/v dose at index (PDC was 80% for 50 mg bid, 83% for 100 mg bid, and 85% for 200 mg bid).
Conclusion: Both persistence and compliance with s/v were high during the first year after index. The use of higher s/v dose was associated with increased compliance.

1546

Impact of patisiran on norfolk QOL-DN in patients with hereditary transthyretin-mediated amyloidosis: results from the cardiac subpopulation in the phase 3 apollo study

G Merlini[1]; S Solomon[2]; D Adams[3]; T Coelho[4]; T Damy[5]; M Mauer[6]; AM Partisano[7]; J Chen[7]; V Karsten[7]; J Vest[7]; OLE Suhr[8]; A Kristen[9]
[1]IRCCS Policolinico San Matteo, Pavia, Italy; *[2]Brigham and Women' s, Boston, United States of America*; *[3]National Reference Center for FAP (NNERF)/ APHP/ INSERM U 1195/ CHU Bicêtre, Le Kremlin-Bicêtre, France*; *[4]Hosptial de Santo Antonio, Porto, Portugal*; *[5]Universite Paris-Est Creteil Val De Marne , Paris, France*; *[6]HCM Center at New York-Presbyterian Hospital/Columbia University Medical Center, New York, United States of America*; *[7]Alnylam Pharmaceuticals , Cambridge, United States of America*; *[8]Umea University Hospital, Umea, Sweden*; *[9]Heidelberg University Hospital, Heidleberg, Germany*

Funding Acknowledgements: Alnylam Pharamceuticals

Background/Introduction: Hereditary transthyretin-mediated (hATTR) amyloidosis is a rare, multi-systemic, progressive, fatal disease. Heterogeneous clinical presentation of hATTR amyloidosis includes sensory, motor and autonomic neuropathy, gastrointestinal symptoms and cardiac involvement resulting in substantial disease burden for patients impacting their quality of life (QOL). Patisiran, an investigational RNAi therapeutic, was evaluated in hATTR patients with polyneuropathy in the APOLLO study and resulted in a statistically significant improvement in the neuropathy (measured by modified neuropathy impairment, mNIS+7) and QOL (measured by Norfolk QOL-DN) scores compared to placebo and was generally well tolerated. To investigate cardiac involvement, APOLLO included a pre-defined cardiac subpopulation.
Purpose: Evaluate the impact of patisiran compared to placebo on Norfolk QOL-DN scores in the pre-defined cardiac subpopulation enrolled in the APOLLO trial.
Methods: APOLLO was a Phase 3 multi-center, international, randomized (2:1), double-blind, study of patisiran 0.3mg/kg or placebo IV q3W in patients with hATTR amyloidosis (NCT01960348). Pre-defined cardiac subpopulation included patients with baseline left ventricular (LV) wall thickness = 13mm and no medical history of aortic valve disease or hypertension. Norfolk QOL-DN, a secondary endpoint of the trial, assessed 5 domains: small fiber neuropathy, physical functioning/large fiber; autonomic neuropathy; activities of daily living; and symptoms. Scores for this QOL instrument range from -4 to 136 with a lower score indicating QOL improvement.
Results: APOLLO enrolled 225 patients, the cardiac subpopulation comprised 56% of the total population and had a mean age 61 years (54-67); 78% males; 27% V30M. Mean (95% CI) baseline Norfolk QOL-DN values for patisiran (n = 90) and placebo (n = 35) in the cardiac subpopulation were 61 (17,102) and 64 (5,119), respectively. In the cardiac subpopulation, patisiran treatment led to significant improvement relative to placebo in Norfolk QOL-DN at 18 months, with a LS mean (95% CI) decrease (improvement) compared to baseline of -3 (-7, 2) points in the patisiran group compared to an LS mean (95% CI) increase (worsening) compared to baseline of 20 (13, 28) points in placebo patients with an overall treatment difference (patisiran –placebo) LS mean (95%CI) -23 (-32, 14). Additionally, patisiran resulted in improvement across all domains relative to placebo. Detailed data will be presented.
Conclusions: These results show that treatment with patisiran improved QOL compared to placebo in hATTR amyloidosis patients with evidence of cardiac involvement. These results are consistent with the outcomes in the overall population, thereby demonstrating that patisiran provides clinical benefit to hATTR amyloidosis patients with both polyneuropathy and cardiomyopathy.

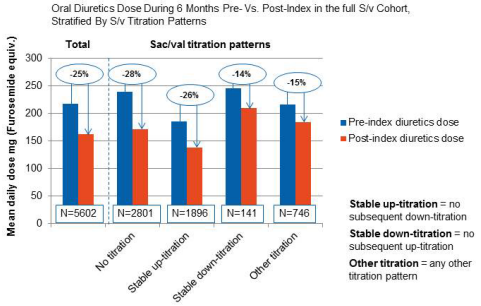
1547

Concomitant use of heart failure medication amongst patients with sacubitril/valsartan therapy in germany, a retrospective cohort study using a longitudinal pharmacy database

R Wachter[1]; AF Fonseca[2]; S Klebs[3]; B Balas[4]; CC Proenca[2]; M Dworak[3]; R Schlienger[4]; J Engelhard[5]; T Maier[4]; S Bruce Wirta[6]; K Kostev[5]
[1]Universitätsklinikum Leipzig, Leipzig, Germany; *[2]Wellmera AG, Basel, Switzerland*; *[3]Novartis Pharma GmbH, Nuremberg, Germany*; *[4]Novartis Pharma AG, Basel, Switzerland*; *[5]IQVIA, Frankfurt, Germany*; *[6]Novartis Sweden AB, Stockholm, Sweden*

Funding Acknowledgements: Novartis Pharma AG

Background: The angiotensin receptor neprilysin inhibitor sacubitril/valsartan (s/v) was launched in Germany in January 2016 for the treatment of symptomatic heart failure with reduced ejection fraction.
Purpose: To characterize real-world concomitant use of beta-blockers (BB) and mineralocorticoid receptor antagonists (MRA) in s/v patients, and to describe the use of oral diuretics with different s/v titration patterns.
Methods: Patients with a first s/v prescription (Rx) between Jan 2016 and Dec 2016, and a minimum of 12months of pre-index data (first s/v Rx = index date), and at least one additional s/v Rx following index, were identified in the longitudinal pharmacy database (IMS LRx), covering approximately 60% of all dispensed Rx from public health insured patients. Prescriber specialty, s/v dose at index, and patient-level s/v titration patterns were analysed. The dose of the four most frequently prescribed oral diuretics (furosemide, torasemide, hydrochlorothiazide, and xipamide) was calculated and normalized per substance to the defined daily dose (DDD, WHO definition). The DDD per patient was calculated as dispensed DDD divided by the time until the next dispensation. Pre- and post-index doses were compared in patients with recorded pre-index diuretics. For calculations purposes, no post-index diuretic dispensation was defined as a dose of zero. For interpretation, DDD was transformed to the furosemide equivalent dose.
Results: A total of 10,556 adult patients (= 18 years old) fulfilled the inclusion criteria. Post-index use of BB was similar between general practitioner (GP) and cardiologist patients (84% vs 86%); while MRA use was lower in GP versus cardiologist patients (54% vs 63%).
Oral diuretics were dispensed in 77% of all s/v patients during the 6 months pre-index period compared to 73% in the 6months post-index ($p < 0.001$); 64% of all s/v patients had diuretics dispensed in both pre- and post-index, while 12% discontinued and 9% started diuretics after index. Post-index daily diuretic dose was 47% higher in GP patients compared to cardiologist patients ($p < 0.001$).
In the entire s/v cohort, the mean furosemide equivalent dose was 218mg during the 6 months pre-index and 163mg in the 6 months after index. Daily diuretic dose decreased from pre to post-index by 48mg (-26%) in patients up-titrated on s/v ($p < 0.001$), decreased by 67mg (-28%) in patients with no s/v titration ($p < 0.001$) and decreased by 35mg (-14%) in those who were down-titrated on s/v ($p = 0.003$)-Figure.
Conclusions: Concomitant use of BB and MRA remained high following s/v index. GPs generally prescribed less MRA and higher doses of oral diuretics than cardiologists. Lower diuretic doses and more frequent down-titration of diuretics after s/v index was observed in patients who were up-titrated on s/v compared with those who had s/v down-titrated. This suggests that an adjustment of oral diuretic doses may need to be considered during s/v initiation and titration.



Oral Diuretics Dose During 6 Months

1549

The association between implantable defibrillators and all-cause mortality in left ventricular assist device carriers - initial results of a propensity score adjusted analysis

M Cikes[1]; N Jakus[1]; JJ Brugts[2]; P Rubis[3]; G Burneikaite[4]; E Van Craenenbroeck[5]; AC Pouleur[6]; E Barge-Caballero[7]; A Gkouziouta[8]; D D'amario[9]; S Grundmann[10]; LH Lund[11]; A Flammer[12]; D Milicic[1]; F Ruschitzka[12]
[1]University of Zagreb School of Medicine, Department of Cardiovascular Diseases, Zagreb, Croatia; *[2]Erasmus Medical Center, Rotterdam, Netherlands*; *[3]John Paul II Hospital, Krakow, Poland*; *[4]Vilnius University Hospital, Vilnius, Lithuania*; *[5]University Hospital Antwerp, Antwerp, Belgium*; *[6]Cliniques Saint-Luc UCL, Division of Cardiology, Brussels, Belgium*; *[7]Hospital Universitario de A Coruña, A Coruña, Spain*; *[8]Onassis Cardiac Surgery Center, Athens, Greece*; *[9]Catholic University of the Sacred Heart, Rome, Italy*; *[10]Universitäts-Herzzentrum , Freiburg-Bad Krozingen, Germany*; *[11]Karolinska Institute, Department of Medicine, Stockholm, Sweden*; *[12]University Hospital Zurich, Clinic for Cardiology, Zurich, Switzerland*

On behalf of: The PCHF VAD-ICD/CRT Registry

Introduction: The role of multiple devices frequently implanted in patients with advanced heart failure requires further insight from diverse patient cohorts. We have formed a registry of ventricular assist device (VAD) carriers through a network of European heart failure centres, aiming to investigate the association between implantable defibrillator and all cause death in VAD recipients.
Methods: At current, the registry includes data on 246 patients with continuous flow LVADs (median age 56 (IQR 48-63), 83% male), 63% of which also received an ICD or CRT-D. We created a propensity score to determine the possibility of having an ICD/CRT-D. This was followed by a propensity score adjusted analysis to assess the relation of ICD or CRT-D device carrier status and the occurrence of the primary event of all-cause death. The median follow-up time was 1.3 years (IQR 0.4-2.0) from index date, defined as time of LVAD or ICD/CRT-D implant, whichever came later.
Results: The baseline characteristics varied significantly according to ICD/CRT-D carrier status (Table 1). The rate of all-cause death was significantly lower in ICD/CRT-D carriers (14.0 (9.8-19.9) vs 31.6 (22.8-43.8) per 100 patient-years) as was the crude hazard ratio for all-cause death (0.43 (0.27-0.71), p = 0.001). After propensity score adjustment for 17 baseline characteristics, the relative risk of all-cause death remained significantly reduced in ICD/CRT-D carriers (HR 0.30 (0.16-0.57), p <0.0001), even after additional adjusting for CRT-P carrier status (HR 0.27 (0.14-0.52), p <0.0001).
Conclusion: The initial results from our registry suggest that ICD/CRT-D might be associated with reduced all-cause death in VAD carriers.

Table 1.

	No ICD/CRT-D (N = 90)	ICD/CRT-D (N = 156)	Group P-value
Age at implant, years	50±13	56±10	<0.001
Male gender, n (%)	69 (76.7%)	134 (85.9%)	0.07
INTERMACS class 1, n (%)	24 (27.3%)	13 (8.4%)	<0.001
INTERMACS class 2, n (%)	24 (27.3%)	33 (21.3%)	
INTERMACS class 3, n (%)	19 (21.6%)	61 (39.4%)	
INTERMACS class 4-7, n (%)	21 (23.9%)	48 (31.0%)	
MCS prior to VAD, n (%)	40 (44.4%)	27 (17.3%)	<0.001
VAD type - HMII, n (%)	56 (62.2%)	66 (42.6%)	0.008
VAD type - HW, n (%)	16 (17.8%)	47 (30 3%)	
VAD type - HM3, n (%)	15 (16.7%)	41 (26.5%)	
VAD type - Other, n (%)	3 (3.3%)	1 (0.6%)	

Baseline characteristics of patients according to ICD/CRT-D carrier status.

1550

Are there differences in the outcomes of ischemic and non-ischemic cardiomyopathy in the current era?

R Raed Odeh[1]; RO Odeh[1]; MK Alkhateeb[1]; MM Almallah[1]; AA Ahmad[1]; AH Ardah[1]
[1]King Abdulaziz Medical City, Riyadh, Saudi Arabia

Background: There has been conflicting evidence on whether the outcomes of ischemic (ICM) and non ischemic (NICM) exit. While older studies suggested the ICMP have worse outcomes, recent data suggest that the outcomes may be the same. The aim of this analysis is to explore the differences between ICM and NICMP in a well-treated contemporary cohort with heart failure with reduced ejection fraction (HFrEF).
Methods: A post hoc analysis of 2,805 (HFrEF) patients (Mean age 57.4, 70% females) were included. ICMP was defined HFrEF in the presence of obstructive coronary artery disease or myocardial infarction. Patients were followed up for a median duration of 4.4 years for all cause mortality.
Result: A total of 1,675 patients had ICM while 1,130 patients had NICMP. Patients with ICMP were older, more often females, with higher prevalence of hypertension, diabetes, and dyslipidemia. NICMP patient had lower ejection fraction (33.6 ± 8.7 vs. 31.5 ± 11.1, p= <0.0001). Patients with NICMP were more often treated with beta blocker and aldactone, with no differences in ACEI/ARB. After a median follow-up duration of 4.4 years, 436 patients died (147(14.7%) in the NICMP and 289 (18.86%)in the ICMP). After adjusting for confounders, including differences in medical therapy, ICMP was associated with increased risk of all-cause mortality (Hazarad ratio 1.62, 95% CI 1.32-2.04)
Conclusion: In the current era, ischemic cardiomyopathy continues to be associated with worse outcomes. This may be partially attributed to differences in medical therapies'.

1548

Noninvasive recognition of experimental cardiac allograft rejection by molecular targeting of apoptotic process with radiolabeled duramycin in vivo

M Adapoe[1]; A Petrov[1]; F Chaudhry[1]; N Narula[1]; B Gray[2]; Y Pak[2]; HW Strauss[1]; P Heeger[1]; J Narula[1]
[1]Icahn School of Medicine at Mount Sinai, New York, United States of America; *[2]Molecular Targeting Technologies Inc, West Chester, United States of America*

Background: Myocardial apoptosis, a cellular death process distinctly different from the cellular necrosis has been described as an obligatory component of moderate and severe cardiac allograft rejection (CAR) in addition to interstitial inflammation. In clinical practice, CAR is universally detected by an invasive endomyocardial biopsy repeated at least 10-12 times in the first year after heart transplantation. Therefore, the importance of a noninvasive test can hardly be overstated.
Objective: Since apoptosis almost always accompanies CAR, and offers cell membrane signatures of the death process in form of asymmetric exposure of phosphatidylserine and phosphatidylethanolamine (PE), we evaluated the usefulness of radiolabeled PE-targeting agent- Technetium-99m-labeled duramycin (D) by microSPECT/CT imaging.
Methods: 16 mice received abdominal heterotopic cardiac allografts in 4 groups of 4 animals each. Group 1: BALB/c (H-2d) donor to B6 (H-2b) recipient (allogeneic transplant, ALO). Group 2: B6 donor to B6 recipient (syngeneic control transplant, CON). Group 3: BALB/c donor to B6 recipient treated with CTLA4-IG (allogeneic transplant and immunosuppressed, IMS). Group 4: Bm12 H-2bm12) donor to B6 recipient (class II MHC disparate transplant to test for chronic CAR, CHR). ALO and CON were sacrificed 6-7 days following transplant. IMS animals were sacrificed 14-15 days following transplant. CHR animals were sacrificed 21 days following transplant (all grafts were beating at the time of harvest). MicroSPECT/CT imaging of the heterotopic transplant was performed in vivo and ex vivo after intravenous D administration. The transplant was collected for quantitative injected dose/gram uptake (%ID/g) of radiotracer. Hearts were then pathologically characterized using the ISHLT grading rubric.
Results: The in vivo and ex vivo imaging, and the quantitative uptake (expressed in mean %ID/g ± SD) of the radiotracer demonstrated the most intense uptake in ALO (5.8 ± 2.2 %ID/g), followed by CHR (1.8 ± 1.5 %ID/g), then IMS (1.2 ± 0.4 %ID/g), and finally CON (0.90 ± 0.04 %ID/g). One-way ANOVA with Tukey post-hoc test revealed ALO had significantly higher uptake than that of the CON and IMS groups ($P < 0.05$). Pathology demonstrated ISHLT Grade 3R rejection in ALO (3 out of 4 animals), no rejection in CON and Grade 1-2R in IMS and CHR groups. Chronic vasculopathy was also observed in the CHR group.
Conclusion: Noninvasive molecular imaging of apoptosis in CAR is feasible with radiolabeled D, which can identify various shades of graft rejection verified by histopathological characterization.

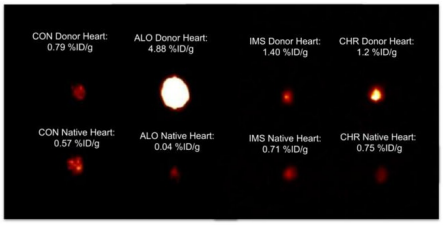


Figure 1. Ex vivo SPECT imaging of hearts are shown with their respective uptake values (%ID/g). Top row contains heterotopic donor transplanted hearts. Bottom row contain native recipient hearts

Moderated Posters - Advanced heart failure

1551

Surfactant proteins changes after acute hemodynamic improvement in patients with advanced chronic heart failure treated with levosimendan

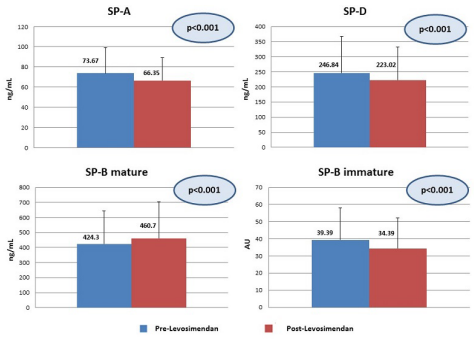
M Mapelli[1]; J Campodonico[1]; C Banfi[1]; E Spadafora[1]; E Salvioni[1]; C Vignati[1]; S Sciomer[2]; A Del Torto[1]; F Nicoli[1]; N Corrieri[1]; M Contini[1]; PG Agostoni[1]
[1]Cardiology Center Monzino IRCCS, Milan, Italy; *[2]Sapienza University of Rome, Rome, Italy*

Background: Alveolar-capillary membrane diffusion evaluated by carbon monoxide diffusion (DLCO) plays an important role in heart failure (HF). Cardiopulmonary exercise test (CPET) is a powerful diagnostic and prognostic tool in this context. Surfactant Proteins (SPs) have also been suggested as a worthwhile marker in these patients. In HF, Levosimendan improves cardiopulmonary hemodynamics and reduces lung fluids but associated SPs and DLCO changes are unknown.

Tab1

	Pre-Levosimendan	Post-Levosimendan	p value
Hemoglobin	12.91±1.93	12.44±1.77	ns
BUN (mg/dl)	78.14±36.43	75.14±34.33	ns
Creatinine (mg/dl)	1.55±0.55	1.51±0.56	ns
BNP (pg/ml)	1277.06±994.02	578.03±591.01	<0.01
Peak VO2 (ml/Kg/min)	10.07±2.36	11.50±2.30	<0.01
Watts	44.45±18.29	51.15±18.34	<0.01
VO2/work slope	8.99±1.87	9.64±1.51	<0.01
VE/VCO2	41.98±9.86	36.36±7.13	<0.01
FEV1 (L)	2.09±0.56	2.26±0.63	<0.01
DLCO (mL/mmHg/min)	18.00±4.51	17.74±4.06	ns

Laboratory, spirometry and CPET changes



SPs changes after Levosimendan infusion

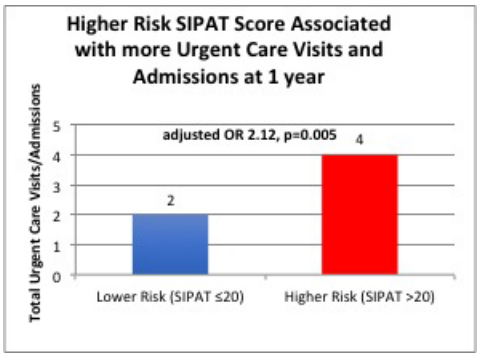
Purpose: To show changes in serum SPs values and in CPET parameters after Levosimendan administration in patients with advanced HF.
Methods: Sixty-five advanced HF patients (NYHA class III/IV, VO2 = 12 underwent complete spirometry, CPET and SPs determination before and after Levosimendan infusion.
Results: Levosimendan caused a significant natriuretic peptide-B (BNP) reduction (from 954 to 370 ng/ml*), peakVO2 increase (from 10.1 ± 2.4 to 11.5 ± 2.3 mL/kg/min*) and VE/VCO2 slope reduction (from 42 ± 10 to 36 ± 7*) (* = p < 0.01, Tab.1). FEV1, FVC and alveolar volume increased but DLCO did not. SP-A, SP-D and immature SP-B reduced while mature SP-B increased (Fig.1). Spirometry, BNP and CPET changes suggest an hemodynamic improvement and lung fluid reduction after inotropic drug infusion. In parallel SP-A, SP-D and immature SP-B reduction indicates an alveolar-capillary membrane hemodynamic and general inflammatory stress reduction. Conversely, mature SP-B increase suggests an alveolar cell function restoration.
Conclusions: Levosimendan improves VO2 peak, decreases VE/VCO2 slope and decreases plasma levels of BNP. Hemodynamic improvement and acute lung fluid reduction is associated with SPs but not DLCO changes. SPs are fast responders to alveolar-capillary membrane condition changes.

1552

Stanford integrated psychosocial assessment for transplantation scores track with intermacs profile and predict readmissions in patients undergoing left ventricular assist device implantation

M Matthew Cagliostro[1]; A Bromley[1]; P Ting[1]; J Donehey[2]; K Parks[2]; E Palumbo[2]; D Mancini[3]; A Anyanwu[1]; A Pawale[1]; S Pinney[3]; N Moss[3]; A Lala[3]
[1]Mount Sinai School of Medicine, New York, United States of America; *[2]Mount Sinai Medical Center, New York, United States of America*; *[3]The Zena and Michael A. Wiener Cardiovascular Institute, New York, United States of America*

Background: Psychosocial assessment is integral to evaluation of advanced therapies in patients with end-stage heart failure. The Stanford Integrated Psychosocial Assessment for Transplantation (SIPAT) is a standardised tool used to predict outcomes in heart transplantation but is not established for utility in patients undergoing left ventricular assist device (LVAD) implantation.
Purpose: To determine the association of SIPAT scores, demographics and INTERMACS profiles in patients undergoing LVAD implantation as well as to explore the relationship between SIPAT scores and outcomes post LVAD.
Methods: SIPAT assessments are routinely performed for patients undergoing LVAD evaluation at Mount Sinai Hospital. Data were collected for consecutive patients implanted from January 2014 through December 2016. Baseline characteristics were evaluated for all patients and compared based on SIPAT scores = 20 (excellent or good candidates) versus >20 (minimally acceptable or high-risk candidates). Outcomes included urgent visits or readmission, death, and adverse events, and were adjusted for age and INTERMACS profile.



Results: During the study period, 111 patients (26% female, 39% white, 66% INTERMACS profile = 3) were implanted with an LVAD and had SIPAT scores available for analysis. The median SIPAT score was 12 (SD 9.95, IQR 8-20), with most patients categorised as excellent or good (77%, n = 85). Higher risk (SIPAT>20) and lower risk (SIPAT = 20) patients were similar in age, gender, ethnicity and medical history, but INTERMACS profiles were significantly different. The higher risk SIPAT group had a greater proportion of INTERMACS profiles 1 and 2 (p = 0.03). At 1-year post LVAD implant, 22 patients were transplanted, and 68 patients experienced an adverse event, including 12 deaths. Higher risk patients had more urgent visits and admissions (4 vs 2, p = 0.005) with a trend towards spending a greater number of days in hospital over 1 year (27 vs 14, p = 0.08) compared to lower risk patients. This difference persisted after adjusting for INTERMACS profile and age (OR 2.12, 95% CI 1.26 - 3.6). There was no significant between group difference in adverse

events of pump thrombosis, gastrointestinal bleeding, right heart failure, arrhythmia, cerebrovascular events or survival. However a trend towards more infections in the higher risk SIPAT group was observed (52% vs 31%, p = 0.06).
Conclusions: Higher psychosocial risk as measured by SIPAT score > 20 was more frequently associated with INTERMACS profiles 1 and 2 compared to lower risk patients. High SIPAT scores were also associated with more frequent urgent visits and readmissions, with a trend towards greater number of days in hospital and more infections at 1-year post VAD implantation. SIPAT scores may help identify patients in need of additional LVAD management assistance in the outpatient setting.

1553
What happened to patients being listed for Heart Transplantation who did not arrive to Transplantation? Reasons for coming out of the waiting list and long term follow-up

M A Castel Lavilla[1]; M Farrero[1]; A Garcia[1]; E Santiago[1]; F Perez-Villa[1]
[1]*Hospital Clinic de Barcelona, Cardiology Department, Barcelona, Spain*

Introduction and Objectives: Waiting time for patients listed for Heart Transplantation (HTx) has been steadily increasing in Spain. There are registers of patients dying in the waiting list but there is little information about patients coming out of the waiting list for other reasons. The objective of this study is analyzing all patients delisted after being listed for HTx, the reason for delisting and their outcomes after long follow-up.
Methods: We investigated all patients from a single center officially listed for HTx in Spain between January 2000 and March 2017. Date entering and date leaving the waiting list were recorded. We investigated reasons for delisting, basal characteristics and mortality at long term. Data of follow-up was obtained in 99% of patients through the hospital records or by the region's shared medical history.
Results: From a total of 399 patients who were listed for Htx, 310 patients reached transplantation and 89 patients were delisted without reaching HTx. Mean age of patients was 54.6 ± 12.6 yrs (12-70 yrs), 82.2% males. Cause of exclusion was death while listed in 31 pat. (34.8%; 7.8% of total), clinical worsening in 31 (34%; 7.8% of total), clinical improvement in 26 (29%; 6.5%) and patient's wish to leave in 2 patients (2.2%; 0.5%). Mean waiting time in list was 123 ± 187 days, after a median follow up of 189 days (IQR 18, 741 days) 76% of patients who came out of list died. Total mortality of patients who were excluded because of clinical worsening was 89.6% and from patients with clinical improvement was 38.5%. From all patients excluded 60% were on elective list, 29% in Urgency status 0 and 10% in Urgency status 1. Total mortality was associated to time in waiting list (p < 0.001) but there was no relationship to urgency status, age, size or time of transplantation.
Conclusions: In our experience mortality of patients awaiting Htx is underestimated. Most patients leaving the waiting list due to clinical worsening died, also an important percentage of patients who improved and were delisted died at long term. Most of patients who left the list were on elective urgency status.

1554
Impact of an interatrial shunt device on survival and heart failure hospitalization in patients with preserved ejection fraction

D M Kaye[1]; MC Petrie[2]; S Mckenzie[3]; G Hassenfus[4]; F Malek[5]; R Doughty[6]; J Trochu[7]; F Gustafsson[8]; A Kolodzei[9]; M Penicka[10]; M Rosenberg[11]; P Raake[12]; M Bergmann[13]; P Ponikowski[9]; C Hayward[14]
[1]*The Alfred Hospital, Melbourne, Australia*; [2]*Golden Jubilee National Hospital, Glasgow, United Kingdom*; [3]*The Prince Charles Hospital, Brisbane, Australia*; [4]*Georg-August University, Gottingen, Germany*; [5]*Na Homolce Hospital, Prague, Czech Republic*; [6]*The University of Auckland, Auckland, New Zealand*; [7]*University Hospital of Nantes, Nantes, France*; [8]*Rigshospitalet - Copenhagen University Hospital, Copenhagen, Denmark*; [9]*4th Military Hospital, Wroclaw, Poland*; [10]*Olv Hospital Aalst, Aalst, Belgium*; [11]*University Medical Center of Schleswig-Holstein, Kiel, Germany*; [12]*University of Heidelberg, Heidelberg, Germany*; [13]*University Heart Center Hamburg, Hamburg, Germany*; [14]*St Vincent's Hospital, Sydney, Australia*

Funding Acknowledgements: Corvia Medical

Background: HFpEF is one of the most challenging disorders in contemporary cardiology. The pathophysiology is complex. Impaired LV diastolic function leading to elevated LA pressures, particularly during exertion, is a key driver of symptoms and outcomes. To date pharmacologic therapies have been primarily ineffective. A mechanical approach (interatrial shunt device, IASD) to reducing LA pressures in HFpEF patients by LA decompression has been shown to be safe and to be associated with short-term hemodynamic and symptomatic benefit. The effects of IASD placement on HFpEF survival and heart failure hospitalization (HFH) in the intermediate to longer term is unknown.
Methods: HFpEF patients (n = 64) participating the REDUCE LAP-HF trial (Corvia Medical) of an IASD were followed for up to 3 years post IASD implant (median 739 days). An invasive rest and exercise hemodynamic assessment was included in the assessment for trial eligibility. The theoretical impact of IASD implantation on HFpEF outcomes was investigated by estimating the survival probability of the study cohort at baseline using the MAGGIC score. Observed and predicted survival curves were compared over the follow-up period using a log rank test. Baseline and post IASD implant parameters associated with HFH were also investigated.
Results: Based upon the baseline clinical and demographic HF features of the cohort, the MAGGIC score predicted mortality rate of the cohort 10.2/100pt years compared with an observed rate of 3.4/100pt years, representing a 33% lower rate (p = 0.02). By Kaplan Meier analysis, observed survival in IASD patients was greater than predicted (p = 0.014). For patients experiencing a HFH event, first hospitalization events occurred at a median of 182 days post IASD. Baseline parameters were not predictive of future HFH, however post IASD a poorer exercise tolerance (6 minute walk distance: 312 ± 23 vs 375 ± 14m, p <0.05) and higher workload corrected exercise pulmonary capillary wedge pressure (94 ± 13 vs 60 ± 5 mmHg/(W/kg), p <0.05) were associated with HFH.
Conclusions: The current study suggests IASD implantation may be associated with a reduction in mortality in HFpEF. Large scale ongoing randomized studies are required to confirm this finding.

1555
Prognosis of patients with cardiac amyloidosis referred in the French national referral Centre for Cardiac Amyloidosis

D Bodez[1]; M Kharoubi[1]; A Galat[1]; S Guendouz[1]; S Rouffiac[1]; J Badie[1]; V Plante-Bordeneuve[2]; A Amiot[3]; C Radu[4]; F Le Bras[5]; L Hittinger[1]; T Damy[1]
[1]*University Hospital Henri Mondor, Cardiology & Amyloid Research Institute, Creteil, France*; [2]*University Hospital Henri Mondor, Neurology & Amyloid Research Institute, Creteil, France*; [3]*University Hospital Henri Mondor, Gastroenterology & Amyloid Research Institute, Creteil, France*; [4]*University Hospital Henri Mondor, Cardiac Surgery & Amyloid Research Institute, Creteil, France*; [5]*University Hospital Henri Mondor, Lymphoid Malignancies unit & Amyloid Research Institute, Creteil, France*

Funding Acknowledgements: APHP & AREMCAR

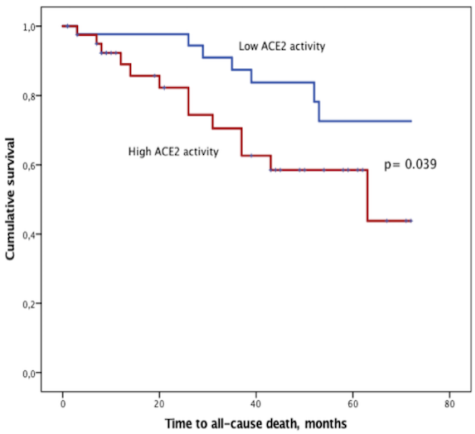
Background: Cardiac amyloidoses (CA) are distinct diseases caused by the extracellular infiltration of the myocardium by different types of amyloid proteins (immunoglulin, transthyretin...). The most frequent CA are light chain (AL) amyloidosis, hereditary transthyretin (TTR-h) and wild-type transthyretin (wt-TTR).
Aim: To describe baseline clinical, biological, echocardiographic characteristics and prognosis of patients referred for suspicion of CA in the French National Referral center for CA.
Methods: From 2010 to July 2016, all patients referred for suspicion of CA were included. Baseline demographic, clinical, laboratory and ultrasound characteristics were recorded. Patients were followed-up for major events (MACE) including death, cardiac transplantation and left ventricular assistance implant.
Results: Of the 942 patients referred for suspicion of CA, 502 had confirmed CA of whom 162 had AL amyloidosis, 203 h-TTR and 141 wt-TTR. CA were men in 60%, the median age was 69 years w-TTR amyloidosis were older (83 [79; 87], p < 0.001) and more men (86%, p < 0.001) than the two other types of CA. NYHA III-IV dyspnea was more frequent in AL amyloidosis (60%) and wt-TTR (54%, p < 0.001) compared to h-TTR, while neurological symptoms were more predominant in h-TTR (62% p < 0.001). Creatinine, NT-proBNP and troponin were higher in AL amyloidosis and w-TTR (p < 0.001) than in h-TTR. Wt-TTR amyloidosis had thicker Interventricular septum thicker, lower LVEF, higher global strain E/A and E/Ea ratios than other groups. During a median follow-up of 22 (8;36) months, 137 major events occurred. The survival without MACE was 59% for AL amyloidosis, 79% for w-TTR, 81% for h-TTR versus 88% for patients without amyloidosis (p < 0.001). In multivariate analysis (including only CA), NYHA class III-IV, hyponatremia, elevation of creatinine, troponin and NTproBNP were independent prognostic factors (p < 0.001).
Conclusion: Cardiac amyloidosis is more frequent than initially thought, with very different layouts depending on the type of amyloid protein involved, and a poor prognosis. The challenge is to achieve earlier diagnosis to improve prognosis.

1556
Angiotensin based biomarkers predict outcome in HFpEF-patients

C Binder[1]; M Poglitsch[2]; FD Duca[1]; C Zotter-Tufaro[1]; AAK Kammerlander[1]; SA Aschauer[1]; C Nitsche[1]; J Mascherbauer[1]; DB Bonderman[1]
[1]*Medical University of Vienna, AKH - Vienna, Cardiology Clinic, Vienna, Austria*; [2]*Attoquant Diagnostics, Vienna, Austria*

Background: The importance of the renin-angiotensin system (RAS) on the development and progression of heart failure (HF) has been studied extensively. In patients with HF with reduced ejection fraction (HFrEF), inhibition of angiotensin-converting enzyme (ACE) is an effective treatment strategy, not only by reducing Angiotensin II (Ang II) but also by increasing its metabolites Ang 1-7 and Ang 1-5 which are produced via ACE2 action and mediate cardio-protective effects. In contrast, studies

have failed to show benefits of RAS inhibiting (RASi) therapy in patients with HF with preserved ejection fraction (HFpEF).
Purpose: We aimed to investigate the RAS profiles of HFpEF patients to gain more insight into the
pathogenesis and to evaluate the prognostic impact of RAS metabolites in this disease.
Methods: Consecutive patients were included in a prospective registry at our dedicated HFpEF outpatient clinic at the Medical University of Vienna. Baseline parameters were assessed and serum samples analyzed by RAS-Fingerprint (Attoquant, Vienna Austria) using mass spectroscopy to quantify equilibrium angiotensin levels for each patient. The sum of Ang 1-7 and Ang 1-5 was calculated as a surrogate for ACE2 activity and patients were then stratified into tertiles. The lowest tertile was compared to the highest tertile regarding baseline characteristics and the primary outcome variable, all-cause death.
Results: RAS-Fingerprint analysis was performed in serum samples of 137 HFpEF patients. 26 patients were only on ACE inhibitors, 94 patients were treated with other RASi and 17 patients did not receive RASi. Notably, baseline parameters associated with advanced disease progression were associated with higher Ang 1-7 levels. During a mean follow- up time of 135 ± 23.6 months, 22 patients (16.1%) died. Of these, 11 (50.0%) patients died of cardiac causes. Univariate Cox regression analysis identified the ACE2 surrogate marker as a predictor for all-cause death with a hazard ratio of 1.005 (95% CI 1.002-1.008), p= 0.005), and remained predictive even after adjusting for common risk factors including age, N-terminal pro-brain natriuretic peptide and glomerular filtration rate (HR 1.005 (95% CI 1.002-1.008), p = 0.004). Furthermore, we found that higher plasma renin was associated with worse outcomes, indicating a higher RAS activity in patients with advanced HF, independent of ACEi therapy (HR 2.781 (95% CI 1.364-5.670), p= 0.005).
Conclusion: We hypothesize, that much like NT-proBNP, ACE2 activity is enhanced in progressive HF to counteract the detrimental effects of Ang II. Angiotensin based biomarkers not only serve as predictors of outcome in patients with HFpEF but also give insight into the individual state of the RAS, which in turn could potentially identify patients who would benefit from RAS inhibiting therapies. Furthermore, it could help characterize patients with respect to therapeutic response for future recombinant ACE2 treatment strategies.



All-cause death according to ACE2 activt

1557

Cardiogenic shock and acute coronary syndrome: could the vascular access influence our patients outcome?

H Miranda[1]; I Almeida[1]; C Sousa[1]; D Mesquita[1]; S Almeida[1]; J Chin[1]
[1]*Centro Hospitalar Barreiro Montijo, Cardiology, Barreiro, Portugal*

On behalf of: Portuguese National Registry of Acute Coronary Syndromes

Introduction: Cardiogenic shock (CS) is the leading cause of death in patients with acute coronary syndrome (ACS), with a 70-90% mortality rate in the absence of early intervention. It's crucial to ensure rapid revascularization, since hospital mortality increases with waiting time until reperfusion.
Objectives: To determine if vascular access (femoral versus radial) for percutaneous coronary intervention (PCI), in patients admitted with CS, had an influence on the outcome.
Material and Methods: Retrospective study, based on the Portuguese National Registry of Acute Coronary Syndrome (ACS), from 10/10/2010 to 19/09/2017. All patients admitted for CS in the context of ACS were selected. Exclusion criteria: Killip class I-III, lack of information on coronary angiography and vascular access.
Results: The initial pool was comprised of 318 patients with ACS. After applying the exclusion criteria, only 258 ended up being included. Male predominance (65.1%). Mean age 68 ± 13 years. Hypertension (69.8%), diabetes (50.2%) and dyslipidaemia (32.1%) were the most frequent comorbidities. 68.24% of the included patients had a diagnosis of ACS with elevation of the ST segment. Mean time symptoms-reperfusion and 1st medical contact-reperfusion contact of 319 and 148 minutes, respectively. PCI was performed, using the femoral access, in 62.02% of the cases.
We found out a greater use of intra-aortic balloon and temporary pacemaker in patients with femoral access (p-value of 0.039 and 0.001, respectively), as well as a higher prevalence of atrioventricular block and hospital death (p-value 0.002 and 0.001, respectively) when compared to radial access. We also found out that the main predictors of death in CS were age over 65 years, haemoglobin above or equal to 12mg / dl, cardiac arrest as the predominant symptom, right bundle branch block on admission's electrocardiogram, hospital medication performed (ACEI, statin and inotropes) and left ventricular function < 40%. There was no significant association between type of access and hospital death (OR 0.51, CI 0.16-1.68, p-value 0.270).
Conclusion: Early and definitive restoration of coronary blood flow is the standard therapy in patients admitted for CS in the context of myocardial ischemia. According to our findings, the vascular access had no impact on mortality in this type of patients.

Clinical Case Corner 5 - New treatments and interventions on the horizon

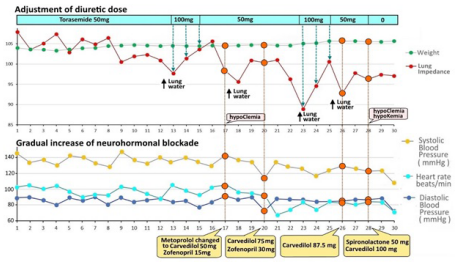
1558

Lung impedance as a sensitive non-invasive tool for home monitoring of lung water in the vulnerable phase

E Paleviciute[1]; E Lycholip[1]; IT Aamodt[2]; I Lie[2]; J Celutkiene[1]
[1]Vilnius University Hospital Santaros Clinics, Clinic of Cardiac and Vascular Diseases, Centre of Cardiology and Angiology, Vilnius, Lithuania; [2]Oslo University Hospital, Centre for patient centered heart and lung research, Department of Cardiothoracic surgery, Oslo, Norway

On behalf of: The Symptom Monitoring After CongeStive Heart Failure study
Funding Acknowledgements: This research was supported by NordForsk. "Nordic Programme on Health and Welfare" Project no.: 76015.

Clinical problem: A key factor in the management of heart failure (HF) patients is an accurate assessment of volume status. The sensitivity of transthoracic impedance (TI) to monitor pulmonary congestion in an individual patient was previously questioned. Recently it has been shown, that the use of a high sensitive non-invasive device measuring lung impedance (LI) reduces hospitalizations for HF and cardiovascular and all-cause mortality. We present a case 1-month follow up of the patient discharged after an episode of acute HF using home LI measurements.
Technique for patient monitoring
Edema guard monitor is based on an algorithm calculating the chest wall impedance that is a preponderant component of the total electrical TI. Subtraction of the chest wall impedance from the latter yields the net LI, which composes only a small fraction of the overall TI. Decreasing LI values represent increase of lung fluid. Measurements are done using 3 electrodes on each side of the chest wall. Before discharge the patient and his caregivers were trained to perform measurements of LI values, arterial blood pressure, heart rate and reported these data to HF nurse by a call or SMS daily.



Case description: A 62-year old man with chronic ischemic HF with reduced ejection fraction was hospitalized due to deterioration accompanied by dyspnea, fatigue, feet edema. On the electrocardiogram paroxysms of ventricular tachycardia were seen, led by cold sweat and extreme weakness. During 17 hospitalization days the patient was treated medically, a biventricular defibrillator was implanted. Medications on discharge included metoprolol 100 mg b.i.d., spironolactone 25 mg q.d., zofenopril 7,5 mg q.d., amiodarone 200 mg q.d., torasemide 50 mg q.d., anticoagulation with warfarin; discharge LI value was 107.9. During 1 month after discharge treatment has been adjusted 6 times. Decrease of LI by -9% and -18% compared with baseline LI twice was treated increasing the dose of torasemide. According to heart rate and arterial blood pressure, dosage of beta-blockers and ACE inhibitors were up-titrated 3 and 2 times, respectively. Laboratory assessment of creatinine and electrolytes was performed 3 times, twice diuretic dose was not raised as hypochloremia and hyponatremia was detected, despite decrease of LI values. In 30 days patient's weight fluctuated between 103.3-105.7 kg. In 4 days, when LI decreased most, weight increased by average 200 g (0.2%), compared with the previous day. After 30 days, patient's status improved compared with the discharge - NT-proBNP level decreased (2061 vs 3485 ng/l), left ventricular ejection fraction increased (28 vs 20%), estimated pulmonary capillary wedge pressure decreased (16.5 vs 20.6 mmHg).
Conclusion: Significant fluctuation of lung water amount is registered by high sensitive LI measurements. Non-invasive daily monitoring of lung impedance seems to be an important component of successful transition from acute to stable phase of HF.

1559

Frailty syndrome: the same age does not mean the same health status

MH Lisiak[1]; I Uchmanowicz[1]
[1]Wroclaw Medical University, Department of Clinical Nursing , Wroclaw, Poland

Introduction: Frailty syndrome (FS) is a multidimensional problem associated with high dependency and mortality rate. The evidence shows that early identification of FS can improve management and outcomes in elderly patients. The relationship between age and frailty is not completely understood. Individuals of the same chronological age vary in terms of their biological age, which depends on the stage of aging processes and the number of co-morbidities. Multiple conditions in a frail person can trigger physical, psychological or social decline.
Case report description: A multidimensional FS assessment was carried out in two women (WA and WB) of the same age (70 y/o) hospitalized in Intensive Cardiac Unit. Data (ICU) on pre-existing diseases and test results were obtained from medical records. Both of them were widows, supported by their children. WA did not work while WB was still professionally active. The women differed in the some aspects. WA had many co-morbidities, such as: chronic heart failure (HF), NYHA III/IV (with triple decompensation in 2017), hypertension, diabetes type 2, chronic kidney disease, arrhythmias, history of heart attacks (PCI treatment and ultimately CABG in 2006). On admission due to decompensation of HF and heart attack she complained of cardiac symptoms, shortness of breath, dizziness and reduced exercise tolerance. In turn, WB was admitted to the ICU due to acute coronary syndrome (ACS) STEMI (stenocardial pain lasted only for an hour) and the only with dyslipidemia and kidney stones. She did not complain of any pain but sometimes she felt anxiety associated with hospitalization. The following screening tools were used: Mini Mental State Examination (MMSE) for cognitive function (CF), Tilburg Frailty Indicator (TFI), Edmonton Frail Scale (EFS), FRAIL scale (FSc) for FS, WHOQOL-Bref for quality of life (QoL), EPWORTH scale (ES) for sleep problems and Center for Epidemiologic Studies Depression Scale (CES-D) for depressive symptoms (DS). The results obtained by the women (A and B, respectively) were as follows: MMSE (pts): 24 (cognitive impairment (CI)) vs. 28 (no CI); TFI (pts): 11 (FS) vs. 1 (no FS); EFS (pts): 10 (moderate FS) vs. 1 (no FS); FSc (pts): 4 (FS) vs. 0 (robust); ES (pts): 15 (moderate excessive) vs. 3 (lower normal) daytime sleepiness; CES-D (pts): 27 (DS) vs. 10 (no DS). In all QoL domains, WA chose the poor or neither satisfied nor dissatisfied answers, while WB always reported good or very satisfied QoL.
Conclusions: All the scores in all the measures revealed that woman A had CI with FS, poor QoL and high DS while woman B had no FS, proper CF, good QoL and no DS. The comparison confirmed that the same age does not have to mean that two different patients are at the same level of multiple biopsychosocial decline. Only a multidisciplinary approach and frailty screening tools in acute care can be useful in identifying FS, planning complex assessment, creating appropriate care plan and discharge.

1560

Progressive heart failure in patient with ccTGA after double switch operation performed in early adulthood.

M Marketa Hegarova[1]; J Vrbska[1]; V Melenovsky[1]; I Malek[1]; J Pirk[2]
[1]Institute for Clinical and Experimental Medicine (IKEM), Department of Cardiology, Prague, Czech Republic; [2]Institute for Clinical and Experimental Medicine, Department of cardiovascular surgery, Prague, Czech Republic

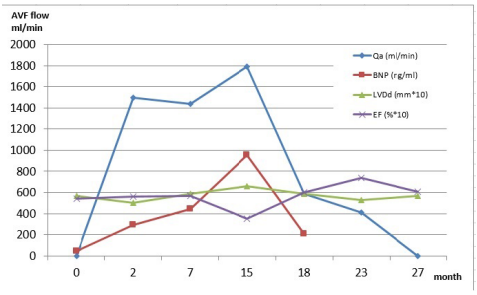
Introduction: Anatomic repair of congenitally corrected transposition of the great arteries (ccTGA) , a double switch operation (venous switch and great vessel switch wherein morphologic left ventricle (MLV) becomes the systemic ventricle) is considered to be superior procedure in order to improve patients' long term outcome. The late retraining of MLV is very controversial because of different response of an immature growing myocardium and matured myocardium to increased pressure overload. Aim: Presentation of the case with a fast progression of heart failure after double switch for ccTGA who was succesfully treated by heart transplantation.

Case report: Female 18 years old (born 1998) with ccTGA. From 2010 she was treated at a foreign heart clinic where the pulmonary artery banding was performed twice (2010, 2011, in age 12 and 13 years) for MLV retraining. She received DDD pacemaker due to complete AV block. Although the pt was doing well, in May 24, 2016 double switch operation was there performed. Immediately after the surgery, the MLV function deteriorated considerably, followed by a slight improvement after six weeks. Despite complete pharmacotherapy, chronic heart failure developed. In August 2016 she was hospitalized twice for severe decompensation with need for levosimendan treatment in the Children's Heart centre Motol university Hospital in Prague Czech Republic. In September 16, 2016 she was referred to our institution as heart transplant candidate. Upon admission she had signs of advanced heart failure, tachycardia, gallop, signs of malnutrition, BMI 14,5, severe systolic dysfunction of the MLV with mild mitral regurgitation and moderate dysfunction of right ventricle. Despite intensive pharmacotherapy she developed terminal heart failure requiring combined inotropic therapy. A successful heart transplantation (OHTx) was performed in October 7, 2016, 18 weeks after the double switch operation. Due to increased gradient on superior vena cava has been extended by CorMatrix patch two days later.
On standard immunosuppressive prophylaxis (MMF, tacrolimus, prednisone) graft function remains normal. Only one episode of cellular rejection was detected by protocolar endomyocardial biopsy without the need for antirejection therapy. Coronary angiography findings were normal one year after OHTx. Nowadays (1/2018) pt is doing well, she is in good clinical condition.
Conclusion: Despite the retrained MLV the double switch operation in ccTGA in early adulthood is very risky. We present a case of very rapid development of MLV dysfunction after the procedure with subsequent progressive deterioration, which resulted in terminal heart failure despite intensive pharmacotherapy.

1561
The role of arteriovenous fistula flow on heart failure in a dialysis patient

J Jan Malik[1]
[1]*Charles University, 1st Faculty of Medicine , Prague, Czech Republic*

Introduction: Creation of arteriovenous fistula (AVF) as the dialysis access leads to a low-resistance circuit with substantial increase in flow volume (Qa). Typical Qa values reach 500-1500 ml/min, but cases with significantly higher values are not rare and usually are well tolerated. Heart failure and pulmonary hypertension represent possible complications due to increased demands on cardiac output. Heart failure is very common in end-stage renal disease patients due to many mechanisms. Safe values of Qa are still a matter of debate.
Case: Here is presented a case of a 52-years old hemodialysis patient (due to polycystic kidney disease) with no prior cardiovascular history, who was cardiologically examined in detail repeatedly. She tolerated the creation of vascular access well. Later the increase in Qa led to the increase of BNP and to the dilatation of the left ventricle - see the Graph. Otherwise, the only echo abnormity was concentric left ventricular hypertrophy.
Graph legend: Qa = AVF flow volume; LVDd = left ventricular end-diastolic diameter (the values in mm times 10 to make them better visible); EF = left ventricular ejection fraction (% multiplied by 10 to make them better visible)
First examination was performed before AVF creation (far left). The surgery resulted in asymptomatic increase of BNP. After 15 months the patient experienced symptoms of heart failure –Qa rose to 1800 ml/min, which was mirrored by further increase of BNP, with left ventricular dilatation and decrease of its systolic function. AVF banding (arrow) reversed the signs and symptoms. AVF thrombosis developed after another 9 months. Thus, safe Qa was below 1500 ml/min in this patient.
Conclusion: This case documents individual toleration of Qa. Calculation of Qa should be a part of cardiological examination of dialysis patients with heart failure. Even usual Qa values can be too high for individual patients.



Graph

1562
MitraClip in a refractory heart failure patient: last but not the least

L Zamfir[1]; D Botezatu[1]; D Benea[1]; G Cerin[1]; M Hakimpour[1]; G Musica[1]; M Diena[1]; L Laudisa[2]
[1]*San Gaudenzio Clinic, Cardiothoracic Surgery, Novara, Italy*; [2]*San Gaudenzio Clinic, Novara, Italy*

Background: MitraClip procedure may improve clinical status in heart failure patients. Moreover, in case of recurrent hospitalization this procedure is of financial benefit.
Purpose: This is a case report of a successfully MitraClip treatment in a patient with numerous hospitalizations for heart failure and one last episode of decompensation refractory to medical treatment.
Methods: a 84 years old female patient that suffered numerous hospitalizations for heart failure. She had a history of a lateral miocardial infarction (1980) and severe residual systolic dysfunction (EFVS 30%). For the primary prophylaxis a cardiac defibrilator was implanted. The attempt to CRT upgrading was unsuccessfull because of the coronary sinus anatomy. Five years ago she had an acute pulmonary edema and was diagnosed with severe functional mitral insufficiency. Although she had frequent hospital recoveries under optimal medical therapy no additional treatment was considered so far. The patient was hospitalized in our Clinic for cardiogenic shock (NYHA IV functional class) that needed CPAP and inotropic therapy support (Levosimendan). The transthoracic echocardiogram showed dilated left ventricle (end diastolic volume 220 ml, 130 ml/m^2) with severe systolic dysfunction (FEVS 15%), severe functional mitral insufficiency and associated pulmonary hypertension (systolic pulmonary artery pressure 70mmHg). The coronarography didn't detect significant coronary artery stenosis.
Results: As the patient was unresponsive to medical therapy the MitraClip procedure was considered as a last alternative in a patient with cardiogenic shock and multiple organ failure. Because of the extension of the mitral jet insufficiency, 2 clips were implanted. The final result was good with mild residual mitral insufficiency, no mitral stenosis (medium gradient 2.46mmHg and 3.8cmq of mitral valvular area) and significant reduction of the polmonary pressure (PAPs 40 mmHg). The patient was hospitalized for 5 days after the procedure and was dicharged home with a significant improvement of the NYHA functional class (IIb). The 15 month follow-up showed stabile ecocardiographic and clinical data with no other hospitalization.
Conclusions: Traditionally, patients undergo corrective surgery. MitraClip is a less-invasive treatment for mitral regurgitation in high surgical risk patients. Our case illustrates the spectacular clinical response even when other therapies are of no significant benefit. As it is eficient in reducing simptoms and in decreasing medical costs MitraClip shouldn't be the last therapeutical alternative in heart failure patients.

1563
Diuretic resistance overcome by mannitol infusion

H Altay[1]; F Ozkalayci[1]; S Pehlivanoglu[1]
[1]*Baskent University Istanbul Hospital , Cardiology, Istanbul, Turkey*

Introduction: Case description 1: 64 years-old man admitted to our hospital with volume overload . The patient had a history of heart failure (HF), coronary artery disease(CAD), hypertension and atrial fibrillation . In the past year, he had had three hospitalization with decompansated HF. Blood pressure was 150/90mmhg, heart rate 100/minute. Bibasiller rales and severe pretibial edema was present. Notable admission labs included amino terminal pro-BNP level 4310pg/ml and creatinine (Cr) 1,26 mg/dl. Echocardiography revealed an ejection fraction (EF) of 20%. He was treated with diuretic infusion at a rate of 5mg/h. Despite stepwise increase in furosemide dose, desired diuretic response was not achieved. Then dobuatmine infusion was tried but didn't bring decongestion and renal function worsened. Before the ultimate treatment with ultrafilltration, 20% mannitol 150 ml three times a day was added in addition to furosemide. Diuresis of the patient increased. After 3 days the patient was decongested .The patient weaned off mannitol and discharged with furosemide.
Case description 2: 82 years-old male patient presented to cardiology outpatient with pretibial oedema and dyspnea. The patient had a history of CAD, anemia, diabetes , hypertension and chronic kidney disease..His blood pressure was 150/90mmhg, pulse rate 100 b.p.m. He had severe pretibial edema with clear lung sounds. Notable labs were NT-proBNP 11,321pg/ml, creatinine 2,3 mg/dl. Echocardiography revealed an EF of %55. We started diuretic infusion at a rate of 10 mg/h, low dose dopamine and perlinganit infusion. At the end of 48 hours, diuresis was 60ml/h, and Cr level increased to 3,1 mg/dl. Peripheric congestion persisted. Mannitol was added to the treatment regime . Average diuresis increased to 212ml/h. At day 3, Cr was decreased to 1.8 mg/dl , NT-proBNP was 6230 pg/ml and pretibial oedema regressed . He was discharged with furosemide 80 mg.
We reported two cases of diuretic resistance one with HF with reduced EF(HFrEF) and one with HF with preserved EF(HFpEF) both of which were overcome by mannitol treatment . Despite escalating doses of furosemide infusion and inotropic

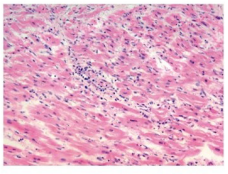
support, our attemps to decongest patient were complicated with worsening renal function. Diuretic resistance is an important clinical problem in patients with acute heart failure, particularly advanced HF and HfpEF with underlying renal disease. Mannitol is an osmotic diuretic that acts primarily on the loop of Henle and the proximal tubule where large amounts of sodium is reabsorbed by increasing the osmotic pressure of glomerular filtrate, thus inhibiting tubular reabsorption. It has the potential to increase diuresis on top of furosemide by sequential nephron blockade mechanism.
Conclusion and implications for clinical practice: Diuretic resistance is a frequent problem in acue HF. Adding mannitol on top of furosemide may be beneficial in these patients circumventing ultrafiltration.

1564

Acute heart failure due to myocarditis under mitral valve replacement in patient with active infective endocarditis

N Safarova[1]; A Pisaryuk[2]; N Povalyaev[1]; M Sorokina[1]; M Teterina[2]; A Chukalin[3]; E Kotova[4]; P Kakhktsyan[3]; I Merai[2]; J Karaulova[4]; A Safarova[2]; A Milto[2]
[1]M.V. Lomonosov Moscow State University, Moscow, Russian Federation; *[2]City Clinical Hospital No 64, cardiology department, Moscow, Russian Federation*; *[3]Bakoulev Center for Cardiovascular Surgery RAMS, Moscow, Russian Federation*; *[4]Peoples Friendship University of Russia (PFUR), Moscow, Russian Federation*

Introduction: Post-infectious immune-mediated myocarditis is an uncommon complication of an IE. IVIG may be used in myocarditis, both viral and autoimmune, particularly if aab-mediated.
Case description: A 69-year old white male patient with hypertension and prior stroke (1999; 2010) admitted to our hospital with fever (39-40C) for 3 months. Physical examination was notable for Lukin spots, digital clubbing and systolic murmur on the apex. TEE was performed, which showed myxomatous degeneration of the MV, vegetations and severe MR. IE was diagnosed and empiric therapy was started with oxacillin (12 g/day), ampicillin (12g/day) and gentamycin (240mg/day) end was changed on oxacillin after a positive blood culture (S. haemolyticus), then patient underwent CABG, mitral valve replacement with a mechanical prosthesis. Three weeks later he had an edema and a decrease in LVEF - 38%, GLPS -8,6% and enlarged LV (LVEDV 60 mm), NTproBNP level 3286 ng/ml. Coronarography was performed which ruled out a bypass failure. Further investigation revealed a high level of troponine I (0.9 ng/ml) and a positive IgG to Parvovirus B19. Myocardial perfusion imaging has showed LV dilatation and no signs of a focal scarring. Biopsy has showed a diffuse cellular infiltrate and a myocyte necrosis, positive viral PCR Parvovirus B19. The Patient was treated with 10 g human immunoglobulin G iv in addition to a standard therapy HF. After the therapy patient had a slight increase and a stabilization of LVEF 44%, GLPS -10.8%. Furthermore, contractility of the apical segments improved, but there still was hypokinesis in septal segments. After 3 months of follow-up after IG-therapy the patients had no clinical sings of heart failure.
Questions and issues: After a successful cardiac surgery, there are many reasons for the development of an acute heart failure, but the immune complications of endocarditis are rare. Myocarditis is the only complication for which treatment is possible with immunomodulation. The nature of the myocardial inflammation could not be clearly defined with a differential diagnosis between postviral (Parvovirus B19) and aab-mediated-myocarditis.
Answers and Discussion: The primary cause of the heart failure in this patient was myocarditis, although a coronary artery disease or a bypass failure could be excluded in a presence of multiple risk factors. Parvovirus-B19 can be a random findings in the myocardium. In our case, there was a normal IgM titer and a high IgG titer to Parvovirus-B19. Nevertheless, IVIG recommended to treat of both immune and postviral myocarditis.
Conclusion: Subacute long-term course of an infective endocarditis can lead to various immune complications, in rare cases to myocarditis that presents several diagnostic and treatment challenges, with a possibility of a favourable outcome in case of a timely treatment.



1565

Description of a clinical turning point after barostim therapy: is permanent atrial fibrillation always permanent?

G Giovanni Tilocca[1]; L Lazzari[1]; A Tordini[1]; C Marini[1]; S Donzelli[1]; G Carreras[1]; E Boschetti[1]; G Ambrosio[2]
[1]Az. Osp. "S. Maria", Cardiology Department, Terni, Italy; *[2]Hospital Santa Maria Della Misericordia, Cardiology Department, Perugia, Italy*

C.F. is a 70 years old man with an ischaemic cardiopathy resulting in ventricular dilatation and severe systolic dysfunction (FE 25%): in 2003 a coronary bypass grafting was performed (LIMA to LAD and two venous grafts, one to the posterior interventricular branch of the RCA and the other one to the first Obtuse Marginal branch), in 2014 a PTCA in proximal LAD was carried out.
The patient is suffering from chronic kidney disease (KDOQI- V stage) with severe hypertension due to a right renal artery stenosis previously treated with percutaneous transluminal angioplasty (PTA).
Because of renal disease, heart failure (HF) therapy was not optimized: being limited to a beta-blocker and a loop diuretic (furosemide), the former being directed to AF rate control as well.
As far as the atrial fibrillation was concerned, we decided to adopt a "rate control" strategy after several ineffective attempts to restore sinus rhythm.
In 2015 a CRT-D was implanted for primary prevention of sudden cardiac death.
A transthoracic echocardiogram performed in July 2015 showed severe dilatation of the LV (EDV 210 ml) with severe systolic dysfunction (Biplane EF 20%), dilatation of the left atrium (area 30 cm2), moderate secondary mitral regurgitation and systolic dysfunction of the RV (TAPSE 10 mm).
In the following months the patient was referred several times to our Unit for acutely decompensated chronic HF, he developed diuretic resistance and a progressive worsening in functional class (NYHA IV and a very poor 6 minute walking test).
The recurrence of several HF hospitalizations led us to implant an endovascular carotid baroreceptor stimulator in February 2016, that allowed to partially overcome diuretic resistance (the sequential nephron blockade therapy, that was our first strategy, was reduced to metolazone 2.5 mg once a week with stable dry weight maintenance) and to improve the functional class (NYHA III and an increase of the 6 minute walk distance) and the self-reported quality of life.
In September 2016 a spontaneous reversion to sinus rhythm from permanent atrial fibrillation (after 6 months of Barostim Therapy) was observed.
An echocardiographic follow-up showed an improvement of the echo parameters (EDV 180 ml, EF raised up to 38% and mild mitral regurgitation).
Thus, because of sinus rhythm restoration and cardiac state improvement, we decided to upgrade the device adding an atrial electrocatheter.
In conclusion this patient showed a dramatic clinical improvement after Barostim therapy with the restoration of sinus rhytm and, as a consequence, of the atrial contribution to the diastolic filling. Since the implantation of Barostim the patient has been no longer hospitalized for decompensated HF. The baroreflex activation therapy allowed the opportunity to antagonize neurohormonal activation, which could not have been persued by pharmacological therapy alone.

1566

Remote monitoring with cardiac implantable electronic device to follow-up pharmacodynamic effects of sacubitril/valsartan treatment: a case report

U O Turk[1]; E Alioglu[1]
[1]Central Hospital, Izmir, Turkey

Introduction: Cardiac implantable electronic devices (CIEDs) collect diagnostic information from continuous monitoring of several physiological variables. The variables includes intrathoracic impedance (ITI), patient activity (PA), and heart rate variability (HRV). Sacubitril/Valsartan is recommended by current guidelines as foundational therapy for patients with symptomatic HFrEF.
However, temporal relationship between sacubitril/valsartan treatment and these variables has not yet been reported.

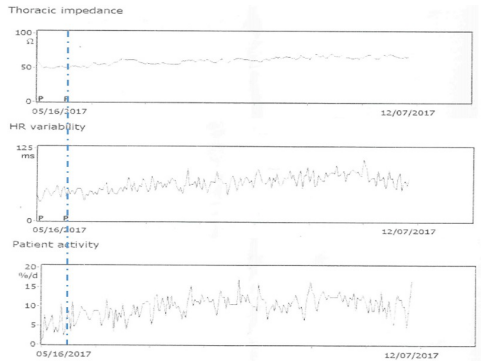


Figure.

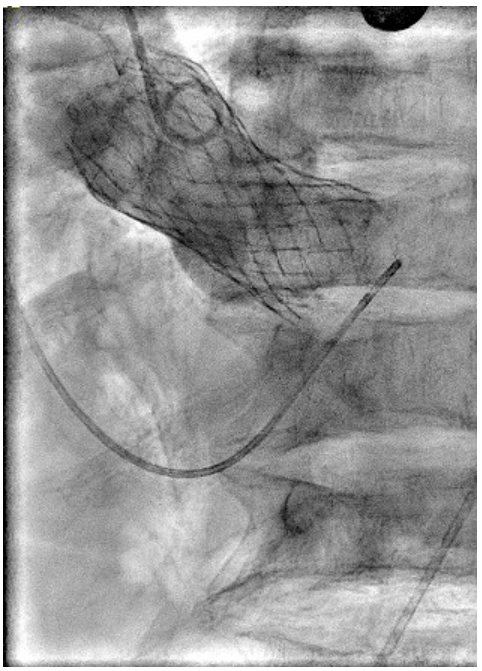
Case Report: A 59-year-old physician with HFrEF admitted to with exertional dyspnoea. He has a past medical history of CABG operation, and a dual chamber ICD (Itrevia 5 DR-T, Biotronik, Berlin, Germany) implantation at May 2017. He was receiving Ramipril 10 mg od, atorvastatin 40 mg od, carvedilol 12.5 mg bid, furosemide 40 mg od, spironolactone 25 mg od, aspirin 100 mg od and insulin therapy. Blood pressure was 125/80 mmHg, heart rate was 88 bpm. Transthoracic echocardiography demonstrated akinetic left ventricular septum, anterior wall and apex. Left ventricular ejection fraction calculated as 32% with modified Simpson method. ICD counter revealed no any atrial or ventricular pacing. Serum B-type natriuretic peptide level was 105 pg/mL (normal <35 pg/mL). After comprehensive evaluation, ramipril 10 mg treatment was replaced with Sacubitril/Valsartan 97/103 mg twice daily. at June 2017. The patient admitted to outpatient clinic for scheduled visit six months later. Patient reported improving his symptoms of exertional dyspnoea, fatigue as well as increasing in his ordinary physical activities. ICD interrogation revealed stable increasing in ITI (from 51 to 73 ohm), HRV (from 42 to 66 millisecond) and PA values (from 5% to13%/day). (Figure)
Discussion: PARADIGM-HF trial demonstrated the superiority of sacubitril/valsartan over enalapril on physical capacity and symptoms, quality of life which measured with Kansas City Cardiomyopathy Questionnaire (KCCQ). KCCQ have limitations such as absence of appropriate reference standards for the various domains, and its patients' perspective fashion (subjectivity). Investigators and many physicians often rely on physiologic variables, such as LVEF or NT-proBNP levels to monitor therapy in HFrEF population. However, such surrogate markers may not always be useful. CIEDs include remote monitoring functions allow to monitor particular physiologic function day by day. They serve objective measurements with high temporal resolution that permitting to follow any trend. In this case, patients' self-reported improvements in symptoms and PA levels confirmed by CIED monitoring functions objectively. To the best of our knowledge, this is the first case documenting improvements in ITI, PA, and HRV levels with sacubitril/valsartan treatment. CHILISALT Study (NCT03359967) will obtain more information in these patient population.
Figure Legend: Vertical lines denotes the date of sacubitril/valsartan initiation.

1567

Transcatheter aortic valve implantation in a patient with sickle-cell disease

E Zhiduleva[1]; O Moiseeva[1]; D Strelkov[1]; D Zverev[1]
[1]*Almazov National Medical Research Centre, Saint Petersburg, Russian Federation*

Introduction: Heart diseases represent a significant cause of mortality and morbidity in hereditary haemoglobin disorders. Peri-operative hemolysis is the serious problem during open-heart surgery. We report a case of successful transcatheter aortic valve implantation (TAVI) in a patient with sickle-cell disease (SCD).



Description. A 64-year-old Caucasian man was hospitalized because of deterioration of congestive heart failure. Clinical sympthomps included dispnea, orthopnea, massive lower limb edema and repeated syncope associated with excercise. He had a past medical history of SCD with vaso-occlusive crises from the age of 35. Hemoglobin level was 90 g/l. Heart chambers dilation with reduced left ventricular systolic function (LVEF = 31%) was revealed by ECHO. Severe aortic valve stenosis (peak aortic jet velocity 4 m/sec, mean gradient 33 mmHg, AVA 0.9 cm2) and severe pulmonary hypertension (systolic pulmonary arterial pressure (PAP) 83 mm Hg) were also detected. The coronary angiography showed normal vessels, but the patent ductus arteriosus (PDA) was presented by aortography. The transcatheter occlusion of PDA was performed as the first step. Because of high risk of hemorrhagic complications the patient underwent TAVI (transfemoral access). Blood transfusion was performed before surgery. At the the 6th day of the postoperative period a permanent pacemaker was implanted because of the transient complete atrioventricular block. We didn't observe significant hemoglobin level decrease, major bleedings, stroke or vascular complications in postoperative period. Control ECHO after TAVI described decrease of systolic PAP (67 mm Hg). Paravalvular aortic regurgitation wasn't presented. Despite the absence of left ventricular systolic function improvement dyspnea reduced (Borg from 8 to 4), six-minute walk distance increased from 150 to 300 m.
Discussion: Acceleration of degerative aortic stenosis formation in patient with tricuspid aortic valve and SCD might be potentially associated with high output state and elastic tissue defects. Left ventricular disfunction is described in hereditary haemoglobinopathies, its pathogenetic mechanisms include high output state, iron overload, vascular disease, myocardial ischaemia, myocarditis, and valvular disease too. Pulmonary hypertension occurs in approximately one third of patients with homozygous SCA and has multifuctorial mechanisms due to haemolysis, impaired nitric oxide bioavailability, chronic hypoxaemia, thromboembolism, parenchymal and vascular injury because of sequestration of sickle erythrocytes. Additional impact to increased PAP was done by left heart disease and PDA. The preferable method of treatment in this case was TAVI. The most significant complication we observed was complete atrioventricular block that was described as one of the most common complications seen after TAVI.
Conclusion: TAVI is considered as a safely procedure in patients with SCD that could improve their life quality.

1568

Treatment of cardiorenal syndrome with haemodialysis: a case report

B Leskovar[1]; T Furlan[1]; S Poznic[1]; D Kosuta[1]; A Adamlje[2]
[1]*Trbovlje General Hospital, Department of Internal Medicine, Trbovlje, Slovenia*;
[2]*Trbovlje General Hospital, Department of Hemodialyisis, Trbovlje, Slovenia*

Introduction: Cardiorenal syndrome (CRS) is characterised by diuretic-resistant heart failure with congestion and concomitant progressive worsening of kidney

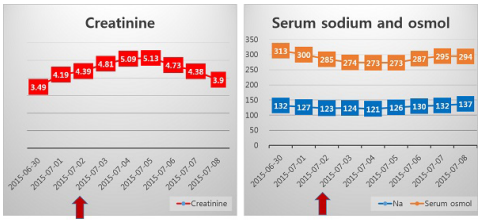
function, even more pronounced with up-titration of heart failure therapy. Ultrafiltration has been proposed as an alternative to diuretics in severe congestion in ESC guidelines (class IIa, evidence level B). The effect of chronic haemodialysis (HD) on long-term outcome and survival in CRS has not yet been extensively evaluated.
Case report: 64-year-old patient with arterial hypertension, diabetes type 2, paroxysmal atrial fibrillation, PAD, COPD and Pickwick syndrome was admitted to our hospital in June 2015 due to first decompensation of heart failure with preserved ejection fraction and concomitant acute worsening of chronic kidney disease. We introduced heart failure therapy with beta blocker, diuretic and angiotensin receptor blocker. In the next 18 months, he was hospitalized 6 times for decompensated heart failure and required several thoracenteses and abdominal paracenteses despite maximal dose of diuretic. Due to hyperkalaemia and progressive worsening of kidney function we could not successfully titrate the dose of angiotensin receptor blocker. He was persistently NYHA class IV with poor quality of life. In March 2017, during another heart failure decompensation, we decided to start with chronic HD. We inserted a tunnelled central venous catheter through the right internal jugular vein and started with low-efficiency bicarbonate HD three times a week. Since the start of HD, he was not hospitalized for to heart failure, his weight decreased for 22 kg, we up-titrated angiotensin receptor blocker to target dose (chronic HD assured good electrolyte control), his quality of life increased significantly, he is currently NYHA II functional class (6MWT) and requires no nocturnal BiPAP support anymore. In the last months, we were able to reduce the frequency of HD to twice a week.
Discussion: Between July 2004 and January 2015, we have treated 67 heart failure patients with HD. Indications for HD were terminal, symptomatic heart failure in NYHA IV patients with uncontrollable hypervolemia and/or metabolic acidosis and/or hyperkalaemia. All patients were receiving maximally-tolerated dose of diuretics and most of them were treated with inotropes and vasopressors before starting HD. We observed a significant decrease in hospitalization rate due to heart failure after the start of HD (before HD: $0,79 \pm 1,32$; after the start of HD $0,22 \pm 0,65$, $p = 0,001$) and a significantly longer survival of NYHA IV patients (1-year survival 81%, 3-year 52%, 5-year 39%)
Conclusion: In our experience, chronic HD is a feasible, safe and effective treatment modality in NYHA IV heart failure patients with uncontrollable hypervolemia, acidosis and hyperkalaemia as a bridge to definite therapy and for patients who are not candidates for heart transplantation.

1569

Impact of tolvaptan in acute heart failure who did not respond to loop diuretics alone

SK Lee[1]; MS Park[1]; SW Choi[1]; JC Youn[1]; SW Han[1]; EJ Kim[2]; KH Ryu[1]
[1]Hallym University, Cardiovascular center , Dongtan, Korea Republic of; *[2]Korea University Guro Hospital, Cardiovascular Center, Korea University Guro Hospital, Seoul, Korea Republic of*

Introduction: Patients with acute heart failure (AHF) and renal dysfunction have prolonged hospital admission and high mortality rates. More efficacious and safer decongestive therapy is clearly needed, but optimal treatment strategies remain unclear.
Case: A 63-year-old female with a chronic kidney disease (CKD, stage IV) visited for newly onset chest pain. She had a history of percutaneous coronary intervention (PCI) in left anterior descending (LAD) and left circumflex artery 1 year ago. On admission, her laboratory tests revealed serum creatinine of 3.46 mg/dL, serum sodium 132 mmol/L, CK-MB 7.88 ng/mL, Troponin T 0.243 ng/mL. Coronary angiography revealed multiple severe restenosis in a previous stent in the LAD. Next day, the patient underwent PCI in the LAD with two drug-eluting stents and follow-up angiogram showed good immediate results. However, her renal function worsened after PCI and urine volume reduced gradually along with progression of dyspnea regardless of incremental doses of intravenous furosemide (max: 320mg/day). At day 3 after PCI, her serum creatinine increased up to 4.81 mg/dL, and sodium level gradually decreased to 124 mmol/L. Because she had no option other than hemodialysis, we decided to start tolavaptan as the last option. After administration of tolvaptan, her urine volume started to increase eventually even in condition with increasing serum creatinine levels. At day 5 from tolvaptan administration, her congestion was successfully treated with decreased levels of serum creatinine. Serum sodium level was also restored to 137 mmol/L without any neuorologic symptoms (Figure). She recovered without any sequelae and discharged at the day 15 of admission. At 3 months follow-up, her performance status was excellent, and her creatinine level decreased to 3.12 mg/dL. Problems: Patients with diuretic resistance may require higher diuretic doses, and even more dosage is needed when renal dysfunction is combined, and this may result to worsening of renal function in the acute phase of HF. In addition, loop diuretics which are most commonly used in HF patients may increase the neuro-hormonal cascade, which is detrimental for the patients of AHF.
Discussion: Tolvaptan shows an effect by antagonizing the V2 receptors present in the collecting ducts in kidney, and produces diuresis largely by increasing free water diuresis. This may explanation for no further worsening of the renal function even in situation of increasing urine volume in our case. In contrast to loop diuretics, tolvaptan acts as a diuretic without activating the neuro-hormonal system. This may result in the improvement in pulmonary edema, and symptoms of heart failure without progressive deterioration of LV function.
Conclusions: Our present findings indicate that the administration of tolvaptan might be considered in AHF patients with renal insufficiency who show no response to loop diuretics.



Tolvaptan 15mg with IV continuous furosemide (320mg/day)

1570

Importance of tissue characterization with cardiac magnetic resonance in diagnosis of acute myocarditis

M Shah[1]; H Singh[2]; R Rastko Rakocevic[3]; A Lucev[2]; B Kim[2]; R Berkowitz[2]; K Satya[2]
[1]New Jersey Medical School, Cardiology, Newark, United States of America; *[2]Hackensack University Medical Center , Cardiology, Hackensack, United States of America*; *[3]New Jersey Medical School, Internal Medicine, Newark, United States of America*

Acute myocarditis can progress to chronic myocarditis or dilated cardiomyopathy that has poor prognosis. Cardiac magnetic resonance CMR can delineate the severity of myocarditis for risk stratification and can help guide management with its tissue characterization properties.
A 35 year old otherwise healthy Ecuadorian soldier presented to the emergency room with sudden onset of substernal chest pain, dyspnea, rigors and chills. His ECG showed sinus tachycardia at 171 beats/min and ST segment elevation in the infero-lateral leads. Initial troponin and BNP were 117 ng/mL and 1850 pg/mL, respectively. Emergent cardiac catheterization showed no coronary artery lesions and a left ventricular ejection fraction (LVEF) < 15% by ventriculogram. Intra-aortic Balloon Pump (IABP) was placed and hemodynamics measurements by pulmonary artery catheterisation showed right atrial pressure of 12 mm Hg, mean pulmonary artery pressure 41 mm Hg, pulmonary artery wedge pressure of 33 mm Hg, systemic vascular resistance of 17 wood units and cardiac index of 2.7 L/min/m2. Mean arterial pressure was 78 mm Hg while on high dose norepinephrine and IABP support. Transthoracic echocardiogram showed LVEF of < 20% and global hypokinesis.
Further workup to determine the etiology of myocardial dysfunction was negative for rheumatoid factor, antinuclear antibody, RPR, lyme ELISA. Blood cultures and virology PCR (including for adenovirus, HHV-6, HIV, Parvovirus, CMV, Coxsackie A/B, EBV) were all negative. With mechanical ventilation, low dose norepinephrine and broad spectrum IV antibiotics patient improved clinically in 48-72 hours. Blood cultures remained sterile. Repeat transthoracic echocardiogram five days from admission revealed left ventricular ejection fraction of 40%. CMR was performed one week after presentation. There was diffuse hypokinesis of the left ventricle on cine images with LVEF of 46%. Right ventricular function and tissue characterization were normal. Short TI inversion recovery (STIR) images with triple inversion recovery showed increased intensity suggesting diffuse myocardial edema affecting all myocardial walls. On late gadolinium enhancement (LGE) images, there was diffuse hyperenhancement of all myocardial segments from base to apex. Basal to apical septum had mid myocardial hyperenhancement whereas the remaining myocardium showed subepicardial hyperenhancement with sparing of the endocardium. All these findings are suggestive of acute myocarditis.
Novel CMR techniques such as native T1 mapping, extracellular volumes (ECV) of distribution and T2 mapping have shown promising results in the assessment of myocarditis. ECV quantification and LGE imaging markedly improved diagnostic accuracy for myocarditis compared to Lake Louise criteria. This case is a perfect example of using these CMR techniques to make a definitive diagnosis of acute myocarditis in the setting of severe myocardial dysfunction with negative standard workup.

Acute heart failure: how to improve survival

1615

The usefulness of the MEESSI score for risk stratification of patients with acute heart failure at the emergency department: validation in a new Spanish cohort.

O Miro[1]; X Rossello[2]; V Gil[1]; H Bueno[2]; P Llorens[3]; FJ Martin-Sanchez[4]; J Jacob[5]; P Herrero-Puente[6]; R Escoda[1]; S Aguilo[1]; C Sanchez[1]; J Marco-Hernandez[1]; G Martinez[1]; V Rico[1]; SJ Pocock[2]
[1]Hospital Clinic de Barcelona, Emergency Department, Barcelona, Spain; [2]National Centre for Cardiovascular Research (CNIC), Madrid, Spain; [3]General University Hospital of Alicante, Emergency Department, Alicante, Spain; [4]Hospital Clinic San Carlos, Emergency Department, Madrid, Spain; [5]University Hospital of Bellvitge, Emergency Department, Barcelona, Spain; [6]University Hospital Central de Asturias, Emergency Department, Oviedo, Spain

On behalf of: ICA-SEMES Research Group
Funding Acknowledgements: ISCIII (Spanish Ministry of Health) and FEDER (PI15/01019 and PI15/00773), Fundació La Marató de TV3 (2015/2510) and Calalan Govern (GRC 2014/0313)

Aims: The MEESSI (Multiple Estimation of risk based on the Emergency department Spanish Score In patients with acute heart failure –AHF-) scale is a new tool to stratify AHF patients at the emergency department (ED) according to the 30-day mortality risk. We aimed to validate the MEESSI risk score in a new cohort of Spanish patients to assess its accuracy in stratifying patients by risk and to compare its performance in different settings.
Methods: We included consecutive patients diagnosed with AHF in 30 EDs during January and February 2016 (60 fays). The MEESSI score was calculated for each patient. The area under the curve of the receiver operating characteristic (AUC ROC) measured the discriminatory capacity to predict 30-day mortality of the MEESSI full model (13 variables) and the 7 secondary models (lacking the Barthel Index, troponin or NT-ProBNP, in any combination). Further comparisons were made between subgroups of patients from university and community hospitals, EDs with high, medium or low activity and EDs that recruited or not patients in the original MEESSI derivation cohort.

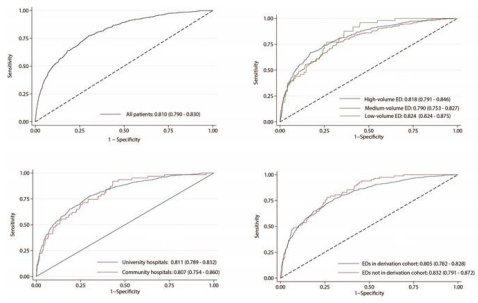


Figure 1

Results: We analyzed 4711 patients (university/community hospitals: 3811/900; high-/medium-/low-activity EDs: 2695/1479/537; EDs participating/not participating in the previous MEESSI derivation study: 3892/819). The distribution of patients according to the MEESSI risk categories was: 1673 (35.5%) low-risk, 2023 (42.9%) intermediate-risk, 530 (11.3%) high-risk and 485 (10.3%) very high-risk, with 30-day mortality of 2.0%, 7.8%, 17.9% and 41.4%, respectively. The AUC ROC for the full model was 0.810 (95% CI: 0.790-0.830), and ranged from 0.731 to 0.785 for the subsequent secondary models. The discriminatory capacity of the MEESSI risk score was similar among subgroups of hospital type, ED activity, and original recruiter EDs (Figure 1).

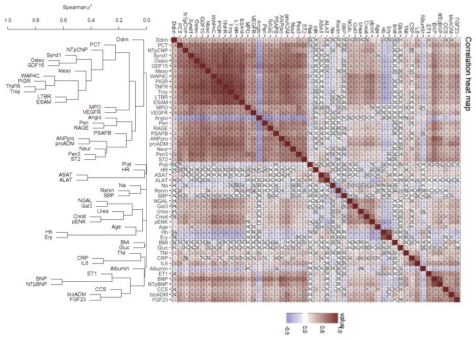
Conclusion: The MEESSI risk score successfully stratifies AHF patients at the ED according to the 30-day mortality risk, potentially helping clinicians in the decision-making process for hospitalizing patients.

1617

Bio-adrenomedullin is strongly related to congestion and poor outcome in patients with worsening heart failure

J M Jozine Ter Maaten[1]; D Kremer[1]; BG Demissei[1]; J Struck[2]; AA Voors[1]
[1]University Medical Center Groningen, Groningen, Netherlands; [2]Sphingotec, Hennigsdorf, Germany

Background: Adrenomedullin (ADM) is a vasodilatory hormone with natriuretic effects that has been postulated to play a role in tissue congestion. Its specific pathophysiological function however remains unclear. We therefore evaluated clinical and biological factors associated with plasma biologically active ADM (bio-ADM).
Methods: Plasma bio-ADM was measured in 2,189 patients with acute or worsening heart failure enrolled in the BIOSTAT-CHF study. We utilized regression models and network analysis tools to identify associations of bio-ADM with clinical and biological variables. Prognostic value of bio-ADM was analyzed using Cox regression.
Results: Acute or worsening heart failure patients with higher bio-ADM levels were significantly older, had a higher BMI and NYHA class and had more signs and symptoms of congestion (all $p < 0.01$). In multivariable regression analysis, higher plasma bio-ADM levels were associated with higher BMI and more severe edema, as well as higher FGF23, aldosterone, and CRP levels (all $p < 0.03$). Conversely higher plasma bio-ADM was significantly associated with lower sodium levels. Interestingly, plasma bio-ADM clustered strongly with markers of congestion, such as FGF23, (NT-pro)BNP and a clinical congestion score (CCS). Plasma bio-ADM was independently associated with an increased risk of all-cause mortality and heart failure rehospitalization (Hazard ratio: 1.18 per log increase (1.08-1.30), $p < 0.001$).
Conclusions: Bio-ADM is strongly associated with clinical variables and biomarkers related to congestion, RAAS activation and inflammation. Also, higher bio-ADM levels are associated with an increased risk of adverse outcome. As such, bio-ADM may play a significant role in heart failure pathophysiology and might be used for risk stratification and to guide treatment.



Heatmap bio-ADM in worsening HF

1619

Catherter-based enhancement of lymphatic drainage in fluid overloaded acute decompensated heart failure: First in human experience

D Dan Haberman[1]; M Jonas[1]; L Zilberman[1]; I Fungenfirov[1]; S Goland[1]; K George[1]; MR Costanzo[2]; WT Abraham[3]
[1]Kaplan Medical Center, Heart Center, Rehovot, Israel; [2]Advocate Heart Institute, Naperville, United States of America; [3]Ohio State University Hospital, Division of Cardiovascular Medicine, Ohio, United States of America

Funding Acknowledgements: WhiteSwell

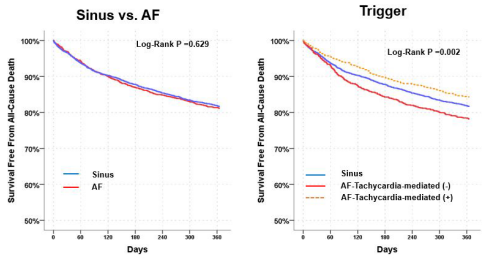
Background: Fluid overload leading to pulmonary and peripheral edema causes about 90% of all acute decompensated heart failure (ADHF) admissions. This excess in extracellular fluid volume resides in both the intravascular and interstitial spaces. Removal of fluid from the intravascular space is usually accomplished with diuretic therapy, while there is currently no direct means for enhancing fluid removal from the interstitial space, frequently resulting in intravascular volume depletion, hypotension, worsening renal function (WRF), and poor patient outcomes. We evaluated a novel catheter-based system for the enhancement of lymphatic drainage in a first-in-human proof of concept study.
Methods: The White Swell System (White Swell Medical Ltd, Herzliya, Israel) increases the movement of interstitial fluid, via enhanced lymphatic system drainage, to the intravascular space and thus enables total body fluid volume excess to be removed from the body via the kidneys. This prospective, multi-center, single arm study evaluated the safety, feasibility, and preliminary efficacy of the White Swell System in in ADHF patients. Performance measures of interest included device functioning, volume removal (diuresis), and changes in renal function, during treatment.
Results: Ten hospitalized ADHF patients with signs of fluid over load were enrolled and 8 underwent the procedure; 2 patients did not complete the procedure due to technical issues. The average age was 73 ± 6.7 years; 75% were men; 62.5% had reduced left ventricle ejection fraction (mean 29.25 ± 8.1%). On average, procedure duration was 6.4 ± 2.44 hours, reduction in CVP was 6.4 ± 4.3 mmH2O, urine output was 1.76 ± 0.45 liters, and no WRF was observed. In fact, there was a mild post procedure reduction of creatinine levels seen in 7 out of 8 patients. There were no serious adverse events related to the procedure and no readmissions at 30-day follow up.
Conclusion: In this pilot study, we found the White Swell system to be safe and feasible with initial promising results for the reduction of total body fluid overload in patients with ADHF. The combination of high volume diuresis with preservation or slight improvement in renal function supports additional clinical trials of this approach.

1620
The effect of trigger on the prognosis of patients with heart failure and atrial fibrillation: tachycardia-mediated acute decompensation

J J Jin Joo Park[1]; IY Oh[1]; DJ Choi[1]
[1]*Seoul National University Bundang Hospital, Division of Cardiology,, Seongnam, Korea Republic of*

On behalf of: Korea Acute Heart Failure (KorAHF) Registry Investigators
Funding Acknowledgements: This work was supported by Research of Korea Centers for Disease Control and Prevention [2010-E63003-00, 2011-E63002-00, 2012-E63005-00, 2013-E63003-0

Background: Atrial fibrillation (AF) is common in heart failure (HF) patients. There exists controversy on the prognostic value of AF in HF patients. Patients with AF and HF, who experience acute decompensation mediated by tachycardia may have different prognosis than those whose decompensation is triggered by other factors, because tachycardia may be an acute and reversible event.
Purpose: We investigated the effect of tachycardia-mediated acute decompensation on the clinical outcomes.
Methods: The Korea Acute Heart Failure (KorAHF) registry consecutively enrolled 5,625 patients. The trigger for acute decompensation was classified as either tachycardia-mediated (TM) or not. Atrial fibrillation was confirmed in ECG taken during hospital admission. The primary outcomes were in-hospital mortality and 1-year all cause mortality according to rhythm and trigger.



1-Year All Cause Mortality

Results: Among 5,625 patients, 3665 (65%) patients had sinus rhythm and 1961 (35%) had AF. Among patients with AF, 928 (47%) had TM acute decompensation. Patients with sinus rhythm was older than those with AF (Sinus: 67 ± 15 years, AF-TM(-): 71 ± 12 years, AF-TM (+): 70 ± 12 years, P < 0.001). Patients with AF-TM(+) had lowest NT-proBNP level (sinus: 9900 ± 11464 pg/microL, AF-TM(-): 8252 ± 9296 pg/microL AF-TM (+): 7462 ± 8945 pg/microL, P < 0.001).
Regarding the clinical outcomes, patients with AF-TM(+) had the lowest in-hospital mortality (Sinus: 5.1%, AF-TM(-): 6.5%, AF-TM (+): 1.7%, P < 0.001). In multivariable analysis, AF-TM (+) was associated with 53% reduced risk (HR, 0.47; 95% CI, 0.24-0.93).
Regarding the 1-year all-cause death, there was no difference in 1-year survival between patients with sinus and AF (P = 0.629). When stratifying the patients according to trigger, AF-TM(+) had the best prognosis, followed by those with sinus rhythm, while AF-TM(-) had the worse prognosis (P = 0.002). However, in multivariable analysis, AF-TM (+) was not associated with reduced risk for 1-year all-cause mortality (HR, 0.91; 95% CI, 0.71-1.17).
Conclusions: HF patients with AF whose acute decompensation is triggered by tachycardia have better in-hospital but similar post discharge outcomes like HF patients with sinus rhythm or those with AF who are decompensated by other factors.

1624
Clinical manifestations and outcome of acute heart failure in Chagas cardiomyopathy patients in comparison do other etiologies: results of the I Brazilian Heart Failure Registry

MV Marcus Vinicius Simoes[1]; CH Miranda[1]; DC Albuquerque[2]; LC Danzmann[3]; S Rassi[4]; HP Guimaraes[5]; MF Canesin[6]; LEP Rohde[7]
[1]*Medical School of Ribeirão Preto - University of São Paulo, Brazil, Ribeirão Preto, Brazil*; [2]*State University of Rio de Janeiro (UFRJ), Cardiology, Rio de Janeiro, Brazil*; [3]*Lutheran University of Brazil, Cardiology, Porto Alegre, Brazil*; [4]*Federal University of Goias, Cardiology, Goiania, Brazil*; [5]*Hospital for the Heart (Hcor), Cardiology, Sao Paulo, Brazil*; [6]*University Hospital, State University of Londrina, Cardiology, Londrina, Brazil*; [7]*Federal University of Rio Grande do Sul, Cardiology, Porto Alegre, Brazil*

On behalf of: BREATHE - Brazilian Heart Failure Registry
Funding Acknowledgements: DEIC - Heart Failure Department of the Brazilian Society of Cardiology

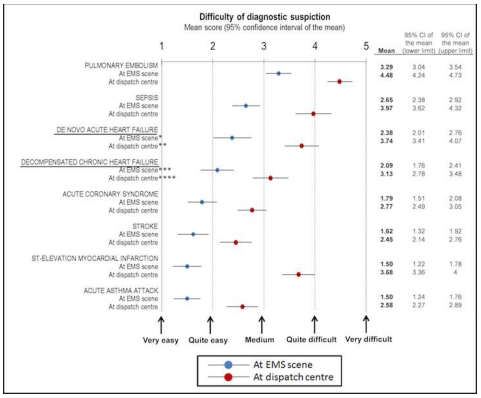
Background: Chagas cardiomyopathy (CC) is a prevalent cause of heart failure in Latin America countries and has recently been spread to Europe owing globalization and migratory waves from endemic regions. Studies describing clinical manifestations and outcomes of heart failure associated to CC are scarce and restricted to single center reports.
Purpose: Report the results of the I Brazilian Heart Failure Registry (BREATHE) addressing the clinical characteristics and outcomes of patients with acute heart failures (AHF) due to CC in comparison to other etiologies.
Methods: BREATHE was a multicenter observational nationwide prospective registry, conducted in 51 Brazilian hospitals, including private and public institutions, from different Brazilian regions. BREATHE included 1,253 patients, >18 years-old patients hospitalized with primary diagnosis of AHF. We proceeded the comparative analysis between patient group with CC etiology (n = 136, 10.9% of the sample) and patients with other etiology (n = 1,117, 89.1% of the sample), concerning demographic, physical examination changes at admission, non-invasive clinical/hemodynamic profile, LVEF on Echocardiogram, use of intravenous inotropic drugs, and death rate during hospital stay and 3, 6 and 12 months after discharge. The categorical variables were compared by using Fisher Exact test and the continuous variables were compared by using Mann-Whitney non-parametric test.
Results: CC patients, in comparison to other etiologies, were younger (62.5 ± 15.2 vs 69.9 ± 16.1 y.o., p < 0.01), presented lower systolic blood pressure (104.2 ± 24.9 vs 127.0 ± 31.4 mmHg, p < 0.001), lower heart rate (76.8 ± 23.3 vs 89.1 ± 22.3 bpm, p < 0.001), lower rate of jugular vein distension (63.2% vs 44.8%, p < 0.001) and hepatomegaly (59.6% vs 34.4%, p < 0.001), lower rate of pulmonary crackles (64.0% vs 73.7%, p = 0.022), higher rate of "cold and wet" clinical hemodynamic profile (36.0 vs 15.7%, p < 0.001), larger diastolic left ventricular diameters (68 [57.2 - 74.0] mm, p = 0.017), lower left ventricular ejection fraction (29.5 [22.2 - 35.5]% vs 37 [26.0 - 49.8]%, p < 0.001), higher rates of intravenous inotropic drugs use (31.5% vs 12.4%, p < 0.001). The CC patients in comparison to non-CC patients presented higher cumulative death rate during hospital stay (20.6% vs 11.7%, p = 0.009), and after discharge at 3-months (34.3% vs 22.1%, p = 0.002, at 6-months (41.0% vs 27.7%, p = 0.002, and at 12-months (53.4% vs 37.8%, p = 0.001).
Conclusions: Patients hospitalized with AHF with CC etiology, in comparison to other etiologies, present more prominent physical signs of systemic congestion, lower arterial blood pressure, more severe left ventricular systolic dysfunction and remodeling, more frequent low cardiac output manifestations and higher use of intravenous inotropic drugs. This higher risk profile was associated to a poorer outcome both in-hospital and after discharge.

1626

The perceived difficulty of identifying acute heart failure in dispatch centre and by emergency medical services on scene compared to other critical medical conditions

P Harjola[1]; VP Harjola[1]; M Kuisma[1]; M Christ[2]; X Escalada[3]; F Martin-Sanchez[4]; O Miro[5]
[1]Helsinki University Hospital, Emergency Care, Helsinki, Finland; *[2]Luzern Hospital, Emergency department, Luzern, Switzerland*; *[3]Hospital Clinic de Barcelona, Sistema d'Emergéncies Médiques, Catalunya, Barcelona, Spain*; *[4]Hospital Clinic San Carlos, Emergency department, Madrid, Spain*; *[5]Hospital Clinic de Barcelona, Emergency department, Barcelona, Spain*

Background: Acute heart failure (AHF) is one of the most important causes for hospital admission. The prehospital treatment of AHF is a novel topic in the recent literature. Real-life data about the readiness of dispatch centres and emergency medical services (EMS) to treat and diagnose AHF is scarce.
Purpose: Our main interest was to find out the difficulty of EMS and dispatch centre to identify AHF. Secondly, we wanted to compare the difficulty of identifying AHF to other common cardiovascular conditions taken care by EMS.
Methods: A survey was sent to EMS leaders on charge of EMS regions covering more than 20% of the countries' population. The study was designed to cover 12 different European countries (Finland, Denmark, Sweden, Norway, Germany, Poland, Czech Republic, France, Spain, Italy, Switzerland, and United Kingdom). The survey included five common conditions: decompensated chronic heart failure (CHF), de novo AHF, stroke, ST-elevation myocardial infarction (STEMI), acute coronary syndrome (ACS), pulmonary embolism (PE), acute asthma attack (AAA), and sepsis. Difficulty of identifying these conditions was graded through a 5-points qualitative scale from very easy to very difficult. Difficulty was compared between EMS and dispatching centre and among the conditions. For comparisons between decompensated CHF and de novo AHF, we used chi-square test. For comparisons between dispatch centre and EMS and between medical conditions results we transformed into quantitative variables and compared by one-way ANOVA.



Diagnostic difficulties in EMS

Results: We received 34 surveys from 3 countries fulfilling the inclusion criteria: 19 from Spain (covering 40.0 million citizens, 86.0% of the population), 9 from Switzerland (covering 2.3 million, 27.1% of population) and 6 from Finland (covering 3.5 million, 63.3% of population). The percentages of responders considering suspicion of decompensated CHF/de novo AHF at dispatch centre as very or quite easy was 29.0/6.5, medium 38.7/35.5, and quite or very difficult 32.3/58.1 ($p = 0.034$ for comparison between decompensated and de novo), while identifying these conditions by EMS was considered very or quite easy in 64.8/55.9, medium in 29.4/29.4, and quite of very difficult in 5.9/14.7 ($p = 0.471$). For all conditions surveyed, difficulty in suspecting these conditions was higher in dispatch centre than in EMS ($p < 0.001$ in all comparisons). The perceived difficulty in identifying the 8 conditions are shown in Figure .
Conclusions: Interestingly, it is considered rather easy to detect de Novo AHF and decompensated CHF in EMS. Whereas in dispatch centre it is rather difficult. Also, a surprising finding is that identifying decompensated CHF is considered easier than de novo AHF. The study also showed that it is more difficult to detect AHF than AAA, STEMI, stroke and ACS but easier than sepsis and PE. A prospective observational study is needed to confirm these findings.

1628

The relationship between peripartum cardiomyopathy with age and other risk factors

SK Lee[1]; MS Park[1]; SW Han[1]; KH Ryu[1]; EJ Kim[2]
[1]Hallym University, Cardiovascular center , Dongtan, Korea Republic of; *[2]Korea University Guro Hospital, Cardiovascular Center, Korea University Guro Hospital, Seoul, Korea Republic of*

Funding Acknowledgements: This study was funded by the Ministry of Health & Welfare, Republic of Korea (Grant Number: HI16C0483)

Background: Peripartum cardiomyopathy (PPCM) is a significant cause of maternal morbidity and mortality, yet its etiology remains unclear. No comprehensive evaluation of the relationship between age and PPCM exists. In addition, little is known regarding the implications of risk factors in PPCM patients.
Purpose: The purpose of this study was to evaluate the associations across quartiles of maternal age and the incidence of PPCM. Moreover, we sought to evaluate not only for independent risk factors of PPCM but also whether the clustering of risk factors of PPCM has a greater impact on PPCM prevalence.
Methods: A systematic search strategy was performed by using the Korea National Health Insurance Claims Database of the Health Insurance Review and Assessment Service.
Results: Patients with PPCM were older compared to control (32.1 ± 4.3 vs 30.9 ± 4.1, < 0.001). Moreover, when divided into quartiles based on age, old maternal age was linearly associated with increasing prevalence of PPCM (P for trend $<$ 0.001, Table). In multivariate analysis, Age = 35 years (OR 1.56, 95% CI 1.32 - 1.83), primiparity (OR 1.18, 95% CI 1.02 - 1.37), multiple pregnancy (OR 2.19, 95% CI 1.64 - 2.93), cesarean section (OR 2.59, 95% CI 2.15 - 3.14), preeclampsia (OR 6.02, 95% CI 4.94 - 7.34), and gestational DM (OR 1.70, 95% CI 1.26 - 2.29) were significantly correlated with PPCM. Intriguingly, the rate of PPCM was exponentially increased when clustering risk factors, and was approximately 200 times greater in patients with = 6 risk factors than in those with none.
Conclusions: The incidence of PPCM was linearly associated with mother's age at birth. PPCM patients were older, more associated with primiparity and multiple pregnancy, and had more pregnancy related complications than control. In addition, the number of risk factors amplifies the PPCM, emphasizing more intensive monitoring on those at high risk.

Table

	Age	P trend†			
	Q1	Q2	Q3	Q4	
Age	<29.9	30-34.9	35-39.9	≥40	
Total delivery number	488,135	653,890	213,164	28,465	
PPCM number	204	363	193	35	
Incidence of PPCM	1:2,393	1:1,801	1:1,104	1:813	<0.001
OR, risk factor adjusted*	1	1.25	1.78	1.96	<0.001

Incidence of peripartum cardiomyopathy in relation to quartiles of age

1616

New renal hemodynamic indices can predict worsening of renal function in acute decompensated heart failure

M Magdy Abdelhamid[1]; K Said[1]; W Ammar[1]; A El Taweel[2]; A Mostafa[1]
[1]Cardiology Department , Cairo University, Cairo, Egypt; *[2]Cairo University, Clinical pathology, Cairo, Egypt*

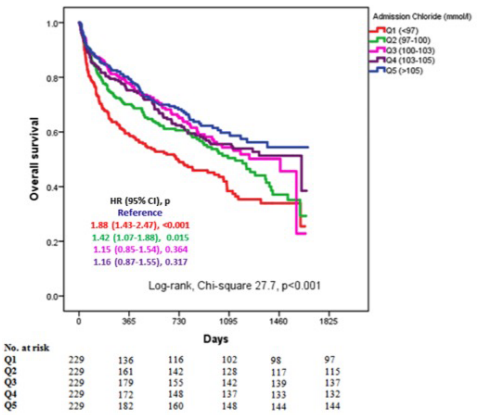
Background: Combined disorders of heart and kidney are classified as cardiorenal syndromes (CRS). CRS type 1 includes acute heart disorder leading to acute kidney injury (AKI) and occurs in ˜25% of patients admitted with acute decompensated heart failure (ADHF). The development of duplex ultrasound has enabled the evaluation of changes in intra-renal blood flow.
Objectives: To evaluate the role of intra-renal duplex parameters in predicting worsening of renal functions (WRF) in hospitalized patients with ADHF.
Methods: Among 90 patients hospitalized with ADHF, intra-renal duplex parameters (resistivity index (RRI), pulsitility index (PI) and acceleration time (AT)) were assessed on admission, after 24 and 72 hours. WRF was defined as rise of the serum creatinine level = 0.3 mg/dL from the baseline. Diuretic efficiency was defined as net daily urine output normalized for the amount of Furosemide received in mg. Adverse in-hospital outcomes were defined as the composite outcome of death, use of vasopressors and need for ultrafiltration.
Results: The mean age of the patients was 57.5 ± 11.1 years with 62% of them males. WRF developed in 40% of the patients. The Mean value of RRI on admission was 0.717 ± 0.08 and it showed significant increase at 24 and 72 hours follow up

(p= 0.001 for both). The independent predictors of WRF by multivariate regression analysis were AT at 24 hours follow up, urea on admission, RRI on admission, LVEF and plasma cystatin C on admission. Patients with lower diuretic response had higher levels of admission RRI and higher levels of PASP on admission. The independent predictors of development of the composite outcome were LVESD, WRF and E/e'.
Conclusions: The intra-renal duplex parameters RRI and AT are independent predictors of WRF in hospitalized patients with ADHF on diuretic therapy. Higher admission RRI is associated with lower diuretic response. WRF is among the independent predictors of adverse outcome in hospitalized patients with ADHF.

1618
Prognostic importance of serum chloride concentration in patients hospitalized due to worsening heart failure

A Urbinati[1]; P Pellicori[2]; J Cuthbert[3]; D Pan[3]; S Kazmi[3]; F Guerra[1]; A Capucci[1]; AL Clark[3]; JG Cleland[2]
[1]Marche Polytechnic University of Ancona, Ancona, Italy; *[2]University of Glasgow, Glasgow, United Kingdom*; *[3]Castle Hill Hospital, Hull, United Kingdom*

Background: Blood electrolyte disorders are common in patients hospitalized for heart failure: serum chloride is usually measured but rarely considered.
Methods and **Results:** Between October 2012 and November 2016, patients hospitalized with worsening heart failure enrolled in the OPERA-HF, a single-centre, prospective, observational study had serum chloride measured at admission and discharge. 1145 patients (mean age 75 ± 12 years, median NTproBNP 4999 (IQR: 2331-10971) ng/l, of whom 62% had HFrEF on echocardiography, were enrolled. Hypochloraemia (serum chloride < 96 mmol/l) was present in 161 patients (14%) at admission and in 390 patients (34%) at discharge. Compared to patients in the highest quintile (median chloride 107 mmol/l; range 105-117 mmol/l), those in the lowest quintile of serum chloride at admission (median 94 mmol/l, range 76-97 mmol/l) were more likely to die (hazard ratio [HR]: 1.88; 95% confidence interval [CI]: 1.43-2.47, p < 0.001). Increasing chloride, but not sodium or potassium, levels at admission were independently associated with lower all-cause mortality (HR 0.94; 95% CI 0.89 to 0.99; p = 0.035). Compared to those who had normal chloride levels at admission and discharge, those who developed hypochloraemia during admission (HR:1.58; 95% CI 1.29-1.93, p < 0.001), or those who remained hypochloraemic (HR: 2.07; 95% CI 1.61-2.66, p < 0.001) had a higher mortality. Patients in whom hypochloraemia was corrected during hospitalisation had the same survival as those who were never hypochloraemic (HR: 1.08; 95% CI 0.65-1.79, p = 0.761).
Conclusion: Hypochloraemia is a common electrolyte disorder in patients admitted with worsening heart failure and is a powerful predictor of increasing mortality.



Quintiles of chloride and ACM

1621
Long-term (10-year) outcomes of patients admitted with decompensated heart failure in a tertiary care centre in India.

S Sivadasanpillai Harikrishnan[1]; G Sanjay[1]; P Jeemon[1]
[1]Sree Chitra Tirunal Institute for Medical Sciences & Technology (SCTIMST), Cardiology, Trivandrum, India

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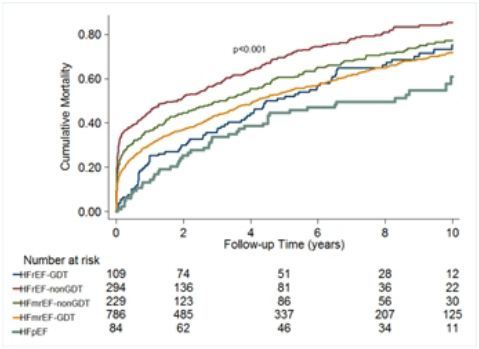
Introduction: Heart failure (HF) is emerging as a leading cause of hospitalization in India. There is paucity of long term outcomes of HF from India.
Objective: To assess the long-term outcome of patients admitted with acute decompensated HF(ADHF) at a tertiary care hospital in Kerala, India.
Methods: The data of consecutive patients from the state of Kerala who were admitted during 2001-2010 with a diagnosis of HF (satisfying European Society of Cardiology Criteria) at SCTIMST were retrospectively collected. Follow-up data were obtained until June 2017 and the follow-up was right censored at ten years.
Results: The data of 1502 patients were collected (mean age:51.1 years (SD = 14.3); females: 37.7%). Diabetes and hypertension was prevalent in 27.4% and 28.6% of participants at baseline, respectively. The most common etiology was ischemic heart disease (36%) followed by rheumatic heart disease (RHD) (34%), Others were non-RHD valve disease (8.2%), dilated cardiomyopathy (4.8%), other cardiomyopathies (6.4%; restrictive, hypertrophic and endomyocardial fibrosis) and grown-up congenital heart disease (4.8%). One third (33%) of patients were in atrial fibrillation or atrial flutter(AF). When the patients were classified based on ejection fraction (EF), HFpEF (57.9%) was the commonest condition followed by HFrEF (26.8%) and HFmrEF (15.3%) (p-preserved, r-reduced, mr-mid-range). We got the follow-up data in 92% of the patients at June 2017.
The total time at risk was 6248 person-years. Almost three fourths of the patients (n = 1051; 72.24%, 95% CI 0.70-0.74) died during the follow-up. The median survival time was 3.7 years and the death rate was 16.8 per 100 person years of follow-up (95% CI: 15.8 to 17.8). One of six patients with HFrEF received guideline directed therapy - GDT (combination of ACE inhibitor/ARB and beta-blocker). Those who received guideline directed therapy reported better cumulative survival rate in both HFrEF and HFmrEF groups (Figure). The survival benefit was however well established in the first three months of follow-up itself.
Conclusions: Compared to data from the west, HF patients in Kerala are relatively younger and predominantly males. Although RHD is a major contributor to HF in this region, ischemic heart disease is the most prevalent etiological condition. Median survival time of 3.7 years is comparatively lower than the Western data. Importantly, guideline directed therapy reduced the mortality in both HFrEF and HFmrEF. Additionally, HF patients with preserved ejection fraction (HFpEF) reported the lowest mortality. This is the first study from India showing long term outcomes of ADHF.



Survival analysis of long term outcome

1622
Five-year follow-up in patients with peripartum cardiomyopathy (PPCM) shows high and stable recovery rate and longterm use of cardiovascular medication

V Abou Moulig[1]; T Pfeffer[1]; M Ricke-Hoch[1]; S Schlothauer[1]; M Kasten[1]; D Berliner[1]; T Koenig[1]; J Schwab[2]; J Bauersachs[1]; D Hilfiker-Kleiner[1]
[1]Hannover Medical School, Klinik für Kardiologie und Angiologie, Hannover, Germany; *[2]Nuremberg Hospital South, Nuremberg, Germany*

Background: Peripartum cardiomyopathy (PPCM) is a rare type of heart failure, defined by reduced left ventricular ejection fraction (LVEF) occurring in previously healthy women during late pregnancy or in the months following delivery. Although many patients recover, PPCM is lethal for some women despite optimal treatment. Longterm studies are rare. Here, we present five-year follow-up data in PPCM patients.
Methods: All patients who were diagnosed with PPCM between February 2006 and May 2013 were included (n = 70). LVEF, medical treatment, adverse events and subsequent pregnancies were recorded. Follow-up data were obtained one and five years after the first diagnosis either by a subsequent visit in our clinic or by requesting the medical report from the treating cardiologist. For 14 patients who did not attend to any cardiologic follow-up, a telephone interview was performed.
Results: Of the 70 patients six were lost to follow-up. Of the remaining 64 patients (mean age 34 ± 5 y) follow-up data after one year (13 ± 2 months) were available for 42 patients and after five years (63 ± 9 months) for 50 patients.

At diagnosis LVEF was reduced (26 ± 10%). 70% of the patients received combination therapy of beta-blocker, angiotensin-converting enzyme (ACE) inhibitor/angiotensin-receptor-blockers (ARB) and mineralocorticoid receptor antagonists (MRA), 28% received two of these drugs and 2% did not get any heart failure medication. In addition 90% were treated with the dopamine agonist bromocriptine.
After one year mean LVEF had improved to 51 ± 11%. 60% of the patients had achieved full cardiac recovery with LVEF = 50%, 31% had recovered partially (LVEF 35-49%), 9% showed no recovery (LVEF < 35% or left ventricular assist device, LVAD) and no patient had died.
After five years mean LVEF had increased to 54 ± 6%. 70% of the patients showed full and 26% partial recovery. No recovery was seen in 4% (two patients needed LVAD of whom one had died). 76% of the patients still took heart failure medication (29% had three drugs, 27% had two drugs and 20% one drug). 20% needed these medications for arterial hypertension or ventricular extrasystoles. Ten patients had a subsequent pregnancy, the mean LVEF after delivery was normal.
Conclusion: Our prospective five-year follow-up study shows a high and stable longterm recovery rate of PPCM with low mortality with standard heart failure treatment combined with prolactin blockers in the acute phase, and longterm cardiovascular drug therapy during the years following the diagnosis. Our results emphasize that the recovery process continues even beyond the first year after diagnosis. Selected patients achieving good LVEF recovery when managed according to this concept seem to have a good chance for successful subsequent pregnancies without relapse. However, a high percentage of patients had developed hypertension and arrhythmias, suggesting that PPCM is associated with cardiovascular disease even in patients with recovery in LVEF.

1623
Time trends in characteristics, clinical course and outcomes of an unselected sample of 13,791 Spanish patients with acute heart failure (2007-2016)

O Miro[1]; P Javaloyes[2]; V Gil[1]; P Herrero-Puente[3]; FJ Martin-Sanchez[4]; H Bueno[5]; J Parissis[6]; CE Muller[7]; MP Lopez-Diez[8]; JM Garrido[9]; E Salvo[10]; M Fuentes[11]; F Richard[8]; FJ Lucas[12]; P Llorens[2]
[1]Hospital Clinic de Barcelona, Emergency Department, Barcelona, Spain; [2]General University Hospital of Alicante, Emergency Department, Alicante, Spain; [3]University Hospital Central de Asturias, Emergency Department, Oviedo, Spain; [4]Hospital Clinic San Carlos, Emergency Department, Madrid, Spain; [5]National Centre for Cardiovascular Research (CNIC), Madrid, Spain; [6]Attikon University Hospital, Cardiology Department, Athens, Greece; [7]University Hospital Basel, Cardiology Department, Basel, Switzerland; [8]University Hospital of Burgos, Emergency Department, Burgos, Spain; [9]University Hospital of Virgen Macarena, Emergency Department, Seville, Spain; [10]Hospital Universitario y Politécnico La Fe, Emergency Department, Valencia, Spain; [11]Hospital Clínico Universitario, Emergency Department, Salamanca, Spain; [12]Albacete University Hospital, Emergency Department, Albacete, Spain

On behalf of: ICA-SEMES Research Group
Funding Acknowledgements: ISCIII (Spanish Ministry of Health) and FEDER (PI15/01019 and PI15/00773), Fundació La Marató de TV3 (2015/2510) and Calalan Govern (GRC 2014/0313)

Objectives: To analyse time trends in patient characteristics, clinical course, hospitalisation rate, and outcomes in acute heart failure along a 10-year period (2007-2016).
Patients and Methods: The EAHFE registry has prospectively collected 13,971 consecutive AHF patients diagnosed in 41 Spanish emergency departments (EDs) at 5 different time points (2007/2009/2011/2014/2016). Eighty fundamental variables and patient outcomes were described and statistically significant changes along time were evaluated. We also compared our data with large ED- and hospital-based registries.
Results: Compared to other large registries, our patients were older [80 (10) years], more frequently women (55.5%) and had a higher prevalence of hypertension (83.5%) and a lower prevalence of ischaemic cardiomyopathy (29.4%). De novo AHF was observed in 39.6%. 63.6% showed some degree of functional dependence, and 56.1% had preserved left ventricular ejection fraction (LVEF). 56.8% of the patients arrived at the ED by ambulance, 4.5% arrived hypotensive, and 21.3% hypertensive. Direct discharge from the ED home was seen in 24.9%, and internal medicine (32.5%) and cardiology (15.8%) were the main hospital destinations. Triggers for decompensation were identified in 75.4%, the most being frequent infection (35.2%) and rapid atrial fibrillation (14.7%). The AHF phenotypes were: warm/wet 82.0%, warm/dry 6.2%, cold/wet 11.1%, cold/dry 0.7%. The length of hospitalisation was 9.3(8.6) days, and in-hospital, 30-day and 1-year all-cause mortality were 7.8%, 10.2% and 30.3%, respectively; and 30-day re-hospitalisation and ED revisit due to AHF were 16.9% and 24.8%. Thirty-nine of the 80 characteristics studied showed significant changes over time (Figure 1), while all outcomes remained unchanged along the 10-year period.
Conclusions: The EAHFE Registry is the first European ED-based registry describing the characteristics, clinical course and outcomes of a cohort resembling the universe of patients with AHF. Significant changes were observed over time in some aspects of AHF characteristics and management, but not in outcomes.

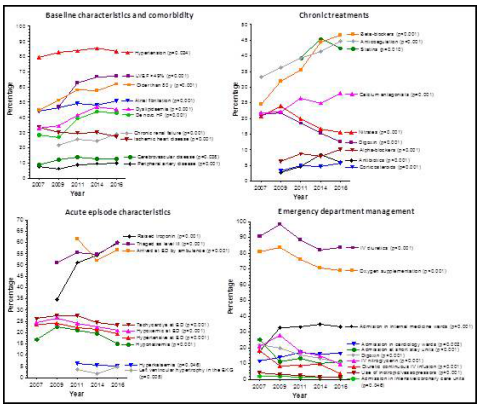


Figure 1

1625
30-Day mortality in the takotsubo syndrome compared to acute coronary syndromes

B Bjorn Redfors[1]; S Jha[1]; O Angeras[1]; C Dworeck[1]; I Haraldsson[1]; S Volz[1]; J Odenstedt[1]; G Hirlekar[1]; P Petursson[1]; E Omerovic[1]
[1]Sahlgrenska Academy, Univ. of Gothenburg, Dept of Molecular & Clinical Medicine/Cardiology, Gothenburg, Sweden

Background: The incidence of the Takotsubo syndrome (TS) has increased over the last decade, but high-quality outcomes data from large TS cohorts are scarce and the impact of TS on prognosis is poorly understood. Whereas prognosis in TS was first believed to be excellent recent reports imply as high risk of dying as for patients with acute myocardial infarction.
Purpose: We sought to compare the 30-day prognosis of patients with TS to that of patients with ST-elevation (STE) and non ST-elevation (NSTE) acute coronary syndromes (ACS).
Methods: Using data from the Swedish Coronary Angiography and Angioplasty Registry on procedures performed between 2009 and 2016 we compared patients with TS to patients with STE and NSTE ACS in regards to 30-day mortality. We adjusted for patient characteristics (age, sex, diabetes, smoking status, hypertension, hyperlipidemia, prior myocardial infarction and prior PCI) using multivariable Cox proportional hazards regression, which accounted for clustering of patients within hospitals.
Results: We identified 1950 patients (1465 [75.0%] women) with TS, 33727 patients (10256 [30.4%] women) with STE-ACS and 88659 patients (28768 [32.5%] women) with NSTE-ACS. The average age was similar among patients with TS (67.0 ± 11.4 years) and STE-ACS (67.1 ± 12.5, p = 0.47), whereas patients with NSTE-ACS were older (67.9 ± 11.1 years, p = 0.0003). The crude 30-day rate of all-cause mortality was 2.9% among patients with TS, which was higher than patients with NSTE-ACS (1.5%, p < 0.0001) but lower than patients with STEMI (6.0%, p < 0.0001). The adjusted 30-day risk of dying associated with TS remained lower than that of STE-ACS (adjusted hazard ratio [HR] 0.45, 95% confidence interval [CI] 0.32-0.63, p < 0.0001) and similar to that of NSTE-ACS (adjusted HR 1.72, 95% CI 1.22-2.44, p < 0.0001).
Conclusion: Patients with TS have unadjusted and adjusted short-term prognosis that is intermediate between NSTE-ACS and STE-ACS.

1627
Short-term outcomes of heart failure patients with reduced and preserved ejection fraction after acute decompensation according to the final destination after emergency department care

O Miro[1]; V Gil[1]; FJ Martin-Sanchez[2]; J Jacob[3]; P Herrero-Puente[4]; S Aguilo[1]; R Escoda[1]; A Dominguez-Rodriguez[5]; J Marco-Hernandez[1]; G Martinez[1]; V Rico[1]; C Sanchez[1]; J Parissis[6]; CE Muller[7]; P Llorens[1]
[1]Hospital Clinic de Barcelona, Emergency Department, Barcelona, Spain; [2]Hospital Clinic San Carlos, Emergency Department, Madrid, Spain; [3]University Hospital of Bellvitge, Emergency Department, Barcelona, Spain; [4]University Hospital Central de Asturias, Emergency Department, Oviedo, Spain; [5]University Hospital of the Canaries, Cardiology Department, Santa Cruz de Tenerife, Spain; [6]Attikon

University Hospital, Cardiology Department, Athens, Greece; [7]*University Hospital Basel, Cardiology Department, Basel, Switzerland*

On behalf of: ICA-SEMES Research Group
Funding Acknowledgements: ISCIII (Spanish Ministry of Health) and FEDER (PI15/01019 and PI15/00773), Fundació La Marató de TV3 (2015/2510) and Calalan Govern (GRC 2014/0313)

Aims: To compare short-term outcomes after an episode of acute heart failure (AHF) in patients with a reduced and preserved ejection fraction (HFrEF, < 40%; and HFpEF, >49%; respectively) according to their destinations after emergency department (ED) care.
Methods and Results: This secondary analysis of the EAHFE Registry (consecutive AHF patients diagnosed in 41 Spanish EDs) investigated 30-day all-cause mortality, in-hospital all-cause mortality, prolonged hospitalisation (<7 days), and 30-day post-discharge ED revisit due to AHF, all-cause death, and combined endpoint (ED revisit/death) in 5,829 patients with echocardiographically documented HFrEF and HfpEF (HFrEF/HFpEF: 1,442/4,387). Adjusted ratios were calculated for patients admitted to internal medicine (IM), short stay unit (SSU), and discharged from the ED without hospitalisation (DEDWH) compared with those admitted to cardiology. For HFrEF, the only significant differences were lower in-hospital mortality (OR = 0.26; 95%CI = 0.08-0.81; p = 0.021) and prolonged hospitalisation (OR = 0.07; 95%CI = 0.04-0.13; p < 0.001) related to SSU admission. For HFpEF, IM admission had a higher post-discharge 30-day mortality (HR = 1.85; 95%CI = 1.05-3.25; p = 0.033) and combined endpoint (HR = 1.24; 95%CI = 1.01-1.64; p = 0.044); SSU admission had a lower in-hospital mortality (OR = 0.43; 95%CI = 0.23-0.80; p = 0.008) and prolonged hospitalisation (OR = 0.17; 95%CI = 0.13-0.23; p < 0.001) but a higher post-discharge 30-day combined endpoint (HR = 1.29; 95%CI = 1.01-1.64; p = 0.041); and DEDDWH had a lower 30-day mortality (HR = 0.46; 95%CI = 0.28-0.75; p = 0.002) but higher post-discharge ED revisit (HR = 1.62; 95%CI = 1.31-2.00; p < 0.001) (Figure 1)
Conclusion: While HFrEF patients have similar short-term outcomes irrespective of the destination after ED care for an AHF episode, HFpEF patients experience worse short-term outcomes when managed by non-cardiology departments, despite adjustment for different clinical patient profiles. Reasons for this heterogeneous specialty-related performance should be investigated.

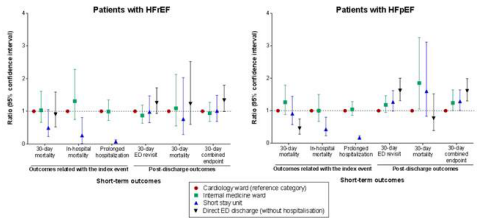


Figure 1

1629
Economic impact of intermittent intravenous outpatient treatment with levosimendan in patients with advanced heart failure

J Comin-Colet[1]; N Manito[1]; C Enjuanes[1]; J Gonzalez-Costello[1]; C Campo[2]; D Rubio-Rodriguez[3]; C Rubio-Terres[3]
[1]*University Hospital of Bellvitge, Cardiology Dpt., Barcelona, Spain*; [2]*Orion Spain, Medical Dpt, Madrid, Spain*; [3]*Health Value, , Health Economics and Outcomes Research Consulting, Madrid, Spain*

On behalf of: LION-HEART Investigators
Funding Acknowledgements: Orion Spain

Background: The LION-HEART study was a multicentre, double-blind, randomised, parallel-group, placebo-controlled trial evaluating the efficacy and safety of intravenous administration of intermittent doses of levosimendan in outpatients with advanced chronic heart failure. In this study, a lower rate of hospitalization for heart failure (HF) was observed in patients treated with levosimendan (22,9%) than in untreated patients (66,7%).
Purpose: Perform a cost analysis to determine whether the lower rate of hospitalizations for HF with levosimendan could generate savings for the Spanish National Health System (NHS), compared to the option of not treating patients with advanced HF.
Methods: An economic model that included hospitalization rates from the LION-HEART study, HF hospitalization costs and acquisition and intravenous administration costs of levosimendan was performed. The time horizon of the analysis was 12 months. Two analyzes were carried out, one deterministic and the other probabilistic (second-order Monte Carlo simulation).
Results: According to the deterministic analysis, the total saving for each patient treated with levosimendan would amount to €1,093.30. The additional cost of the medication (€1,404.61) and its intravenous administration (€480.24) was more than compensated by the savings due to the lower rate of hospitalization with levosimendan (€2,978.16). In the probabilistic analysis, the saving per patient treated with levosimendan would be €1,162.43 (95% CI €286.47; €2,599.65). The probability of savings with levosimendan compared to the no treatment option would be 94.1%.
Conclusion: Intermittent outpatient treatment with levosimendan could generate savings for the Spanish NHS, compared to the option of not treating patients with advanced HF.

Poster Session 3

Atrial Fibrillation - Epidemiology, Prognosis, Outcome

P1630

Clinical characteristics of patients with heart failure with mid-range ejection fraction and atrial fibrillation

A Samaras[1]; G Fotos[1]; G Dividis[1]; E Paschou[1]; J Goulas[1]; D Vasdeki[1]; E Forozidou[1]; P Tsoukra[1]; E Kotsi[1]; A Kartas[1]; H Karvounis[1]; A Tzikas[1]; G Giannakoulas[1]
[1]*Ahepa University Hospital, 1st Cardiology department , Thessaloniki, Greece*

On behalf of: MISOAC-AF investigators

Background: Heart failure (HF) often coexists with non-valvular atrial fibrillation (AF) and this combination increases the risk for thromboembolic events. Data on the population of patients with heart failure with mid-range ejection fraction (HFmrEF) and concomitant AF are currently lacking.
Aim: To determine the clinical characteristics and treatment strategy of rate/rhythm control and anticoagulation of patients with HFmrEF and AF in a dataset of patients who were hospitalized in a tertiary University Hospital.
Methods: Patients with chronic HF were classified into three groups according to the left ventricular ejection fraction (EF) [HF with reduced EF <40% (HFrEF), HF with mid-range EF:40-49% (HFmrEF) and HF with preserved EF = 50% (HFpEF)]. All patients had coexisting AF. A multivariate model using stepwise logistic regression analysis was performed to analyze the differences among the HF subgroups.
Results: In total, 307 patients with HF and AF (mean age75 ± 9.6 years, mean CHA2DS2-VASc score 5.3 ± 1.6) were studied (HFpEF 52%, HFmrEF 19%, HFrEF29%). HFmrEF patients presented more often with palpitations as their main symptom at admission compared with HFrEF (19% vs 6%, OR 5.52, 95%CI 1.43-2.18, p = 0.013) and HFpEF patients (19% vs 11%, OR 7.33, 95%CI 1.80-29.97, p = 0.006). HFmrEF patients were more likely to be male (62% vs 39%,OR 2.23, 95%CI 1.04-4.81, p = 0.039), younger (mean age 74 ± 10 vs 77 ± 9 years, OR 1.07, 95%CI 1.02-1.11, p = 0.003), have concomitant coronary artery disease (66% vs 44%,OR 3.61, 95%CI 1.61-8.09, p = 0.002) and history of prior stroke (25% vs 19%, OR 3.75, 95%CI 1.47-9.59, p = 0.006) in comparison with HFpEF patients. The presence of diabetes mellitus was more frequent in HFmrEF patients compared with HFrEF (45% vs 33%, OR 6.13, 95%CI 1.95-19.23, p = 0.002) and HFpEF (45% vs 40%, OR 9.31, 95%CI 2.73-31.74, p <0.001). Paroxysmal AF pattern was less frequent in HFmrEF compared with HFpEF patients (22% vs 37%, OR 0.33, 95%CI 0.14-0.76, p = 0.01). There was no difference in the CHA2DS2-VASc and HAS-BLED score among the HF subtypes. HFmrEF patients received more frequently beta-blockers compared with HFpEF patients (96% vs 80%, OR 11.78, 95%CI2.41-57.58, p = 0.002) and less often amiodarone at discharge compared with HFrEF patients (7% vs 27%, OR 0.23, 95%CI 0.07-0.78, p = 0.018). There was no difference in the use of anticoagulants (novel oral anticoagulants and vitamin K antagonists) among the three groups.
Conclusions: Among the HF-AF populations, patients with HFmrEF had more frequently a history of coronary artery disease, diabetes mellitus, prior stroke and increased use of beta-blockers. Patients with HFmrEF and AF share similar clinical phenotype and comorbidities with HFrEF-AF patients and have distinct differences from HFpEF-AF patients.

P1631

Mid-term outcomes in heart failure patients treated with non-vitamin K antagonist oral anticoagulants. A real world study.

C Goena Vives[1]; L Quintas Ovejero[1]; R Garcia Martin[1]; I Luis Serret[1]; J Taboada Gomez[2]; I Rilo Miranda[3]; JR Beramendi Calero[3]; C Gomez Ramirez[4]; R Natividad Andres[4]
[1]*Mendaro's Hospital, Cardiology, Mendaro, Spain*; [2]*Mendaro's Hospital, Public Health, Mendaro, Spain*; [3]*Donostia University Hospital, Cardiology, Donostia, Spain*; [4]*Cruces University Hospital, Cardiology, Barakaldo, Spain*

Introduction: New oral anticoagulants (NOAC) have been released for prevention of thromboembolism in non-valvular atrial fibrillation (NVAF).In the general population, each of them has been proven to be at least as effective and safe as warfarin but has to be studied in a real-world setting and in special patient population.
Purpose: Evaluate the mid-term efficacy and safety of NOAC in Heart Failure (HF).
Methods:520 consecutive patients with NVAF and NOAC with HF(158 cases, 30.4 %) or without (no-HF) (362 cases, 69.6%) were retrospectively reviewed.The incidence of HF was 9.4% in 4 years (34 new cases).The efficacy outcome was stroke or systemic embolism.The safety outcome was bleeding or death.
Results: The follow-up days were 507 ± 434.The mean age (75 ± 10), prevalence of previous stroke, HTA and DM was similar in the two groups.HF patients had a higher predicted stroke, renal dysfunction and bleeding risk (see table 1).The NOAC used were Dabigatran, Apixaban, Edoxaban and Rivaroxaban. In HF patients Apixaban was the most used.Differences between groups were statistically significant(see table 1). The global incidence of death (9%), systemic embolism (2.3%:Stroke N = 10, ACS N = 1, peripheral embolism N = 1) and major(3.5%) and minor(10.3%) bleeding was higher comparing the pivotal trials due to the higher predicted risk of population in the study but there were no differences statistically significant between groups.Conclusions:The benefit of NOAC was similar in NVAF patients with and without HF, despite the HF group has an additional risk for adverse effects in our series. Individual potential risk, benefit and harness of treatment must be carefully examined before matching a NOAC to a particular patient. Further research is required concentrating NVAF and heart failure.

Table 1

	No-HF	HF	p
Gender (Female %)	49.17	39.24	0.04
Mean age (years)	76.09±10.31	75.11±12.02	NS
CHADS2VASC2	3.52±1.6	4.78±1.56	<0.001
HASBLED	2.99±1.38	3.69±1.32	0.002
GFR	70.44±19.99	65.37±20.11	0.008
NOAC (N and %)			
Dabigatran	77(21.27%)	25(15.82%)	<0.005
Apixaban	194(53.59%)	91(57.59%)	NS
Rivaroxaban	60(16.57%)	19(12.02%)	NS
Edoxaban	28(7.73%)	22(13.92%)	<0.005

P1632

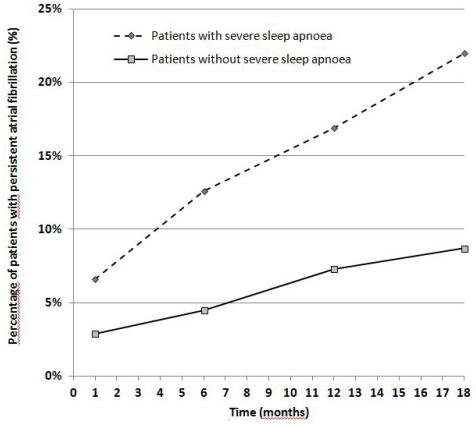
Development of persistent atrial fibrillation over 18 months in the RESPIRE study in unselected pacemaker patients with or without severe sleep apnoea

L Jesel[1]; P Winum[2]; T Moccetti[3]; G Macaluso[4]; L Brandao[5]; JP Elkaim[6]; F Alvarez Salgado[7]; M Pardo[8]; J Plant[9]; H Burri[10]
[1]*Nouvel Hôpital Civil, Strasbourg, France*; [2]*University Hospital of Nimes, Nimes, France*; [3]*Cardiocentro Ticino, Lugano, Switzerland*; [4]*Private Hospital Beauregard, Marseille, France*; [5]*Hospital Garcia de Orta, Almada, Portugal*; [6]*Centre Hospitalier de Douarnenez, Douarnenez, France*; [7]*University Hospital Dr Negrin, Las Palmas De Gran Canaria, Spain*; [8]*Vigo University Hospital Complex, Vigo, Spain*; [9]*LivaNova, Clamart, France*; [10]*Geneva University Hospitals, Geneva, Switzerland*

On behalf of: RESPIRE Study Investigators
Funding Acknowledgements: LivaNova

Background/Introduction: Patients with sleep apnoea (SA) often have atrial fibrillation (AF). Gold-standard diagnosis of SA with polysomnography is costly and often lengthy, making widespread use of this method impractical. The SA monitoring feature in REPLY 200 DR pacemakers analyses and records abnormal night-time breathing events, eg, apnoea and hypopnoea, allowing pre-screening of SA via the measurement of the respiratory disturbance index (RDI).
Purpose: The RESPIRE (Registry of Sleep Apnea Monitoring and Atrial Fibrillation in Pacemaker Patients) study examined the development of persistent AF in an unselected pacemaker population over 18 months, according to the severity of SA.
Methods: RESPIRE was an 18-month multicentre, international, single-arm, open-label study that observed adult patients after implant with an SA monitoring–enabled dual chamber pacemaker. SA severity during sleep was determined from device memory using RDI, the sum of abnormal respiratory events divided by sleep duration. Severe SA was defined as a mean RDI = 20. Persistent

AF was defined as an AF episode lasting for more than 7 consecutive days, based on the duration of fallback mode switch in the device memory. Endpoints included were the development of persistent AF in patients with severe SA and patients without severe SA from implant to 1, 6, 12 and 18 months. Mean intergroup differences (95% confidence intervals) were estimated in successfully implanted patients with valid SA monitoring data for = 80% of nights.
Results: In the 1147 enrolled patients, 56.3% were male and mean age was 75.7 ± 10.3 years. There were
301(36%)/525(64%) patients with severe/non-severe SA at 1 month, 230(34%)/449(66%) at 6 months, 172(31%)/381(69%) at 12 months, and 118(27%)/312(73%) at 18 months. The development of persistent AF in patients with and without severe SA is described in the Figure. Mean intergroup differences in the incidence of persistent AF at 1, 6, 12 and 18 months were 3.8% (0.2% to 7.4%), 8.2% (2.8% to 13.5%), 9.5% (2.5% to 16.6%) and 13.4% (4.1% to 22.7%).
Conclusion(s): In unselected pacemaker patients, persistent AF develops sooner and more often in patients with severe SA than in patients without severe SA.



P1633

Holter monitoring value in cardioembolic stroke: a follow up study

H Helena Nascimento[1]; C Sousa[1]; J Rema[1]; M Braga[1]; A Lebreiro[1]; D Souteiro[1]; P Chaves[1]; M Campelo[1]; MJ Maciel[1]
[1]*Sao Joao Hospital, Porto, Portugal*

Background: Cardioembolic etiology accounts for 14-30% of all cerebral infarctions. As atrial fibrillation (AF) is the most important cause, identification of paroxysmal atrial fibrillation (PAF) may have crucial prognostic impact. Holter monitoring (HM) has been increasingly used in stroke and transient ischemic attack (TIA) patients (pts) as a routine investigation to search for occult PAF. The purpose of this study was to verify the HM prognostic implications in the follow-up of cardioembolic stroke.
Methods: A group of 80 pts selected in the setting of post stroke or TIA, that were in sinus rhythm at the time of the event and performed HM between October 2009 and October 2011 were reviewed and followed up. Clinical, echocardiographic and neuro imaging data were collected an inserted in an uniform base.
Results: In our population 53% were male, with a median age of 63 (range 52-67) years at the index event. Sixty-four pts had a stroke (80%), and 17 a TIA (20%); thrombolysis was performed in 24% of the case. In the HM, PAF occurred in 5% of the pts (4). Comparing PAF and ESVEA groups of pts and sinus rhythm pts, no statistically significant differences were found, neither concerning clinical nor imaging data. During a median follow up (fup) of 82 months (range 58-98), 9 pts developed AF, 7 PAF (78%) and 2 permanent AF. During this period, 9 pts had a recurrent cerebrovascular event: 4 TIA and 5 strokes (only one hemorrhagic). From these pts, 56%were male(5), median age 69 (range 61-82) years, 44% hypertensive, 22% diabetic, 56% dyslipidemia and 33% smokers. Regarding demographic and cardiovascular risk factors, no differences were found between the group of pts with recurrent events and the other pts with no events in fup. Although not statistically significant, we found a tendency towards a higher value ofCHA2DS2-VASc in pts with recurrent cerebral ischemic events (5.4 ± 1.4 vs. 4.9 ± 1.3). Concerning the documentation ofAF, it was detected in only one of recurrent AIT/stroke pts. Still, it must be recognized that only 10 pts repeated the HM during the fup period.
Conclusions: Our study emphasizes that is of paramount importance to detect PAF after acute cerebral ischemia in order to prevent recurrence. HM is an invaluable tool in the workup of suspected cardioembolic stroke. However, new strategies like prolonged Holter monitoring and loop recorders are needed. Moreover, our investigation suggests a potential role of CHA2DS2-VASc score as a predictor of recurrent events even in patients without fibrillation.

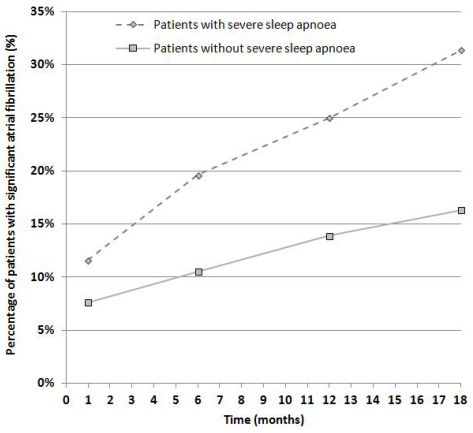
P1634

Development of significant atrial fibrillation over 18 months in the RESPIRE study in unselected pacemaker patients with or without severe sleep apnoea

P Pedro Marques[1]; JA Santos[2]; C Steinwender[3]; P Bechetoille[4]; NC Roche[5]; S Fynn[6]; T De Geyer[7]; J Marti-Almor[8]
[1]*Hospital de Santa Maria, Lisbon, Portugal*; [2]*Centro Hospitalar do Baixo Vouga, Aveiro, Portugal*; [3]*General Hospital (AKH) of Linz, Linz, Austria*; [4]*Centre Hospitalier d'Ardéche Nord, Annonay, France*; [5]*Hôpital d'instruction des armées Bégin, Saint-Mandé, France*; [6]*Papworth Hospital NHS Trust, Cambridge, United Kingdom*; [7]*LivaNova, Clamart, France*; [8]*Hospital del Mar, Barcelona, Spain*

On behalf of: RESPIRE Study Investigators
Funding Acknowledgements: LivaNova

Background/Introduction: Patients with sleep apnoea (SA) often have atrial fibrillation (AF). Diagnosing SA with polysomnography is costly and often lengthy, making widespread diagnosis with this method impractical. Some pacemakers are able to pre-screen SA via the measurement of the respiratory disturbance index (RDI). One of these, the REPLY 200 DR pacemaker, has an SA monitoring feature that analyses and records abnormal night-time breathing events, eg, apnoea and hypopnoea.
Purpose: The RESPIRE (Registry of Sleep Apnea Monitoring and Atrial Fibrillation in Pacemaker Patients) study examined the development of significant AF in an unselected pacemaker population, according to the severity of SA.
Methods: RESPIRE was an 18-month multicentre, international, single-arm, open-label study that observed adult patients after implant with an SA monitoring–enabled dual chamber pacemaker. SA severity during sleep was determined from device memory using RDI, the sum of abnormal respiratory events divided by sleep duration. Severe SA was defined as a mean RDI = 20. Significant AF was defined as cumulative AF episodes lasting = 24 hours over 2 consecutive days, based on duration of fallback mode switch. Endpoints included the development of significant AF from implant to 1, 6, 12 and 18 months, according to SA severity. Mean differences and 95% confidence intervals between the two groups (with versus without severe SA) were estimated in successfully implanted patients with valid SA monitoring data for = 80% of nights.
Results: In the 1147 enrolled patients, 56.3% were male and mean age was 75.7 ± 10.3 years. There were 301(36%)/525(64%) patients with severe/non-severe SA at 1 month, 230(34%)/449(66%) at 6 months, 172(31%)/381(69%) at 12 months and 118(27%)/312(73%) at 18 months. The development of significant AF over time in severe and non-severe SA patients is described in the Figure. Mean differences in the incidence of significant AF at 1, 6, 12 and 18 months were 4.0% (-0.3% to 8.3%), 9.1% (3.2% to 15.0%), 11.1% (3.7% to 18.4%) and 15.0% (5.7% to 24.3%).
Conclusion(s): In unselected pacemaker patients, significant AF develops sooner and more often in patients with severe SA than in those without.



Ventricular Arrhythmias and SCD - Treatment

P1635
Targeted temperature management after cardiac arrest

C Catarina Ruivo[1]; C Jesus[1]; J Morais[1]; J Correia[1]; P Viana[1]
[1]*Hospital Santo Andre, Cardiology, Leiria, Portugal*

Introduction and Purpose: Targeted Temperature Management (TTM) for patients with return of spontaneous circulation (ROSC) after cardiac arrest (CA) remain a matter of debate. Doubts remain about management, target temperature and duration. In the present study we describe the experience of a non-tertiary care center with TTM after CA and seek predictors of mortality and neurological outcome.
Methods and Results: 2279 patients were hospitalized in the intensive care unit and 82 of them had diagnosis of CA with ROSC. 15 patients were submitted to TTM, 47.3 ± 14 years, 10 (67.0%) male. The CA occured out-of-hospital (n = 11; 73.3%) or in-hospital (n = 4; 26.7%), in initial shockable (n = 10; 66.7%) or nonshockable (n = 5, 33.3%) rhythm. The average time from CA to ROSC (CA-ROSC) was 44.7 ± 36.5 min. All patients met the 24 hour target temperature of 33°C. The average value of neuron specific enolase (NSE) was 93.7 ± 109.0 μg/L. Patients who survived with good cerebral performance (n = 7; 46.7%) had lower median age (38.4 ± 10.1 vs 55.1 ± 13.2 years; p = 0.032), shorter CA-ROSC (22.9 ± 12.9 vs 63.8 ± 40.4 min; p = 0.048), lower measurements of NSE (42.6 ± 35.1 vs 138.4 ± 133.4 μg/L; p = 0.020) and initial ventricular fibrillation rhythm (p = ns) than those who died (n = 8; 53.3%).
Conclusions: The effectiveness of TTM seems related with younger age, shockable initial rhythm and reduced CA-ROSC time. These results point out some lines of research that appropriate prospective studies should develop. The role of biomarkers to predict prognosis is an open issue for debate, with the NSE occupying a particular role in this field.

P1636
Role of catheter ablation in electrical storm treatment

S Garkina[1]; R Tatarsky[1]; E Mikhaylov[1]; V Lebedeva[1]; V Orshanskaya[1]; YU Miller[1]; A Kamenev[1]; S Gureev[1]; D Lebedev[1]
[1]*Almazov National Medical Research Centre, Saint-Petersburg, Russian Federation*

Background: Electrical storm (ES) is a life threating situation that involves recurrent episodes of ventricular tachyarrhythmias (VTA). It is defined as 3 or more sustained episodes of ventricular tachycardia (VT), ventricular fibrillation (VF) or appropriate implantable cardioverter-defibrillator (ICD) shocks during 24 hours. Several clinical studies demonstrated the rate of ES about 9-12% after ICD implantation due to both primary and secondary prevention while 7% of patients developed it during first year of follow up. Radiofrequency (RF) ablation of triggering ventricular premature beats or substrate-based catheter treatment are considered to be effective in ICD patients with heart failure (HF) and drug-refractory, repetitive polymorphic ventricular tachycardias (VT) after myocardial infarction (MI).
The purpose of the study was to evaluate the effectiveness of early and delayed radiofrequency ablation (RFA) in ES patients with severe HF, implanted ICD and postinfarction ventricular arrhythmias.
Materials and methods. We enrolled 14 consecutive patients with ES (mean age 61 + 12 years, 11 male) which underwent endocardial electrophysiological (EP) study and catheter ablation using the nonfluoroscopic navigation and mapping system. Average rate of appropriate ICD shocks during ES was 12,2 ± 14,1 per day whereas ICD was implanted 3,4 ± 3,2 years before the first ES episode. Only 3 patients were treated with ICD for primary prevention while 11 patients required secondary prevention of sudden cardiac death (SCD). Chronic heart failure (CHF) with NYHA III-IV functional class and left ventricular ejection fraction of 32 ± 12% was diagnosed in 10 patients (71%) among those who underwent emergency RFA. Catheter treatment was performed in 1-3 days after admission when potential reversible causes of ES were excluded. The procedure also included mapping during hemodynamically tolerated clinically relevant VT or clinical VTA triggers with subsequent homogenization of the scar. Patients with "fast" VT underwent primary scar homogenization.
Results: Acute effectiveness of emergency RFA in patients with clinically relevant VT was 64% (9 patients). During the first year of follow-up, 6 patients experienced recurrent VT episodes (43%) in 5 ± 3 months after discharge. The overall survival rate was 25%. Long-term effectiveness of ES elimination was 100% while freedom from clinically significant VTA was up to 79% due to repeated ablation procedures. We also observed improvement of NYHA functional class in 80% of patients. Conclusion. Catheter ablation of ES may be effective treatment in patients with sustained VTA resistant to drug therapy both in acute period and long term follow up. It also may be effective in improvement of heart failure NYHA functional class in some patients.

Implantable Cardioverter / Defibrillator

P1637
Occurrence of ventricular tachyarrhythmias in left ventricular assist devices patients with implantable defibrillators

M Sasov[1]; P Lesny[1]; M Svetlosak[1]; P Margitfalvi[1]; R Hatala[1]; E Goncalvesova[1]
[1]*National Institute of Cardiovascular Diseases, Bratislava, Slovak Republic*

Background: Primary prevention of sudden death with implantable defibrillators (ICD) in patients (pts) with left ventricular assist devices (LVAD) is still studied. Information on the impact of LVAD on malignant ventricular tachyarrhythmias (VTA) - ventricular tachycardia / fibrillation (VT/VF) and inappropriate ICD therapies is limited.
Purpose: Retrospective analysis of occurrence and type of VTAs and ICD interventions prior and post LVAD implantation in a single tertiary care centre.
Patients and Methods: 33 pts with end-stage systolic heart failure with implanted LVAD and ICDs or pacemakers were included. LVADs were implanted during years 2008-2015: all were continuous flow devices. Six pts (18%) died within 30 days after LVAD implantation. From the 27 surviving pts indications for LVADs were bridge to transplant (16 pts), bridge to candidacy (10 pts), destination therapy (1 pt). The aetiology of heart failure was dilated cardiomyopathy in 17 pts, coronary heart disease in 9 pts and congenital heart disease in 1 pt. 17 pts had implanted ICD (8 pts CRT-D), 1 pt had CRT-P and 1 pt dual-chamber pacemaker. Twenty three were men, mean age of the cohort was 47.7 ± 10.7 years. At the time of LVAD implant mean INTERMACS score was 2.56 ± 1.15, mean LVEF 18.8 ± 4.7%, mean CI 1.82 ± 0.37 l/min/m2. Mean follow-up duration was 29.9 ± 34.6 months before LVAD implantation and 17.2 ± 11.9 months after LVAD implantation. At the end of follow-up 14 pts underwent heart transplantation (52%), 10 pts died (37%), 2 pts were on waiting list for transplantation (7%) and LVAD was destination therapy in 1 pts (4%).
Results: Prior to LVAD implantation 9 pts (33%) had overall 40 VT episodes and 9 VF episodes. Following LVAD implantation 5 pts (19%) had 68 VT episodes and 11 VF episodes. Seventeen pts (63%) were free of VT/VF. Total annual per patient incidence of VTA increased post LVAD implantations from 0.59 to 1.75 and from 0.13 to 0.28 (episodes/pt/year) for VT and VF, respectively. In 6 pts with pre-LVAD occurrence of VT/VF the arrhythmia burden was reduced after LVAD, in 3 pts the burden increased. New VT/VF episodes after LVAD implant was diagnosed only in 1 pt. Inappropriate ICD interventions were diagnosed in 5/25 pts (20%) and accounted for 32% of all anti-tachycardia interventions. Annual incidence of inappropriate ICD interventions post-LVAD was 0.68 episodes/pt/year.
Conclusions: In our retrospective analysis VTA episodes post LVAD implant occurred mainly in those pts who had VTA episodes already prior to LVAD. Patients without VTA prior to LVAD implantation manifested a relatively low risk of VTA post-LVAD. Number of pts with VT/VF post LVAD implantation decreased, but total burden of VT/VF episodes increased. Almost 1/3 of ICD interventions post LVAD were inappropriate. Based on our observations in pts without ICD prior to LVAD implantation we recommend ICD implantation post-LVAD only for secondary prevention of VTA.

P1638
Cardiac device-related infective endocarditis: a challenge condition

H Helena Nascimento[1]; M Braga[1]; L Flores[1]; V Ribeiro[1]; F Melao[2]; D Paula[2]; MJ Maciel[2]
[1]*Sao Joao Hospital, Porto, Portugal*; [2]*Hospital Centre do Tamega e Sousa, Cardiology, Penafiel, Portugal*

Introduction and Purpose: In the last decades, the number of cardiac devices has grown exponentially. Cardiac device-related infective endocarditis (CDRIE) is a fearful complication, accounting for 10-23% of all cardiac device infections. Diagnosis and management of this condition remains a challenge. The aim of this study was to assess clinical and prognostic profile of CDRIE patients (pts).
Methods: A retrospective study of 173 consecutive diagnosed infective endocarditis (IE),admitted to several departments in a tertiary center from 2011 to 2014. Data were collected from the electronic clinical process and registered in an uniform base.
Results: Among theIE cases studied, 16 cases were CDRIE (9%). Mean age was 62 ± 22 years-old and 63%were males. The most common comorbidity was diabetes (25%). Intracardiac device was a pacemaker in 12 cases and a implantable cardioversor-defibrillator in the other 4. Average time from device implantation/replacement procedure to diagnosis was 64 months (range 7-86). No previous cases of IE were present; 50% of the cases were health-care associated IE. Fever was the predominating signal at hospital presentation (69%). Staphylococci species were the main causative microorganisms (25% coagulase negative and 44% S.aureus) and almost one fifth of the episodes were caused by methicillin resistant strains. Most pts had isolated infection of the cardiac leads (75%), however 3 pts

had also involvement of the tricuspid valve and 1 patient had also left side involvement. Lead vegetations were identified in 44% by transthoracic echocardiography and in 56% by transesophageal approach; vegetations were multiple in 11 cases and large (<10mm) in 2 cases. Complications developed during the clinical course were renal failure (19%), persistent infection (50%), heart failure (31%), shock (25%) and systemic embolism (19%). Most of the patients underwent surgical or percutaneous removal of the infected system (88%). Three pts died during the hospital stay.
Conclusion: CDRIE is a rising problem, with major diagnostic and therapeutic barriers. The clinical evolution is characterized by serious complications. Therefore, a high level of suspicion is of paramount importance to an accurate CDRIE diagnosis and treatment.

Cardiac Resynchronization Therapy

P1639
Minute ventilation sensor driven rate response as part of resynchronization therapy optimization

C Lenz[1]; S Fischer[2]; C Hansen[3]; A Werner[4]; C Beaudoint[5]; T Kayser[5]; N Cielen[5]; RC Braun-Dullaeus[6]; S Vikman[7]; B Zrenner[8]; S Pakarinen[9]
[1]UKB Berlin, Cardiology, Berlin, Germany; [2]Harzklinikum D. Ch. Erxleben, Internal Medizin, Quedlinburg, Germany; [3]Herz- und Gefäßzentrum am Krankenhaus Neu-Bethlehem Göttingen, Göttingen, Germany; [4]Clinic Oldenburg, Klinik für Kardiologie, Oldenburg, Germany; [5]Boston Scientific, Clinical RM, Diegem, Belgium; [6]Otto-von-Guericke University of Magdeburg, Klinik für Kardiologie und Angiologie , Magdeburg, Germany; [7]Tampere University Hospital, Heart Center, Tampere, Finland; [8]Hospital Landshut-Achdorf, Cardiology, Landshut-Achdorf, Germany; [9]Helsinki University Central Hospital, Division of Cardiology, Helsinki, Finland

Background: With increasing life expectancy and optimized pharmacological treatment, more patients (pts) show signs of chronotropic incompetence (CI) and heart failure (HF). Currently, not much data is available on the use of minute ventilation sensor (MVs) in those pts.

Table 1

Variable	Cohort 1 (n = 35)	Cohort 2 (n = 11)					
0 to 1 Month MVs off	1 to 3 Month MVs on	P value between time MVs off/ on	0 to 1 Month MVs off	1 to 3 Month MVs off	P value within off	P value between cohorts	
Age	71	75	0.205				
80% APMHR (bpm)	120	116	0.268				
Resting Heart Rate (bpm)	72	70	0.297	74	70	0.344	0.571
Maximum Heart Rate (MHR) during 6mWT (bpm)	95	101	0.038	101	108	0.365	0.246
6MWD (meters)	349	376	0.004	359	349	0.537	0.942
% Atrial Pacing (% AP)	40	49	0.047	3	6	0.062	< 0.001
* between group p value from the repeated measure ANOVA model.							
* within group p value from Wilconson signed-rank test							

Objective: To assess the clinical impact of optimized rate adaptive pacing (RAP) by MVs alone in HF patients following 6 minute walking test (6mWT).
Methods: A total of 61 pts with well established indication for CRT-P were enrolled into the study; participants were implanted with a device capable of rate adaption based on a minute ventilation driven algorithm. All patients suffered from symptomatic heart failure (NYHA class II or greater).
At pre-discharge, all pts were programmed in DDD mode, unless they had a known need for RAP. At 1 Month (mo), a 6mWT was performed in a non-RAP mode and walking distance was collected. When max. HR (MHR) was < 100min-1 or < 80% Age predicted MHR (APMHR), MVs was turned ON. At 3 Mo, the 6mWT was repeated in DDDR. Demographics, resting and MHR and % atrial pacing (AP) were collected.
Results: Implanted pts (n = 61; mean age: 73.3 ± 10.1 years) had LVEF of 41.1 ± 11.6% and NYHA value of 2.6 ± 0.64. After 6mWT at 1Mo, 35 pts had MVs turned ON , 11 pts remained in DDD and 15 pts were excluded (other programming, incomplete datasets). Pts with MVs ON resulted at 3 month FU in a higher % AP, allowed an increase of the MHR similar to subjects with no CI, and improved 6mWT distance. No MVs related adverse events have been reported.
Conclusion: This study showed beneficial clinical effects of using MVs only in a CRT-P cohort who could not reach 80% APMHR at 1 mo 6mWT. Patients under optimal medical therapy have an underestimated need of sensor driven HR frequency which is supporting CRT therapy.

P1640
The change pattern of doses in loop diuretics according to cardiac resynchronization therapy response is associated with clinical outcomes in patients with heart failure and reduced left ventricular e

J Jaewon Oh[1]; JS Uhm[1]; IJ Cho[1]; TH Kim[1]; HN Pak[1]; MH Lee[1]; B Joung[1]; SM Kang[1]
[1]Yonsei University College of Medicine, Cardiology Division, Seoul, Korea Republic of

Introduction: Cardiac resynchronization therapy (CRT) improves cardiac hemodynamics. Recently, down-titration of loop diuretics was associated with improved clinical outcomes after CRT. Therefore, we evaluated the change pattern of doses in loop diuretics according to CRT response and its association with clinical outcomes in patients with heart failure with reduced ejection fraction (HFrEF).
Methods: We retrospectively investigated 76 HFrEF patients (M:F= 41:35) with CRT implantation from January 2010 to October 2015. Pre-defined echocardiographic responses 6 months after CRT implant were: 1) negative responder (increased LV end systolic volume, LVESV), 2) non-responder (decreased LVESV, 0-14%), 3) responder (decreased LVESV, 15-29%), and, 4) super-responder (decreased LVESV = 30%). Loop diuretics dose (daily furosemide equivalent) was assessed before and 6 months after CRT implant. Clinical outcomes including all-cause mortality and HF rehospitalization were assessed during follow-up period (median 555 days)
Results: Mean age, baseline LVEF and ischemic HF were 67 ± 10 years, 24.3 ± 6.1% and, 14.5%, respectively. There were 53 (69.7%) patients with down-titration or no loop diuretics (34.2%) and unchanged diuretics dose (35.5%). The prevalence of these pattern of diuretic users were 43.8% in negative responders (n = 7/16), 66.7% in non-responders (n = 18/27), 88.9% in responders (n = 8/9) and 83.3% in super-responders (n = 20/24) (p = 0.031). Up-titration of loop diuretics (30.3%) was associated with higher all-cause mortality (47.8 vs. 13.2%, p = 0.005) and HF rehospitalization (52.2 vs. 18.9%, p = 0.006) compared with other patterns of diuretic users.
Conclusion: After CRT, down-titration or no loop diuretics and unchanged diuretics dose are significantly less common in negative responder compared to other responder groups. Up-titration of loop diuretics was associated with poor clinical outcomes after CRT in HFrEF patients.

P1641
Mild to moderate functional mitral regurgitation and cardiac resynchronization therapy: Evaluation and prognosis

JL Jose Luis Martins[1]; J Milner[2]; N Antonio[2]; L Elvas[2]; J Viana[1]; M Pego[2]; J Santos[1]
[1]Centro Hospitalar do Baixo Vouga, Cardiology, Aveiro, Portugal; [2]University Hospitals of Coimbra, Cardiology, Coimbra, Portugal

Introduction: Functional mitral regurgitation (MR) may be a consequence of systolic dysfunction, changes in geometry or occur in the presence of dyssynchrony. Degree reduction of severe functional MR after cardiac resynchronization (CRT) therapy appears to have a mortality impact. On the other hand, the long-term prognosis of mild to moderate MR changes after CRT implantation is not well established.
Methods: We retrospectively studied patients submitted to cardiac resynchronization therapy with pre-implantation MR. The patients were divided in 4 groups according to MR severity changes: grade 1 or 2 worsened MR (Group 1); improved or unchanged grade 1 or 2 MR (Group 2); worsened or unchanged grade 3 or 4 (Group 3); improved grade 3 or 4 (Group 4). Mortality and echocardiographic measurements were evaluated during mean follow-up of 1303 ± 634 days.

Results: The study included 144 patients with MR pre-CRT implantation (age 63 ± 11years, 75% male, 30% ischemic etiology). Preclinical grade 1 MR was present in 44% of patients and grade 2 in 29% of patients. Super-responders rate was 21%; 24% responders and 54% non-responders. Pré-implantation left ventricular final diastolic volume (LVEDV) was 234 ± 83 ml compared to 203 ± 96 ml LVEDV postimplantation (p = 0.001). Pré-implantation left ventricular final systolic volume (LVESV) was 174 ± 78 ml versus 142 ± 86 ml postimplantation LVESV (p < 0.001). There was no difference in mortality between group 1 and 2 (logrank, p = 0.98). There was a tendency for a better survival when there was improvement in the severity degree if the degree was moderate to severe (group 3 versus group 4, logrank, p = 0.1).
Conclusion: Among patients with mild to moderate MR at baseline, the worsening degree of MR does not appear to have a prognostic impact.

P1642
Left ventricular only pacing with dual chamber pacemaker system: Improve left ventricular function in patients with atrioventricular conduction delay and left ventricular systolic dysfunction.

HABIBA Umme Habiba Ferdaushi[1]; ATAHAR M Atahar Ali[1]; SHAILA Shaila Nabi[1]; MAINUL Mainul Islam[1]
[1]*National Institute of Cardiovascular Disease, cardiology, Dhaka, Bangladesh*

Background: In patients with atrioventricular (AV) delay and concomitant left ventricular (LV) systolic dysfunction, conventional right ventricular (RV) apical pacing may lead to further deterioration of LV function and heart failure, particularly in patients with depressed LV function at baseline. Cardiac resynchronization therapy (CRT) improves LV hemodynamics and function in this subset of patients, partially reversing the deleterious effects of RV apical pacing. However, these devices are not affordable to many patients in Bangladesh.
Objective: We aimed to assess the efficacy of LV only pacing using two leads, right atrial (RA) and LV leads with dual chamber pacemaker as a cost effective alternative to conventional CRT in patients with AV block requiring pacing, and concomitant LV systolic dysfunction.
Methods: We implanted right atrial (RA) and LV leads with dual chamber pulse generator in four patients with complete heart block and LV dysfunction with New York Heart Association (NYHA) functional class III/IV symptoms, at the National Institute of Cardiovascular Diseases (NICVD), Dhaka from December 2016 to November 2017. The sensed atrioventricular delay was programmed to pre-excite the LV and achieve fusion beat. Response to therapy was assessed six months post implantation using clinical and echocardiographic parameters.
Results: Four male patients were included. The indication for pacing in all patients was complete heart block. The mean age was 73 ± 1.2 years. Pacing was achieved in all patients. At six months follow up, no patient reported syncope or pacing failure. There was significant improvement of NYHA functional class from 3.3 ± 0.44 to 1.7 ± 0.6 (p <0.001) in all patients. On echocardiography, mean LV end-diastolic diameter (LVEDD) decreased from 65.5 ± 4.65 mm to 54.75 ± 2.21 mm (p <0.001) and mean LV end-systolic diameter (LVESD) decreased from 53.75 ± 4.78 to 43.5 ± 4.35mm (p < 0.001). The mean difference of LVEDD and LVESD pre and post-procedure was 10.25 ± 2.5mm and 9.75 ± .62mm respectively. LV ejection fraction (EF) improved significantly from 30.5 ± 5.3% to 44.25 ± 3%(p <0.001).
Conclusion: RA-LV pacing is a cost-effective alternative to CRT in patients with LV systolic dysfunction and indication for anti-bradycardia pacing. Although the study was performed on a small number of patients, it can be considered that this therapy had favorable haemodynamic effect and improved myocardial structure and function by left ventricular reverse remodeling.

P1643
The impact of left ventricular lead position on long-term clinical outcome: a high volume, single center experience

A Annamaria Kosztin[1]; W Schwertner[1]; A Kovacs[1]; E Zima[1]; L Geller[1]; V Kutyifa[1]; B Merkely[1]
[1]*Semmelweis University, Heart Center, Budapest, Hungary*

Background: There is limited data on the association of left ventricular (LV) lead location with long-term clinical outcomes in patients after cardiac resynchronization therapy (CRT).
Purpose: We evaluated the mid-term echocardiographic response and long-term survival of patients who underwent CRT implantation by LV lead non-apical positions and further characterised by right to left ventricular activation delay (RV-LV AD).
Methods: In our retrospective registry patients underwent CRT implantation according the current guidelines from 2004 to 2017 were registered. Those with non-apical LV lead location was classified into anterior (n = 30), posterior (n = 154), and lateral (n = 370) positions. Primary endpoint was all-cause mortality assessed by Kaplan-Meier and Cox regressional analyses. Secondary endpoint was echocardiographic response within 12 months.
Results: From 554 patients 291 (53%) reached the primary endpoint during the mean follow up time of 4.3 years. Univariate analysis showed patients with lateral position had significantly better outcome compared to others (HR 0.78; 95% CI: 0.61-0.98; p = 0.04), which was also confirmed by Cox analysis (HR 0.79; 95% CI: 0.62-1.01; p = 0.05) after adjusting for RV-LV AD. The mean of RV-LV AD was significantly larger in the lateral group and showed an U-shaped curve by LV lead location. When echocardiographic response was evaluated in the lateral group, ROC analysis showed 100 ms as the optimal cutoff value (AUC 060, 95% CI: 0.51-0.69; p0.03).
Conclusions: Mortality benefit derived from CRT is associated only with lateral LV lead location, moreover the most beneficial echocardiographic response could be expected in those patients where RV-LV AD is longer than 100ms in this group.

Chronic Heart Failure - Pathophysiology and Mechanisms

P1644
Relationship of circulating plasma levels of D-Dimer and outcome in patients with heart failure: findings from BIOSTAT-CHF

P Pellicori[1]; G James-Rae[1]; A Voors[2]; K Dickstein[3]; G Filippatos[4]; F Zannad[5]; S Anker[6]; P Ponikowski[7]; A Mcconnachie[1]; JGF Cleland[1]
[1]*University of Glasgow, Robertson Centre for Biostatistics, Glasgow, United Kingdom*; [2]*University Medical Center Groningen, Groningen, Netherlands*; [3]*University of Bergen, Bergen, Norway*; [4]*National & Kapodistrian University of Athens, Athens, Greece*; [5]*University Hospital of Nancy , Nancy, France*; [6]*Charité - Universitätsmedizin Berlin, Berlin, Germany*; [7]*Wroclaw Medical University, Wroclaw, Poland*

Aims: D-Dimer, is produced by fibrinolysis of cross-linked fibrin, and may be increased in heart failure, reflecting activation of both haemostatic and fibrinolytic systems. Gross elevations may occur with thrombo-embolic disease. We investigated the prognostic significance of increases in D-Dimer in patients with heart failure.
Methods and Results: D-Dimer was measured in 2,358 (94% of the entire cohort) patients enrolled in The BIOlogy Study to TAilored Treatment in Chronic Heart Failure (BIOSTAT-CHF). 1,592 patients (67%) had a D-Dimer equal to, or below, the lower limit of detection (< 102ng/mL), 611 (26%) had values between 102 and 499 ng/mL and 155 (7%) had values = 500 ng/mL (upper limit of normal); 50 (2%) had values >1,000 ng/mL. Compared to out-patients (n = 780, 33%), in-patients (N = 1,578, 67%) were more likely to have an elevated D-Dimer = 500ng/mL (7.9% v 4.0%; p < 0.001). Compared to patients with atrial fibrillation (AF; n = 1070; 45%) those without AF (N = 1288, 55%) were more likely to have an elevated D-Dimer = 500ng/mL (7.5% v 5.4%; p = 0.029). D-Dimer levels were weakly correlated with age (r = 0.076, p < 0.001), NTproBNP (r = 0.136, p < 0.001) and Troponin-I (0.134; p < 0.001) levels, but not with creatinine.
During a median FU of 559 (257-784) days, 148 out-patients (19%) and 456 in-patients (29%) died and 237 out-patients (30%) and 713 in-patients (45%) died or were re-hospitalised with HF (HFH). Overall, patients with an elevated D-Dimer did not have worse outcomes. However, amongst out-patients, risk rose progressively as plasma D-Dimer concentrations exceeded the limit of detection (HR (95% CI) for HFH/ACM; 1.47 (1.09-1.98); p = 0.01 for 102-499 ng/mL and 2.02 (1.17-3.83); p = 0.01 for = 500 ng/mL) and for ACM 1.26 (0.86-1.86); p = 0.24 and 2.41 (1.29-4.49); p = 0.006). Also, for patients without a history of AF, an increase in risk was observed (HR for HFH/ACM: 1.41 (1.15-1.72); p = 0.001 and 1.47 (1.06-2.05); p = 0.02 and for ACM 1.21 (0.93-1.57);p = 0.16 and 1.61 (1.09-2.39);p = 0.018).
Conclusions: Amongst patients with heart failure, plasma D-Dimer concentrations are lower in patients with AF, perhaps reflecting greater use of anticoagulants but higher in hospitalized patients perhaps reflecting greater severity of heart failure or a higher rate of occult venous thrombo-embolism. D-Dimer was most strongly associated with outcome amongst out-patients in sinus rhythm. The prognostic significance of D-Dimer and its modification by anticoagulants requires further investigation.

P1645
Left ventricular ejection fraction, systolic blood pressure and smoking history are good predictors of respiratory muscle weakness in systolic heart failure

NK Naomi Kondo Nakagawa[1]; MA Diz[1]; TS Kawauchi[1]; GN Andrade[1]; IIK Umeda[2]; FM Murakami[1]; JP Oliveira-Maul[1]; JA Nascimento[1]; N Nunes[3]; JY Takada[3]; AP Mansur[3]; LP Cahalin[4]
[1]*Sao Paulo University Medical School, Sao Paulo, Brazil*; [2]*Institute Dante Pazzanese of Cardiology, Sao Paulo, Brazil*; [3]*Heart Institute of the University of Sao Paulo (InCor), Cardiology Department, Sao Paulo, Brazil*; [4]*University of Miami Miller School of Medicine, Physical Therapy Department, Miami, United States of America*

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Introduction: Inspiratory muscle weakness (IMW) has been identified in 30 to 50% of patients with systolic heart failure. However, little is known on possible risk factors for IMW.
Purpose: To assess clinical and echocardiographic characteristics, physical capacity and inflammatory and cardiovascular diseases markers in patients with systolic heart failure.
Methods: Patients with LVEF < 40% (NYHA II and III) were consecutively recruited in a cardiac ambulatory and divided in two-groups: with IMW (IMW) and without IMW (no-IMW). We assessed demographic, echocardiographic and clinical variables, smoking history, pulmonary function, peripheric and respiratory muscle strength, as well as systemic inflammation and cardiovascular diseases markers in blood samples.
Results: Patients (56 years, 46 male, BMI = 27.5 kg/m2) entered into the study and 36 patients presented IMW (55 ± 17 cmH2O) and 34 had no-IMW (88 ± 20 cmH2O). Groups were different in LVEF (27 ± 6 vs 31 ± 6%, p = 0.003), systolic blood pressure (110 ± 21 vs 126 ± 24 mmHg, p = 0.005), diastolic pressure (68 ± 12 vs 75 ± 15 mmHg, p = 0.042), smoking history (25 vs 10 pack-years, p = 0.012), BNP level (256 vs 110 pg/mL, p = 0.020), frequency of pulmonary hypertension (58 vs 34%, p = 0.029), non-dominant quadríceps strength (211 ± 77 vs 261 ± 94 N, p = 0.024), lung function (predicted vital forced capacity: 72 ± 15 vs 81 ± 13%, p = 0.006; predicted forced expiratory volume 1 s: 61 ± 17 and 75 ± 15%, p = 0.022). The other demographic and clinical variables and markers were similar between groups. Stepwise logistic regression model analysis showed that lower LVEF, lower systolic pressure and smoking history can acurately predict IMW (AUC=.79). Conclusion: IMW can be acurately predicted using a simple model that may help in clinical decision-making due treatment of patients with systolic heart failure using the following:
Probability of IMW= exp (6.0694+(0.0315 x Pack-years)-(0.1038 x LVEF)-(0.03 x SBP) [1 + exp (6.0694+ (0.0315 x Pack-years)-(0.1038 x LVEF)-(0.03 x SBP)]

P1646

Correlation between Th1, Th2, Th17, and Treg cytokines serum levels with autonomic function in patients with chronic Chagas disease and systemic arterial hypertension

RB Bestetti[1]; R Dellalibera-Joviliano[1]; G Lopes[1]; R Furlan-Daniel[1]; K Lopes[2]; CHC Domingos[1]
[1]University of Ribeirao Preto, Ribeirao Preto, Brazil; *[2]Clinica Sao Rafael, Piumhi, Brazil*

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Background: Cytokines serum levels have been associated with autonomic function in patients with different types of heart disease. In general, proinflammatory cytokines have positively been correlated with sympathetic nervous system drive, whereas anti-inflammatory cytokines have negatively been associated with parasympathetic activity. Therefore, the autonomic nervous system may influence the innate immunity system response (the so-called inflammatory reflex). In patients with chronic Chagas disease, there is a marked impairment in Parasympathetic Nervous System. No study has previously addressed the association between cytokines serum levels and autonomic function in patients with chronic Chagas heart disease and systemic arterial hypertension (CCHD-SAH).
Purpose: The aim of this study was to correlate the panel of cytokines (Th1, Th2, Th17, and T treg) serum levels with indices of autonomic function in patients with CCHD-SAH.
Methods: This study focus on eight patients with CCHD-SAH in which a 24-hour Holter monitoring was performed, and heart rate variability in the frequency domain was determined. Parasympathetic activity was evaluated by the high-frequency component (HF), whereas the sympathovagal balance was determined by means of the relation between low frequency component (LH)/ HF component of the heart rate variability in the frequency domain. Cytokines serum measurements were made through the double-ligand/sandwich enzyme-linked immunosorbent assay (ELISA). The Spearman test was used to correlate cytokine serum levels with indices of parasympathetic and sympathetic activity obtained in the power spectral analysis.
Results: There was a strong positive correlation between IL-8 serum levels and parasympathetic activity (r = 0.84; p = 0.0085). A strong negative correlation was found between IL-6 serum levels and parasympathetic activity (r= -0.81; p = 0.01), and TGF Beta serum levels and parasympathetic activity (r= -0.75; p = 0.03). A strong negative correlation between IL-6 serum levels and indices of sympathovagal balance was also observed (r= -0.80; p = 0.01). No correlation was detected between TNF alpha, IL-13, IFN gamma, IL-12, IL-17, IL-23, IL-1 Beta, IL-10, IL-2, IL-4, IL-7 serum levels and indices of parasympathetic activity or sympathovagal balance. Conclusion. Cytokines serum levels correlated with autonomic dysfunction, particularly with parasympathetic derangement, in patients with CCHD-SAH. This suggests a role for the inflammatory reflex in the pathogenesis of patients with this condition.

P1647

Impact of left ventricular assist device implantation on right and left ventricular volumes and functions

C Clement Delmas[1]; E Cariou[1]; P Fournier[1]; S Cazalbou[1]; D Carrie[1]; J Roncalli[1]; M Galinier[1]; O Lairez[1]
[1]Toulouse Rangueil University Hospital (CHU), Cardiology department, Toulouse, France

Background: Because the right ventricle is not assisted, its function is a critical determinant of the hemodynamic in patients with left ventricular (LV) assist devices (LVADs) and contributes significantly to postoperative morbidity and mortality. Right ventricular (RV) failure remains a challenge in the area of continuous-flow LVADs. The aim of this study was to evaluate the evolution of RV volumes and function before and after LVAD implantation.
Methods: Fifteen patients underwent tomographic equilibrium radionuclide ventriculography for the assessment of LV and RV volumes and functions before and after LVAD implantation. Evolution of LV and RV volumes and functions after LVAD implantation were analyzed regarding the results of right heart catheterization.
Results - Mean LV and RV ejection fractions before implantation were 18 ± 7 and 43 ± 13%, respectively. LVAD implantation had no impact on RV ejection fraction (43 ± 11% after implantation, P = 0.955) but increased LV ejection fraction (31 ± 19% after implantation, P = 0.008). LVAD led to a decrease of LV end-diastolic volume (? = -129 ± 88 after implantation, P = 0.001) and RV end-diastolic volume (? = -75 ± 49 after implantation, P = 0.001). The decrease of RV end-diastolic volume was inversely correlated with pulmonary arterial wedge pressure before implantation (R = - 0.651, P = 0.009) but not with pulmonary vasculature resistance (R = 0.018, P = 0.949).
Conclusion: In patients with preserved RV ejection fraction, LVAD implantation leads to a decrease of RV volumes without impact on RV ejection fraction. The decrease of RV end-diastolic volume after LVAD implantation could be explained by the decrease of pulmonary arterial wedge pressure. These results highlight the importance of afterload on RV volumes in patients with heart failure.

P1648

The effect of standard treatment of acute decompensation of heart failure at the concentration of omega-3 and omega-6 polyunsaturated fatty acids in whole blood

A Aleksandra Zaplatina[1]; A Vlasov[1]; S Salikova[1]; O Bystrova[2]; G Osipov[2]; V Grinevich[1]
[1]Military medical Academy, therapy of advanced medical, Saint-Petersburg, Russian Federation; *[2]The international research Centre N. D. Zelinsky Institute of Organic Chemistry, Moscow, Russian Federation*

Introduction: Blood levels of polyunsaturated fatty acids (PUFAs) may have prognostic value in chronic heart failure (?HF). Changes in PUFAs in acute decompensation of CHF and background treatment remains unclear.
Objective: To study the effect of standard treatment of acute decompensation of ?HF on the concentration of eicosapentaenoic acid (EPA), docosahexaenoic (DHA), arachidonic (AA) and linoleic (LA) fatty acids (FA), omega-3 index and the ratio of omega-3 / omega-6 polyunsaturated fatty acids (PUFAs) in whole blood.
Material and Methods: We studied the content of 22 FA in the blood of patients with CHF in stable stage (CHF, n = 12) with acute decompensation (ADHF1, n = 24) and after the standard treatment (ADHF2, n = 24). We calculated omega-3 index (the ratio of the sum of EPA and DHA to the sum of all FA) and the ratio of the sum of EPA and DHA to the sum of AK and LK.
Results: Indicators of EPA, DHA, omega-3 index in the group ADHF1 was lower than in group CHF (0.085 (0.06;0.17) vs. 0.26 (0.15;0.4) mmol/ml, p = 0.0005; 0.37 (0.16;0.62) vs 0.84 (0.55;1.10) mmol/ml, p = 0.004; 1.11 (0.65;2.11) vs 2.44 (1.80;3.71) %, p = 0.0008, respectively). After the standard treatment acute decompensation CHF the levels of EPA, DHA, omega-3 index increased and amounted in group ADHF2 to 0.16 (0.11;0.21) mmol/ml, p = 0.0016; 0.46 (0.35;0.76) mmol/ml, p = 0.045; 1.74 (1.14;2.42) %, p = 0.043 respectively.
Statistically significant differences the contents of AK and LK in the blood between patients groups ADHF1 and CHF were not revealed. The indicators of AK and LK in group ADHF1 were 2.74 (1.80;4.15) mmol/ml, p = 0.25 and 6.70 (4.92;9.44) mmol/ml, p = 0.19, respectively. On the background of treatment was observed the increase of the concentration AK in group ADHF2 (3.40 (2.56;4.91) mmol/ml, p = 0.011) and a trend of increasing LK (9.13 (5.08;11.28) mmol/ml, p = 0.09). The concentration of AK patients in group CHF was 3.42 (2.42;4.62) mmol/ml, p = 0.76; the concentration of LK was 7.27 (6.45;11.88) mmol/ml, p = 0.9.

The dynamics of the ratio omega-3 / omega-6 testified to the prevalence of a share of omega-6 in all participants, especially within the decompensated CHF. The ratio omega-3/omega-6 in patients group ADHF1 was 1/22.94 (12.87;36.32), in patient's group CHF was 1/15.63 (11.71;25.32), and patient's group ADHF2 was 1/12.25 (8.25;14.82). After reversal of the syndrome of fluid retention in patients, the ratio was changed due to the increase level of omega-3 PUFA.
Conclusion: During the acute decompensation of CHF observed a significant reduction in patients' blood omega-3 index, the concentration of EPA and DHA. Standard therapy of decompensated CHF increases content in the blood of patients with EPA, DHA, AA, omega-3 index.

P1649
Mortality from cardiovascular diseases among US cancer survivors

K Kathleen Sturgeon[1]; L Deng[2]; S Bluethmann[1]; D Trifiletti[3]; C Jiang[4]; S Kelly[5]; N Zaorsky[6]
[1]Penn State College of Medicine, Public Health Sciences, Hershey, United States of America; *[2]Albert Einstein College of Medicine, Jacobi Medical Center, New York, United States of America*; *[3]Mayo Clinic, Jacksonville, United States of America*; *[4]Mount Sinai School of Medicine, Internal Medicine, New York, United States of America*; *[5]National Institutes of Health, Bethesda, United States of America*; *[6]Penn State Cancer Institute, Radiation Oncology, Hershey, United States of America*

Introduction: Cardiotoxicities from cancer treatment have been shown to increase mortality risk in cancer survivors. But, the specific risk by cancer site and cardiovascular disease (CVD) over time is unknown.
Purpose: We conducted an epidemiological analysis to characterize death from CVDs in multiple cancer sites, with respect to the following: (1) continuous calendar years of diagnosis, (2) follow-up time after diagnosis, and (3) age at diagnosis.
Methods: We analyzed Surveillance, Epidemiology, and End Results (SEER) program data for death from CVDs among 3,234,256 U.S. cancer patients between 1973 and 2013. CVDs were defined as heart disease, hypertension, cerebrovascular disease, atherosclerosis, and aortic aneurysm/dissection. For objective 1, we characterized total deaths due to CVDs in each continuous calendar year of diagnosis in cancer patients by cancer type. For objectives 2 and 3, we calculated standardized mortality ratios (SMRs), which compare the risk of death from CVDs vs the general population; SMRs were characterized as a function of follow-up time since diagnosis (objective 2), and age at diagnosis (objective 3). Analyses were adjusted by age, race, and sex.
Results: Among 28 cancer types, from 1973-2013, 1,228,328 patients (38%) died from cancer and 365,689 patients (11.3%) died from CVDs. Among CVDs, >80% of deaths were due to heart or cerebrovascular disease. The majority of CVD deaths were in patients with cancer of the prostate (23.1%), breast (16.5%), and bladder (7.6%). For objective 1, of 564,129 cancer patients diagnosed from 1973-1982, 19.3% have died of CVDs, compared to 10.6% CVD deaths of cancer patients diagnosed from 1993-2002. In certain cancers (e.g. prostate, breast, rectal, lymphoma), there has been an upward trend in death due to CVDs; in other cancers (e.g. pancreas, lung), the rate remained relatively low. For objective 2, the highest SMR of heart disease (SMR, 3.93 [95% CI, 3.89-3.97]) was within the first year after cancer diagnosis, decreasing at 1-10 years follow-up, and climbing in years 15-20 (SMR, 2.29 [95% CI, 2.26-2.32]) and 20+ (SMR, 2.72 [95% CI, 2.69-2.76]). For objective 3, the highest SMRs of heart disease (<30) were noted in patients diagnosed at < 35 years of age. SMRs of heart disease declined with increasing age of diagnosis (40-44y: SMR, 23.16 [95%CI, 21.36-25.08]; 50-54y: SMR, 15.38 [95%CI, 14.83-15.95]; 60-64y: SMR, 7.29 [95% CI, 7.15-7.43]; 70-74y: SMR, 3.59 [95% CI, 3.55-3.64]; and 80-85y: SMR, 2.17 [95% CI, 2.15-2.19]).
Conclusions: Patients at highest risk to die of CVDs include cancers of the prostate, breast, bladder, or lymphatic system. The risk of death from CVDs (vs the general population) is highest in the first year after diagnosis; this risk declines with time but always remains elevated over the general population. Patients diagnosed with cancer at a younger age should be followed closely for potential CVDs, as they are at higher risk than older survivors.

P1650
Low body mass index and arterial hypotension as early predictors of cardiotoxicity in patients with HER2 + breast cancer

M Marina Vitsenya[1]; A Potekhina[1]; A Ovchinnikov[1]; S Gavryushina[1]; A Skorobogatova[1]; F Ageev[1]; I Chazova[1]
[1]Cardiology Research and Production Center, Outpatient care, Moscow, Russian Federation

Background: Pre-existing cardiovascular risk factors, mainly arterial hypertension (AH), or established cardiovascular disease (CVD), increase the risk for chemotherapy-induced left ventricular (LV) dysfunction and heart failure. The monitoring and management strategies for patients with low cardiovascular risk receiving cardiotoxic therapy require considerable attention.
Aim: To determine the incidence and risk factors of LV dysfunction in hypertensive and normotensive patients with HER2+ breast cancer (BC) receiving anthracycline-containing regimens with trastuzumab.
Methods: 60 women with newly diagnosed HER2+ BC, mean age 49,9 ± 11,8 years without established CVD were enrolled. 43% of patients had AH and antihypertensive therapy with ACE inhibitor or ARB was initiated / optimized. Patients had been receiving neoadjuvant cancer therapy with anthracyclines and trastuzumab with further adjuvant therapy with trastuzumab during one year. Complex cardiological examinations including echocardiography with myocardial global longitudinal strain (GLS) assessment were performed before the start of cancer treatment and every 3 months. Chemotherapy-induced LV dysfunction was considered if LVEF decrease of 10 percentage points, to a value below 50%, and early subclinical cardiotoxicity if a relative percentage reduction of GLS of 15% from baseline occurred.
Results: The hypertensive (HG) and normotensive (NG) groups at baseline demonstrated differences in mean age (58 ± 8.5 vs. 43.7 ± 10.2, p < 0.00001), BMI (28.45 [26, 31.6] vs. 23,5 [20; 28], p < 0.01), lipid and serum glucose levels, LVEF (62 [60, 65] vs. 64 [63, 67]%, p < 0.05) and GLS values (-20,2 [-18.5, -21.8] vs. -22.3 [-21, -23.2]%, p < 0.01). LVEF and GLS decreased significantly in both groups. After completion of therapy LVEF was 59[55;62]%, GLS -17,2[16;18,9]% in HG and 56[53;61]%, -19[-18,2;-20,2]% in NG (p < 0,05 vs. initial values). Chemotherapy-induced LV dysfunction was observed in 6 (10%) of patients, 5 (83,3 %) of them were from NG. 28 patients (46,6 %) developed subclinical cardiotoxisity, 20 (71,4%) of them were from NG. Initial BMI below 25 kg/m2 and arterial hypotension (SAD < 120 mmHg) demonstrated the prognostic significance for the development of early subclinical cardiotoxisity (OR 10,04 (95% CI 3,09-39,21), ? < 0,001 and OR 4,27(95%CI 1,25-14,56), ? = 0,015, respectively).
Conclusion. The incidence of chemotherapy-induced subclinical cardiotoxisity was lower in hypertensive BC patients probably due to prevalence of antihypertensive therapy with cardioprotective effect. Low body mass index and arterial hypotension showed the predictive role for subclinical cardiotoxisity development in HER2+ BC patients receiving anthracycline-containing regimens with trastuzumab.

P1651
Routine use of global longitudinal strain among active breast cancer patients: A Cardio-Oncology registry

LM Michal Laufer-Perl[1]; A Milwidsky[1]; L Mor[1]; D Ravid[1]; N Amrami[1]; M Derakhshesh[1]; J Sherez[1]; G Keren[1]; Y Arbel[1]; Y Topilsky[1]
[1]Tel Aviv Sourasky Medical Center, Cardiology, Tel Aviv, Israel

Background: Increased survival among breast cancer patients exposed a wide range of side effects, with cardiotoxicity being the most significant one. Cancer therapeutic related cardiac dysfunction (CTRCD) is defined as a left ventricular ejection fraction (LVEF) reduction of >10 % points, to a value below 50%. Unfortunately, a detectable drop in LVEF occurs only after the loss of a substantial amount of myocardial tissue, and in up to 58% of these patients the ventricular function will not recover. Therefore, according to the American and European Society of Echocardiography, global longitudinal strain (GLS) is the optimal parameter for early detection of subclinical LV dysfunction, with a relative reduction of = 15% considered to be clinically significant. However, due to the lack of studies routine use of GLS has not been fully adopted.
Objectives: Evaluating the frequency of significant GLS reduction and whether it predicts CTRCD development among active breast cancer patients.
Methods: Data was collected as part of the International Cardio-Oncology Registry (ICOR), enrolling all patients evaluating in the cardio-oncology clinic in our institution. All patients performed at least two GLS examinations by the same vendor, technician and interpreting cardiologist.
Results: Among 103 consecutive patients, 5 (5%) developed CTRCD for which lower baseline GLS (18 ± 3 vs. 21 ± 2, p = 0.016) was a significant predictor. Among 79 patients,
9 (11%) developed significant GLS reduction, of which 44% had no concomitant EF reduction. Median time for GLS reduction was 93 days. There were no significant differences in the baseline cardiac risk factors and no predictors for GLS reductions were identified, including blood tests or echocardiography parameters (diastolic function, right ventricular function or systolic pulmonary artery pressure).
Conclusions: Our study demonstrate that GLS reduction is frequent among breast cancer patients, precedes LVEF reduction and cannot be anticipated by other echocardiographic parameters. Using GLS routinely may lead to an early diagnosis and prevention of cardiotoxicity.

P1652

Dispersion of ventricular repolarization in men treated by hormone therapy for advanced prostatic cancer.

ACD Andrei Cristian Dan Gheorghe[1]; GS Gheorghe[1]; A Ciobanu[1]; AS Hodorogea[1]; IT Nanea[1]
[1]*Clinical Hospital Dr Theodor Burghele, Cardiology, Bucharest, Romania*

Aim: To evaluate the proarrhythmic effects of the treatment with luteinizing hormone-releasing hormone (LHRH) antagonists in advanced prostate cancer by determining the surface ECG parameters of electrical instability.
Method We investigated 24 men (pts) with advanced prostatic cancer treated by orchiectomy and LHRH antagonist degarelix. We noted clinical history and excluded pts with atrial fibrillation, heart failure (HF) NYHA III and IV class, acute myocardial infarction (MI) in the last 6 months, chronic renal disease stages IV-V. We performed ECG, Holter ECG, echocardiography and evaluated QT interval dispersion (QTd), Tpeak-Tend interval (Tpe, in V5), J-T peak interval (JT), Lown class ventricular premature beats (VPB) on Holter ECG, left ventricular ejection fraction (LVEF) before the beginning of the treatment (V1) and after 3 (V2) and 6 months (V3). We used paired t-test for comparing the differences.
Results: Pts were 67.5 +/-10 years old. 18 (75 %) had arterial hypertension, 13 (54.1%) stable angina, 6 (25 %) old myocardial infarction, 5 (20.8 %) diabetes mellitus, 5 (20.8%) chronic renal disease grade 1-3b. They were stable during the study. 18 (75%) pts had an statistical significant (p = 0.02) increase of the QTd (83 +/- 10 ms) and JT (78 +/- 30 ms) intervals between V1 and V3, . Tpe changes were variable. We did not note an increase in the number or severity of VPB between V1, V2 and V3. Mean LVEF was 60+/-5%, stable between V1 and V3.
Conclusion: In pts with advanced prostatic cancer receiving LHRH antagonist for 6 months the values of QTd and JT duration had a rising tendency. TPe changes were variable. No increase was noted in the number or severity of VPB during the first 6 months of treatment

P1653

The use of myocardial deformation imaging to predict cardio toxicity in breast cancer treated with trastuzumab

S Charfeddine[1]; C Yousfi[1]; L Abid[1]; D Abid[1]; S Kammoun[1]; W Ben Kridis[2]; S Sghaier[2]; M Frikha[2]
[1]*Hedi Chaker University Hospital, Cardiology department, Sfax, Tunisia*; [2]*Habib Bourguiba University Hospital, Oncology department , Sfax, Tunisia*

BACKYGROUND: Trastuzumab, a chemotherapeutic agent used in the treatment of breast cancer, could induce cardio toxicity (CT). Although left ventricular ejection fraction (LVEF) is the gold standard to monitor chemotherapy-induced CT, measurement of myocardial deformation using speckle tracking enables more detailed assessment of myocardial contractility.
Purpose: The aim of this study was to determine the value of strain imaging in the early detection and screening of Trastuzumab's cardio toxicity.
Methods: This was a prospective study of 31 breast cancer patients receiving adjuvant Trastuzumab, who underwent 2-dimensional, tissue Doppler, and strain echocardiographic examination at baseline, 4 months and 10 months after therapy. The LV global longitudinal strain (GLS), global circumferential (GCS) and radial strain (GRS), and other echocardiographic parameters were calculated.
Results: At the first follow up, The LV ejection fraction, tissue Doppler parameters, GCS and GRS values did not show any change, whereas significant decreases were observed in GLS value (-20.58+/-2.28% vs. -19.35+/-2.14, p = 0.001) and systolic annular velocity of the lateral LV wall (S' velocity) (10.83+/-2.31 vs. 9.64+/-1.72, p = 0.002). At the last follow up, patients who have presented an earlier significant decrease in GLS value, have developed subclinical LV dysfunction with a significant decrease in LVEF > 10%.
Conclusions:
The two dimensional 2D strain imaging is a new non-invasive technique that can better assess the real state of left ventricular function. Our study confirms the value of global longitudinal strain in the early detection of subclinical cardio toxicity before conventional measures in women undergoing treatment with Trastuzumab for breast cancer.

P1654

Long-term follow up of acute heart failure patients underwent levosimendan infusion: identification of responders and non responders by using hlm classification

P Paolo Severino[1]; M Pucci[1]; M Alfarano[1]; E Pagliaroli[1]; M Straito[1]; S Calcagno[1]; A Fusto[1]; M Mancone[1]; F Fedele[1]
[1]*Sapienza University of Rome, Department of Cardiovascular, Respiratory, Nephrology, Anesthesiology and Geriatric Sciences, Sapien, Rome, Italy*

Introduction: Acute heart failure (AHF) still has poor long-term prognosis with high rehospitalization and mortality rates; Levosimendan (Levo) is an inodilator that seems to reduce mortality in AHF patients. AHF determines involvement of other organs beyond heart; similar to TNM used in oncology, we proposed the HLM staging system to assess prognosis of HF patients, evaluating heart damage (H), lung involvement (L) and malfunction (M) of peripheral organs (JACC 2014;20;63(19):1959-60).
Hypothesis: The aim is to evaluate the outcomes of Levo infusion in AHF patients and, by using HLM classification, to identify the predictors of increased cardiac mortality and rehospitalization for
major cardiovascular and cerebrovascular events (MACCE) risk.
Methods. AHF patients admitted to our Hospital were enrolled. All patients received 24-h Levo i.v. infusion (0.05- 0.2 mcg/kg/min, no bolus) in addition to standard therapy. Pre and post Levo
infusion, clinical, laboratory and imaging data for H, L and M were collected in according to HLM.
At 6 and 12 months all patients were followed up to check for rehospitalization for MACCE and cardiac death.
Results: We enrolled 300 AHF patients, two of which died in hospital. Levo infusion improved HLM stages with a greater impact on L and M parameters (L, M pre vs L, M post; p <0.001). About H parameter, we observed a statistical significative improvement of the left ventricular ejection fraction (p < 0.0001) pre and post Levo infusion as well as reduction of left
ventricular end-systolic volume (p < 0.0098) and pro-BNP (p < 0.338). Patients were also divided into two groups: Group A, with no improvement or only in L or M; Group B, with an improvement of L and M. At 6 and 12 months, Group B showed significant better outcomes in term of cardiac mortality and rehospitalization compared with Group A.
Conclusions: 24-h Levo infusion improves clinical status of AHF patients. HLM identifies patient responder to this inodilator, with a significant reduction of mortality and rehospitalization risk at 6 and 12 months beyond risk factors and AHF etiology. Moreover, using HLM it may be possible to
identify patients with a poorer prognosis that may need repetitive use of Levo or advanced therapy.

P1655

Haemodynamic profiles in type 2 pulmonary hypertension influence response to phosphodiesterase-5 inhibitors

P Patricia Alves[1]; AV Marinho[1]; C Domingues[1]; JA Ferreira[1]; J Milner[1]; R Baptista[1]; F Franco[1]; G Castro[1]; M Pego[1]
[1]*University Hospitals of Coimbra, Cardiology, Coimbra, Portugal*

Background : Pulmonary hypertension (PH) is a complication of left heart disease with a small subset having elevated transpulmonary gradient (TPG), diastolic pulmonary gradient (DPG) or pulmonary vascular resistance (PVR).
Purpose: To assess the effect of phosphodiesterase-5 inhibitors (PDE5i) in type 2 PH hemodynamic profiles.
Methods: We retrospectively enrolled 195 patients with type 2 PH and created the following groups: group A with TPG = 14 mmHg and DPG = 7 mmHg; group B with TPG = 14 and DPG <7; group C with TPG <14 and DPG <7. All groups had PVR = 3.WU Parameters before and after PDE5i were collected.
Results : About 57% of patients were started on PDE5i. Prevalence of the different profiles was: 15% for group A; 39% for group B; 20% group for C. Patients that were started on PDE5i had higher values of MPAP (p <0.001), PVR (p <0.001) and TPG (p <0.001) and lower values of cardiac output (CO) (p = 0.01). No significant differences were observed in DPG values. After institution of PDEi5, there was an overall significant decrease of MPAP (44 to 39, p <0.001), PVR (6.3 to 3.4, p <0.001), capillary wedge pressure (CWP) (25 to 23mmHg, p = 0.03), while CO was significantly increased (3.2 to 3.9 L.min-1, p <0.001). This effect seemed to be driven by group B, as per subgroup analysis showed in the table. PVR reduction was seen in groups A, B and C. CO increase was notorious in group B and also in groups A and C.
Conclusions: : A high prevalence of a hemodynamic profile with high TPG and PVR and low DPG was found. Hemodynamic parameters in patients under PDE5i significantly improved, particularly in the group with isolated high TPG, but not with high DPG.

		Pre-PDE5i	Post-PDE5i	P value
MPAP	A	45.4(±13.8)	40(±12.3)	0.07
B	45.6(±9.6)	38.5(±10.5)	<0.001	
CWP	B	26.4(±7.6)	22.4(±7.8)	0.006
PVR	A	9.5(±8.9)	4.2(±2.8)	0.008
B	6.8(±6.1)	4.1(±3.4)	<0.001	
C	4.4(±1.4)	1.8(±1.9)	0.003	
TPG	A	24.8(±9.1)	17.4(±6.9)	<0.001
B	19.1(±4.6)	16.1(±7.9)	0.004	
CO	A	3.3(±0.8)	3.9(±0.8)	0.06
B	3.2(±0.9)	3.9(±1.1)	<0.001	
C	3.2(±2.5)	3.8(±1.3)	0.05	

P1656

Prognostic impact of chronic kidney disease on long-term mortality in patients with preserved, moderately impared and severely impared left ventricular systolic function after myocardial infarction

L Lidija Savic[1]; I Mrdovic[2]; G Krljanac[2]; M Asanin[2]; R Lasica[2]; D Rajic[2]; D Matic[2]
[1]*Clinical Center of Serbia, Institute for Cardiovascular Disease, Belgrade, Serbia*; [2]*Clinical Center of Serbia, Institute for Cardiovascular Disease, Emergency Hospital, Belgrade, Serbia*

Background/aim: Chronic kidney disease (CKD) is associated with poor cardiovascular outcome in the general population after ST-elevation myocardial infaction (STEMI). The aim of this study was to investigate and compare the prognostic impact of preterminal CKD in patients with preserved, moderately and severely reduced left ventricular systolic function following STEMI.
Method: we included 2436 consecutive STEMI patients treated with primary percutaneous coronary intervention (pPCI). Patients presenting with cardiogenic shock and patients on hemodyalisis were excluded. Left ventricular systolic function was assesed by echocardiographic examination before discharge. According to EF, patients were divided in three groups: preserved left ventricular systolic function - EF >50%, moderately impared left ventricular systolic function - EF 40-50% and severely impared left ventricular systolic function - EF < 40%. The follow-up period was 6 years.
Results: Out of a total of 2436 patients, 1773(72.7%) were men and 663 (37.3%) were women. The average age of the examined patients was 57 (50, 63) years. Preserved, moderately and severely reduced left ventricular systolic function were registered in 741(30.5%), 1367(56.1%) and 328(13.4%) patients, respectively. Baseline CKD was registered in 472(19.3%) patients and the mean eGFR value was 88.5 (67.7, 108.8)ml/min/1.73m2. CKD was registered in 105 (14.2%) patients with preserved systolic function, in 247(18.1%) patients with moderately impared and in 120(36.5%) patients with severely impared systolic function. Over a 6-year follow-up period there were 196 (8.3%) deaths overall. Regardless of the presence of CKD, 6-year mortality rates in patients with preserved, moderately and severely impared systolic function were 2.7%, 5.2% and 31.1% respectively. Within each EF group, patients with CKD had a worse outcome, both in the short- and long term. In cox rgression model CKD remained an independent predictor of all-cause mortality during a 6-year follow-up in patients with moderately and severely reduced systolic function, but not in patients with preserved systolic function: EF >50% (HR 0,59, 95%CI 0,14-1,41, p = 0.461), EF 40-50% (HR 2.52, 95%CI 1.54-3.78, p = 0.001) and EF < 40% (HR 2.84, 95%CI 1.68-5.34, p < 0.001). Conclusion: Although patients with CKD had higher 6-year mortallity following STEMI regardless of the EF, CKD remained a strong independent predictor for 6-year mortality only in patients with moderately and severely reduced systolic function

P1657

Correlation of large arteries stiffness parameters in STEMI patients with systolic and diastolic left ventricular dysfunction

L Salyamova[1]; A Khromova[1]; A Golubeva[1]; N Burko[1]; I Matrosova[1]; V Valentin Oleinikov[1]
[1]*Penza State University, Penza, Russian Federation*

Aim: to study the correlation between central pressure parameters, arterial stiffness and echocardiographic indicis of systolic and/or diastolic left ventricular dysfunction in patients with ST segment elevation myocardial infarction (STEMI).
Methods: the study included 69 patients with STEMI. Inclusion criterion was the presence of significant stenosis of one coronary artery according to the coronary angiography results Patients underwent echocardiography using the MyLab device (Esaote, Italy) at 7-9th day from the disease onset. The end-diastolic volume index (EDVi), and ejection fraction (EF) were determined. Diastolic function was analyzed by the following parameters: E/A peak velocity ratio, deceleration time of early diastolic mitral inflow velocity (DTE), the time of isovolumetric relaxation (IVRT). The structural and functional properties of the large arteries were assessed by the applanation tonometry method using the Sphygmocor device (AtCorMedical, Australia) for the following parameters: aortic systolic (SBPao), diastolic (DBPao) and pulse (PPao) pressure, carotid-femoral pulse wave velocity (cfPWV). Ultrasound of the common carotid arteries with high-frequency RF signal technology was performed on the MyLab device ("Esaote", Italy). Local systolic (locPsys) and diastolic (locPdia) pressure, local pulse wave velocity (locPWV), stiffness index ß, coefficient of transverse distensibility (DC) were recorded. The Spearman rank correlation coefficient was used to determine the correlations.
Results: positive relationship was found between EF and SBPao (r = 0.27, p = 0.03), PPao (r = 0.26, p = 0.03), locPsys (r = 0.32, p = 0.01), negative - between EF and index ß (r=-0.28, p = 0.02). The E/A ration index correlated with DBPao (r=-0.29, p = 0.02), cfPWV (r=-0.26; p = 0.04), locPsys (r=-0.33; p = 0.01), locPdia (r=-0.41, p < 0.01), locPWV (r=-0.28, p = 0.02), the DC coefficient (r = 0.37, p < 0.01). The DTE decrease was associated with lower values of SBPao (r = 0.64, p < 0.01), DBPao (r = 0.30, p = 0.03), PPao (r = 0.45, p < 0.01), locPsys (r = 0.41, p < 0.01), locPdia (r = 0.39, p < 0.01). IVRT also correlated with BP in the aorta and common carotid arteries: SBPao (r = 0.45, p < 0.01), PPao (r = 0.29, p = 0.03), locPsys (r = 0.29, p = 0.03), locPdia (r = 0.30, p = 0.02). The relationship between EDVi and indicators reflecting the structural and functional properties of the aorta and common carotid arteries was not revealed.
Conclusion: the deterioration of systolic and diastolic left ventricular function is associated with lower values of BP in the aorta and common carotid arteries, and increased local vascular rigidity in patients with ST segment elevation myocardial infarction.

P1658

Mid-range ejection fraction: a grey zone in heart failure?

JJ Herrera Paz[1]; N Zareba[1]; CL Gonzalez[1]; CE Sandoval[1]; M Urdapilleta[1]
[1]*FLENI Institute, Cardiology, Buenos Aires, Argentina*

Background: From the use of the terms Heart failure (CHF) with preserved ejection fraction (EF) and reduced ejection fraction, a group of undefined patients remains in the middle of these values (between 40 - 49 of EF), a true grey area. Recently the European Guidelines incorporated this group as mid-range EF. Neither the behavior of this group nor the therapeutic strategy to be implemented are entirely clear.
Objectives: To evaluate in a population of patients hospitalized for HF if the patients with mid-range EF evolve as the reduced EF group or as the preserved ones. For this, we took death during hospitalization; CHF-related hospitalization and death during follow-up as end points.
Materials and methods: We retrospectively evaluated 428 patients hospitalized for CHF in a center in the city of Buenos Aires, Argentina, between 2008 and 2013. The hospitalizations were consecutive and for the first time. All the patients were followed up by telephone for at least one year. The population was divided in three groups, group A, n = 178 patients with preserved EF (< 50%), group B, n = 180 patients with reduced EF (< 39%) and group C, n = 70 patients with mid-range EF (from 40 to 49%)
The Wilcoxon test was performed for the analysis of the variables. For the comparison between EF groups, the chi2 test was carried out and later logistic regression was conducted.
Results: Mortality during hospitalization was 3.9% for group A, 6.6% for group B and 2.8% for group C. During follow up, death was 30% for A, 38% for B and 35% for C. CHF-related hospitalization were and 33% for A, 36% for B and 40% for C.
We found no significant differences between the baseline characteristics of each group. Only one statistical trend was found, the presence of coronary disease between group B and C (p = 0.054).
No statistical relationship was found between group A and C in the end points.
There was a statistically significant relationship between groups B and C in the end points of death and CHF-related hospitalization during follow-up of patients (p < 0.05)
Conclusions: Patients with intermediate EF do not relate in a statistically significant way with preserved EF.
Patients with intermediate EF have a statistically significant association with the group of reduced EF in terms of mortality and CHF-related hospitalization in the follow-up. This could suggest that the grey or mid-range EF group behaves, in this population, similarly to the reduced EF group. Considering this, we could propose a similar therapeutic strategy for this new group.

P1659

Reperfusion and reversible diastolic dysfunction of the left ventricle in patients with ST elevation myocardial infarction

D KH Rakhmanov[1]; S R Kenjaev[2]; A L Alyavi[3]; M L Kenjaev[4]; M S Mirmaksudov[1]; SH B Turg'unboyev[1]
[1]Tashkent Medical Academy, Tashkent, Uzbekistan; *[2]Republican Research Center of Emergency Medicine, Tashkent, Uzbekistan*; *[3]Republican Specialized Scientific-Practical Medical Center Therapy and Medical Rehabilitation, Tashkent, Uzbekistan*; *[4]Bukhara branch of Republican Research Center of Emergency Medicine, Bukhara, Uzbekistan*

Aim: To study the effect of reperfusion on the reversibility of diastolic LV myocardial dysfunction in patients with ST elevation myocardial infarction (STEMI).
Methods: 302 patients with STEMI were included in the study. All patients underwent primary PCI. Depending on the results of myocardial reperfusion, patients were divided into 3 groups. 1st group consisted of 196 patients with successful myocardial reperfusion; 2nd group was 76 patients with partial myocardial reperfusion; and 3rd group was included 30 patients without successful myocardial reperfusion. Stress echocardiography with low dose dobutamine was carried out after stabilizing condition on 3rd-5th days of the disease to evaluate reversible diastolic dysfunction.
Results: In 242 (80.0%) of 302 patients with STEMI, type I of diastolic dysfunction of left ventricle (DDLV) were identified in the first day of the disease, type II (pseudonormal type) and type III were determined in 15 (5%) and 45 (15%) patients respectively. Among patients with adequate reperfusion (1st group), 97% had DDLV as a relaxation disorder and 3% had a pseudonormal type DDLV. In this group, the restrictive type of DDLV was not detected. After injection of low doses of dobutamine in 6 patients with type 2 DDLV, a transformation to type 1 DDLV was noted, which was probably due to an improvement in diastolic properties in the zone of myocardial stunning in response to small doses of dobutamine. In the second group, the administration of low doses of dobutamine also resulted in a reduction in the number of patients with type III DDLV by 51% and type II DDLV by 66%. Consequently, the number of patients with type I DDLV increased from 63 to 83%. The introduction of low doses of dobutamine did not lead to significant changes in 3rd group patients. Restrictive type of diastolic dysfunction was often found among 3rd group patients with absence of myocardial reperfusion, which may be due to severe myocardial dysfunction. Type III of DDLV recorded also in 3rd group (with unsuccessful reperfusion) after injection of low dose dobutamine.
Conclusions: Successful myocardial reperfusion in patients with STEMI helps maintain diastolic LV function. Changes in diastolic LV function during low dose dobutamine echocardiography are associated with the presence of reversible myocardial dysfunction. Effective and early application of reperfusion methods (TLT, PCI) improves the diastolic properties of LV myocardium in the ischemic injury zone, which prevents the development of CHF. An irreversible restrictive type of diastolic dysfunction often develops after unsuccessful myocardial revascularization, which can be predictor of unfavorable post-infarction myocardial remodeling and severe form of CHF.

P1660

Ventriculoatrial remodeling in patients with recurrent atrial fibrillation and diastolic dysfunction: does gender matter?

A Shavarov[1]; E Kokhan[2]; G Kiyakbaev[1]; Z Kobalava[1]
[1]RUDN University, Moscow, Russian Federation; *[2]Lomonosov Moscow State University, Moscow, Russian Federation*

Background: Left ventricular (LV) hypertrophy and left atrial (LA) remodeling are associated with recurrence of atrial fibrillation (AF). There exists a significant gender variability in the response of the LV to increased hemodynamic load. But the data concerning the relationship between LV and LA remodeling depending on gender is scarce.
Purpose: To evaluate the impact of gender on the relationship between LV and LA remodeling in patients with AF, hypertension and diastolic dysfunction (DD).
Methods: The study included 27 men and 28 women (median age of 65 [60;72]) with recurrent non-valvular AF, hypertension, mild to moderate LV DD and preserved ejection fraction (<50%). All patients underwent conventional and speckle tracking echocardiography. Global peak LA longitudinal strain (PALS, %) in the reservoir (r) and contractile (c) phases was assessed using 6 segments in the 4-chamber and 2-chamber views. We calculated diastolic index using the ratio of E/E' to LV-end diastolic volume.
Results: There were no significant differences between men and women in most clinical characteristics including median of hypertension duration (67 vs 65 moths in men and women, respectively; $p = 0.88$) and the prevalence of paroxysmal and persistent AF (10 and 17 pts in men, respectively vs 14 and 14 pts in women, respectively; $p = 0.33$). Despite the fact that DD was more pronounced in women than in men [E/E' (13 vs 11.2; $p = 0.03$) and diastolic index (0.13 vs 0.09 ml-1; $p = 0.001$)], LA structural and functional parameters were similar between the two groups. Compared to men, women also had higher median of LV relative wall thickness (0.53 vs 0.4; $p = 0.03$). In women only the diastolic index was significantly related to LA size ($r = 0.52$; $p = 0.005$ vs $r=-0.32$; $p = 0.14$, respectively); PALSr ($r=-0.53$; $p = 0.004$ vs $r=-0.1$; $p = 0.62$, respectively) and PALSc ($r = 0.51$; $p = 0.005$ vs $r=-0.1$; $p = 0.65$, respectively); p for all interactions < 0.05. Subgroups of patients with paroxysmal and persistent AF differed by diastolic index (0.13 vs 0.16 ml-1; $p = 0.01$ and 0.1 vs 0.08 $p = 0.16$ ml-1 in women and men, respectively) and LV global longitudinal strain (-19 vs -16.5; $p = 0.04$ and -17.5 vs -17.1 $p = 0.41$, respectively for women and men) in women only.
Conclusion: Patients of both genders had similar patterns of LA remodeling. Only in women LV function was significantly related to LA remodeling and type of AF. That may be because a relation between increased afterload, LV and LA remodeling is stronger in women than in men.

P1661

How about heart failure with reduced or preserved diastolic function?

JP Jose Pedro Sousa[1]; M Madeira[1]; L Reis[1]; C Negrier[1]; L Goncalves[1]
[1]Centro Hospitalar e Universitário de Coimbra - Hospital Geral, Cardiology, Coimbra, Portugal

Introduction: Left ventricular ejection fraction (LVEF), the main parameter of systolic function, is a cornerstone for classification, management and outcome prediction in heart failure (HF). Having been more difficult to evaluate, diastolic dysfunction is less studied and the usefulness of its objective measurement in determining clinical care is controversial.
Purpose: To characterize diastolic dysfunction and determine its short term prognostic significance in the setting of acute HF.
Methods: Retrospective single-center study comprising patients consecutively admitted into a cardiac intensive care unit, during six years, presenting with de novo or decompensated acute HF. Demographic, clinical, laboratory, echocardiographic, therapeutic and prognostic data were assessed. Diastolic function was comprehensively evaluated using echocardiography and dysfunction was graded into three patterns: impaired relaxation (IR), pseudonormal (PN) and restrictive (RT). Follow-up (FU) was performed targeting hospital readmission for acute HF and all-cause mortality. All statistical analysis was performed using SPSS version 23 (IBM Corp., Armonk, NY, USA).
Results: 264 patients were included. Mean age was 70 ± 14 years and 22% were female. Median FU was 10 months. In-hospital mortality was 15%, while readmission for HF and death in FU occurred in 46.7% and 42% of patients, respectively. FEVE was 34 ± 12.9% and the distribution of diastolic function across patients was as follows: 13.8% normal, 53.2% IR, 14.7% PN and 18.3% RT. These groups were homogeneous as to sex, whereas IR patients were older than RT patients (72 vs. 64 years, p 0.013). Personal history of arterial hypertension was more common in IR and rarer in RT (p 0.001), while that of type 2 diabetes mellitus was only numerically more frequent in PN (p 0.078). PN showed itself dependent upon coronary artery disease (p 0.005) and chronic kidney disease was found to be at the verge of significance for dependency on diastolic dysfunction as a whole (p 0.068). Both serum creatinine and NT-proBNP, at admission, maximum value and discharge, exhibited no statistically significant differences between groups. LVEF was lower in RT than in all other groups (24 ± 8.7%, $p < 0.001$). Maximum daily dose of furosemide was greater in RT than in IR (202 ± 137 vs. 149 ± 100mg, p 0.011). Similarly, and in spite of independency between diastolic dysfunction and in-hospital mortality, when compared to IR, RT was associated with superior rates of readmission for acute HF (p 0.005) and death during FU (p 0.023).
Conclusions: In the setting of acute HF, diastolic dysfunction is the rule, with IR as the predominant pattern. However, only RT displays association with greater rates of hospital readmission and all-cause mortality during FU.

P1662

Abnormally elevated left-ventricular filling pressure as a prognostic factor in an Advanced Heart Failure Unit

G L Alonso Salinas[1]; S Del Prado Diaz[2]; M Pascual Izco[2]; S Hernandez Jimenez[2]; M Plaza Martin[2]; JM Vieitez Florez[2]; M Abellas[2]; A Lorente[2]; E Gonzalez Ferrer[2]; JL Zamorano[1]
[1]Health Institute Carlos III, CIBERCV, Madrid, Spain; *[2]Hospital Universitario Ramón y Cajal, Cardiology, Madrid, Spain*

Background: The relationship between E wave velocity and e 'wave velocity allow us to non-invasively estimate left ventricle (LV) filling pressure. An increase in LV filling pressure correlates, in previous studies, with the presence of exercise dyspnea, and even with an increase in readmission or mortality rates. The aim of this study is to analyze the population that presents abnormal elevated LV filling pressure in a cohort of Advanced Heart Failure Unit patients.

Methods: Patients followed in an Adavanced Heart Failure Unit were consecutively included. Baseline, analytical and echocardiographic data were collected. Therapeutic strategy was also collected. Functional class was evaluated through 6-minute walking test, and admissions and mortality rate were collected during the follow-up. Abnormal elevated LV filling pressure was defined as those patients with an E/e' ratio greater than or equal to 15.
Results: A total of 136 patients were consecutively included from May 2016 to March 2017. Of them, 60 (44.1%) had increased LV filling pressure. Baseline characteristics are defined in Table 1.
Patients with increased filling pressures were older and tended to receive less beta-blockers. This group of patients presented also a lower functional class in 6-minute walking test, a higher rate of readmissions and a higher mortality rate, although these differences did not reach statistical significance.
Conclusions:
An abnormally elevated LV filling pressure tend to decrease survival in patients with heart failure. Treatment with beta-blockers may decrease filling pressures. The findings suggested by this study should be tested in a larger cohort of patients.

	Increased filling pressures (n = 60)	Normal filling pressures (n = 76)	p
Age (years)	77.3 ± 9	71.4 ± 14.2	0.01
Female sex	23 (38.3%)	28 (36.8%)	0.86
LVEF (%)	36.4 ± 13.2	38.6 ± 11.1	0.29
BNP (pg/ml)	806.4 ± 967.2	572.7 ± 573.9	0.18
ACEIs/ARBs	34 (61.8%)	46 (63.9%)	0.81
Beta-blocker	38 (69.1%)	60 (83.3%)	0.05
Mineralocorticoid Antagonists	35 (63.6%)	42 (58.3%)	0.54
Furosemide daily dose (mg)	82.6 ± 44.3	74.5 ± 50.6	0.41
6-minute walking test (m)	256.7 ± 107.2	290.6 ± 125.2	0.87
Admissions	14 (23.3%)	12 (15.8%)	0.23
Mortality rate	4 (6.7%)	1 (1.3%)	0.10

Table 1

P1663

Myocardial tissue matrix metalloproteinases are associated with left ventricular geometry and ejection fraction improvement in subjects undergoing surgical left ventricular reconstruction

SC Serenella Castelvecchio[1]; FM Francesco Moroni[2]; EB Ekaterina Baryshnikova[1]; GP Giuseppina Palladini[3]; GM Giulia Marazzi[1]; SP Stefano Perlini[3]; LM Lorenzo Menicanti[4]
[1]IRCCS Policlinico San Donato, San Donato Milanese, Milan, Italy; *[2]San Raffaele Hospital of Milan (IRCCS), Milan, Italy*; *[3]IRCCS Policlinic Foundation San Matteo , Department of Internal Medicine, Pavia, Italy*; *[4]IRCCS Policlinico San Donato, Department of Cardiac Surgery, Milan, Italy*

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Background: After a myocardial infarction, the loss of viable tissue initiates a process of complex geometrical alterations leading to adverse remodeling and progressive heart failure (HF). Matrix myocardial proteinases (MMPs) were shown to play a key role in adverse remodeling in several preclinical models.
Purpose: To investigate the role of different myocardial tissue MMPs, i.e. MMP1, MMP2 and MMP9, and their respective inhibitors in subjects with ischemic heart failure (HF) undergoing left ventricular (LV) surgical reconstruction (SVR).
Methods: Twenty-six patients (20 male, 6 female, mean age 63 ± 9) with previous anterior myocardial infarction and HF undergoing elective SVR were recruited. LV function and geometry were evaluated by echocardiography before surgery and at follow-up. LV biopsies were obtained after the opening of the left ventricle. For each patient, two biopsies were harvested: one from the border zone (peri-infarctual area) and one from the remote myocardium. Samples were immediately treated according to the protocol in the operating theatre and stored at -80°C. Plasma samples were collected from each patient before surgery and at follow-up. We analyzed MMP1, MMP2, MMP9, TIMP4, TIMP2 and TIMP1 both in myocardial tissue samples and in plasma. All the subjects were prospectively followed for 12 months after surgery.
Results: Subjects with a more adverse geometrical remodeling, i.e. with a higher systolic sphericity index, had higher myocardial MMP9 in the remote zone (Rho = 0.5, p = 0.01). Furthermore, MMP9/TIMP1 in the remote myocardium significantly correlated with systolic sphericity index (Rho = 0.447, p = 0.03). Conversely, both MMP9 concentrations in the remote and border myocardium negatively correlated with systolic conicity index (Rho=-0.49, p = 0.02 and Rho=-0.42, p = 0.04, respectively). Remote myocardium MMP2 was significantly correlated with NTproBNP (Rho = 0.59, p = 0.003) and LV ejection fraction (EF) (Rho=-0.46, p = 0.02). The highest quartile of LV EF improvement, thereby defining optimal response to SVR, was a postoperative improvement of at least 17%. Subjects with the greatest improvement in terms of LV EF had a significantly lower MMP9 concentration in the border myocardium (9 vs 48, p = 0.006). At the same time, they had a significantly lower concentration of MMP2 both in border myocardium (8.8 vs 29.0, p = 0.006) and in the remote myocardium (7.7 vs 16.8, p = 0.005). On the other hand, MMP1 concentration in the border myocardium was higher in subjects with the greatest improvement in LVEF (3.6 vs 1.4, p = 0.001).
Furthermore, subjects in whom the target ESVi of < 60mL/m2 was obtained had a lower MMP9 concentration in border myocardium (11 vs 17, p = 0.04).
Conclusions-Different MMPs and TIMPs in myocardial tissue appear to associate differentially with diverse parameters of myocardial dysfunction and adverse remodeling. Our data support a heterogeneous role for these molecules in post-infarction remodeling.

P1664

Left ventricle remodeling, blood pressure profile and endothelial dysfunction in hypertensive patients with chronic heart failure

N Nadiia Demikhova[1]; T Rudenko[1]; S Bokova[1]
[1]Sumy State University, Medical Institute, Sumy, Ukraine

Chronic overload of the left ventricle in hypertension leads to structural and morphological reorganization of the myocardium, which combines the concept of "remodeling", which is characterized by the presence of hypertrophy, dilatation and changes in the geometry of the left vetricular (LV).
Objective: To evaluate the relationship of endothelial dysfunction with blood pressure (BP) daily profile and type of LV remodeling in hypertensive patients with chronic heart failure (CHF).
Methods: We examined 98 patients with arterial hypertension and CHF. Assessment of: systolic and diastolic LV function, condition vasomotor endothelial function (doppler brachial artery during reactive hyperemia), daily BP monitoring.
Results: Analsis of vasomotor function in patients with BP profiles showed that the diameter of the brachial artery was the greatest in patients with profile type night-peaker, and was 4.25(3.80;5.00), followed by patients with non-dipper - 4.20(3.70;4.60), dipper - 4.10(3.50;4.65) mm Hg, reduced and most patients over-dipper, while the velocity of the blood was reduced in patients with night-peaker - 0.60(0.53;0.84) m/s.
Vasodilatatory reaction during decompression was the least pronounced in night-peaker patients - 5.47 (3.04;11.72)% (p < 0.00014), in non-dipper patients - 11.63 (7.76;18.92)%, dipper - 8.94 (7.04;15.46)%, over-dipper - 7.24 (5.82;13.32)%.
Vasodilatatory response to nitroglycerin was preserved in most patients with non-dipper, accounting for 16.6(10.52;25.00)%, night-peaker - 13.67(8.01;20.24)%, over-dipper - 11.72(7.54;17.08)%, and decreased in dipper - 9.97(7.04;15.46)%.
Evaluation of correlation of endothelial dysfunction and indices of LV structural and functional properties showed that there is an inverse correlation between endothelial dysfunction in the form of reduced vasodilatatory effects on diagnostic tests and concentric hypertrophy (r=-0,32, p = 0.001), type of BP non-dipper (r=-0.27, p = 0.009), degree of night reduction in diastolic BP (r=-0.25, p = 0.014), systolic index (r=-0.25, p = 0.016), performance dilatation of brachial artery with nitroglycerin (r=-0.24, p = 0.017), normal LV geometry (r=-0.22, p = 0.026), the type of dipper (r=-0.22, p = 0.032), degree of night reduction in systolic BP (r=-0.22, p = 0.030), speed E (r=-0.21, p = 0.037). Direct correlation was between of endothelial dysfunction degree and diastolic dysfunction degree (r = 0.37, p = 0.00038), concentric remodeling (r = 0.25, 0.23), excentric hypertrophy (p = 0.015; p = 0.02), restrictive type of diastolic dysfunction (r = 0.25, p = 0.026), normal LV geometry (r = 0.21, p = 0.036), type of night-peaker (r = 0.23, p = 0.026), LV systolic dysfunction (r = 0.21, p = 0.036).
Conclusion. Endothelial dysfunction is a factor of correlation with LV myocardial remodeling by concentric type, and with the change of BP circadian rhythm as night-peaker in hypertensive patients with CHF.

P1665

Dynamics of chronic heart failure indicators in patients with rapidly progressive left ventricular remodelling after myocardial infarction

L Salyamova[1]; A Khromova[1]; O Kvasova[1]; A Golubeva[1]; V Valentin Oleinikov[1]
[1]Penza State University, Penza, Russian Federation

Aim: to study the dynamics of laboratory parameters of chronic heart failure and exercise tolerance during 48 weeks of follow-up in patients with rapidly progressive left ventricular remodeling after STEMI.

Methods: 97 patients with STEMI were included in the study. Inclusion criterion was the presence of one coronary artery significant stenosis according to the coronary angiography results At the 7-9th day and after 48 weeks of follow-up, all patients had undergone echocardiography on the MyLab apparatus ("Esaote", Italy) with the determination of the end diastolic volume index (EDVi). The patients were divided into two groups. The first group included 52 subjects without echocardiographic signs of LV remodeling: the dynamics of EDVi was < 20% at 48 weeks after STEMI. Group 2 included 45 patients with rapidly progressive LV remodeling (an EDVi increase > 20%). The groups were matched by age, sex, anthropometric data, and treatment. The brain natriuretic peptide (BNP) was determined at the 7th-9th day and at 48 weeks of follow-up using immunochemical analysis. The 6-minute walk test was performed after 12 and 48 weeks.
Results: Initial values of BNP did not differ: in the 1st group - 27.1 (18.2, 45.3) pg/ml, in group 2 - 31.6 (19.9, 52.1) pg/ml (p>0.05). After 48 weeks there was no significant BNP dynamics in patients without pathological EDVi increase (30.2 (19.7, 49.1) pg/ml, p>0.05); the values increased to 59.4 (30.1, 94.3) pg/ml in patients with rapidly progressive LV remodeling (p = 0.001). After 12 weeks of follow-up the average distance traveled during 6-minute walk test was 511.3 ± 72.4 m in group 1. At the same time, FC 0 was detected in 32% of cases, FC 1 - in 56%, FC 2 - in 12%. At 48 weeks after STEMI, the mean distance was 612.2 ± 85.6 m (p = 0.01). FC 0 was detected in 47% of cases, FC 1 - in 48%, FC 2 - in 5% (p>0.05). In group 2 the mean distance initially was 529.1 ± 76.1 m. FC 0 was detected in 35% of cases, FC 1 - in 38%, FC 2 - in 27%. After 48 weeks the indices were 527.4 ± 89.2 m (p>0.05), FC 0 - 41%, FC 1 - 24%, FC 2 - 32%, FC 3 - 3% (p>0, 05), respectively.
Conclusion: in patients with rapidly progressive LV remodeling after STEMI the BNP level increase was detected without reliable decrease in exercise tolerance after 48 weeks of follow-up. While in patients without pathological remodeling, there was an improvement in exercise tolerance without BNP changes.

P1666

The mortality benefit of carvedilol versus bisoprolol in patients with heart failure with reduced ejection fraction : an analysis from Korean Acute Heart Failure (KorAHF) registry

KH Choi[1]; JO Choi[1]; ES Jeon[1]
[1]*Samsung Medical Center, Sungkyunkwan University, Cardiovascular Center, Seoul, Korea Republic of*

On behalf of: KorAHF investigators
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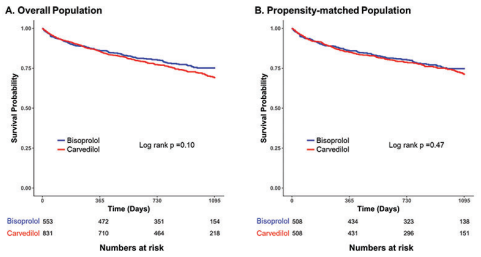
Background/Aims: It is unknown whether different beta-blockers (BBs) have variable effects on the long-term survival of patients with heart failure with reduced ejection fraction (HFrEF). Therefore, this study compares the effects of carvedilol and bisoprolol on survival in patients with HFrEF.



Kaplan-Meier curves for all-cause death

Methods: The KorAHF registry is a prospective multicenter cohort that includes 5,625 patients who were hospitalized for acute heart failure (AHF). We studied 1,384 patients with HFrEF who were prescribed carvedilol or bisoprolol upon discharge. Accordingly, patients were separated into respective groups based on these prescriptions, with a carvedilol group (n = 831) and bisoprolol group (n = 553). Propensity score matching analysis was performed to reduce confounding factors.
Results: Among patients who were prescribed a BB at discharge, 60.5% received carvedilol and 32.7% received bisoprolol. There was a significant reduction in all-cause mortality in those patients with HFrEF prescribed a BB at discharge (n = 1,707) compared to those who were not (n = 1,309) (BB vs. no BB, 26.1% vs. 40.8%, hazard ratio [HR] 0.59, 95% confidence interval [CI] 0.52-0.67, p < 0.001). However, there was no significant difference in the rate of all-cause mortality between those receiving different types of BB (carvedilol vs. bisoprolol, 27.5% vs. 23.5%, HR 1.21, 95% CI 0.99-1.47, p = 0.07). Similar results were observed after propensity score matching analysis (carvedilol vs. bisoprolol, 508 pairs) (26.2% vs. 23.8%, HR 1.10, 95% CI 0.86-1.40, p = 0.47).

Conclusions: In the treatment of AHF with reduced EF after hospitalization, the mortality benefits of carvedilol and bisoprolol were comparable in acute HF patients with reduced EF.

P1667

Relationship between parathyroid hormone and cardiac function and congestion in chronic heart failure: a prospective cohort study

L Kattnig[1]; V Habenicht[1]; M Gangl[1]; E Kolesnik[1]; J Schmid[2]; M Manninger[1]; H Brussee[1]; S Pilz[3]; A Tomaschitz[1]; B Obermayer-Pietsch[3]; D Scherr[1]; F Fruhwald[1]; D Von Lewinski[1]; K Ablasser[1]; N Verheyen[1]
[1]*Medical University of Graz, Department of Cardiology, Graz, Austria*; [2]*Medical University of Graz, Department of Radiology, Graz, Austria*; [3]*Medical University of Graz, Department of Internal Medicine, Division of Endocrinology and Diabetology, Graz, Austria*

On behalf of: Role of Comorbidities in Chronic Heart Failure Study

Background: Chronic heart failure (CHF) is often accompanied by disturbed bone metabolism, but potential mechanistic links are unclear in large parts. High parathyroid hormone (PTH) levels increase the risk of CHF and hyperparathyroidism is common in CHF patients. Few clinical studies aimed to elucidate the role of PTH in CHF, but their majority was limited by the retrospective character and very low sample sizes prohibiting multivariate analyses.
Purpose: We aimed to correlate plasma PTH levels with echocardiographic and laboratory parameters reflecting both cardiac systolic or diastolic function and congestion in CHF patients.
Methods: Subjects were enrolled between September 2016 and December 2017, as part of a single-center prospective cohort study. Main inclusion criteria were age over 18 years, CHF according to the ESC CHF guidelines 2016 and left ventricular ejection fraction (LVEF) < 50%. Stable disease was defined as absence of unplanned hospitalization or change in medication or device therapy within the previous month or major surgery within the previous 3 months. Exclusion criteria were any acute illnesses or more than moderate primary valvular disease. Blood samples were taken after an overnight fast and all laboratory parameters were determined immediately.
Results: We enrolled 99 patients (mean age 64.8 ± SD 9.6 years, 79% males). Mean LVEF was 35.9 +/- 9.0 % and median NT-proBNP was 1301 [IQR 349 - 2750] pg/ml. Hyperparathyroidism was present in 50% of patients and median PTH was 65.0 [47.0 - 94.6] pg/ml.
PTH correlated significantly with NT-proBNP (Pearson r = 0.467, p < 0.001), but not with LVEF, tricuspid annular plane systolic excursion or e'. In multivariate linear regression analyses with adjustment for age, sex, estimated glomerular filtration rate, 25-hydroxyvitamin D and body mass index, PTH remained significantly associated with NT-proBNP (adjusted beta-coefficient 0.331, p = 0.004).
Conclusion: In 99 patients with CHF, PTH was significantly correlated with NT-proBNP, but not with parameters of cardiac function, independently of important potential confounding variables. This observation is in line with previous studies and suggests a mechanistic interweavement between cardiac congestion and PTH secretion. Further investigation will be necessary to elucidate the impact of this possible interaction on bone health in CHF patients.

P1668

Total Left Atrial Emptying Fraction as a novel prognostic marker in HFrEF patients with significant functional mitral regurgitation

G Palmiero[1]; L Ascione[1]; A Ferro[1]; E Melillo[1]; R Ascione[1]; S Severino[1]; P Caso[1]
[1] *AO dei Colli-Monaldi Hospital, Department of Cardiology, Naples, Italy*

Background: A comprehensive risk assessment for prediction of adverse outcomes has been proposed in HF to overwhelm LVEF limitations. LA size and MR are considered prognostically relevant parameters.
Purpose: To assess the effects of significant functional MR on LA function and its prognostic impact in HFrEF patients.
Methods: 97 patients with LVEF = 40%, sinus rhythm and with mild-to-severe FMR were enrolled and underwent a comprehensive echocardiogram. MR severity was evaluated and patients were dichotomized according to the presence of SFMR (3-4+). LAF was evaluated using the phasic method with LA volumes measured at three time-points: before mitral valve opening, at P-wave onset and at MV closure. Different components of LAF were calculated consequently (reservoir as LAEI, conduit as LAPEF, pump as LAAEF and total emptying function as TLAEF). LA dysfunction (LA-Dys) was defined by TLAEF values below the median.
Results: LAF indices were more impaired in SFMR group (Table 1) and the SFMR/LA-Dys+ group showed the worst outcome in terms of survival (Figure 1). At the ROC curve analysis the TLAEF showed the highest predictive value (AUC 0.81) and at the final backward multivariate model (R2 0,31; Beta 0.62; p<.04) it was the only independent predictor of outcome.

Conclusions: SFMR seems to affect the LAF. TLAEF proved to be an important prognostic factor and may represent a novel parameters to consider in risk assessment of HFrEF patients.

Table 1

	FMR (n = 38)	SFMR (n = 59)	P
Age (yrs)	62,5±14,9	66,0±9,7	ns
Men (%)	5 (13,1%)	9 (15,2%)	ns
Ischaemic aetiology (%)	24 (63,1%)	46 (79,6%)	ns
NYHA Class	2,0±0,8	2,7±0,8	0,0001
LVEDV (ml)	174,3±52,9	256,3±72,1	0,0001
LVEF (%)	30,1±3,5	28,4±5,6	ns
LAVI (ml/m^2)	46,3±17,3	67,9±23,2	0,0001
E/E'	17,4±6,9	27,7±10,5	0,0001
EROA (mm^2)	0,11±0,4	0,23±0,8	0,0001
LAAEF (%)	28,0±9,4	19,1±8,9	0,0001
LAPEF (%)	25,1±8,1	18,1±7,5	0,0001
TLAEF (%)	45,8±10,4	33,5±11,0	0,0001
LAEI (%)	92,7±44,8	54,7±26,4	0,0001

Baseline characteristics of the study population, with dichotomization according to the presence or absence of significant mitral regurgitation.

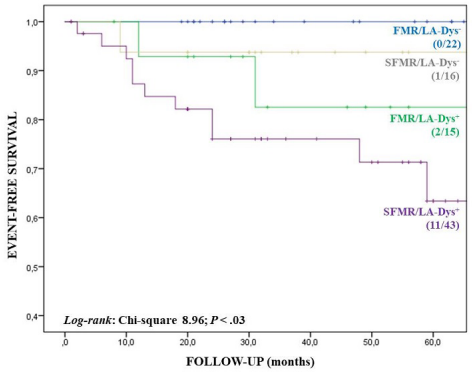


Figure 1

P1669

Serum calcium, phosphate and parathormone homeostasis in patients with heart failure with reduced ejection fraction

E Sawicka[1]; K Ptaszynska-Kopczynska[2]; M Marcinkiewicz-Siemion[1]; E Tarasiuk[2]; A Lisowska[2]; M Witkowski[2]; WJ Musial[2]; B Sobkowicz[2]; KA Kaminski[1]
[1]Medical University of Bialystok, Department of Cardiology, Department of Population Medicine and Civilization Diseases Prevention, Bialystok, Poland; *[2]Medical University of Bialystok, Department of Cardiology, Bialystok, Poland*

Introduction: Heart failure with reduced ejection fraction (HF-REF) is one of the most severe outcomes of cardiovascular diseases. Dysregulation of calcium (Ca) and phosphate (P) homeostasis may play a potential role in the development and progression of this disease. The adverse effect of elevated levels of P and parathormone (PTH) have been described, while the role of abnormal Ca concentration remains unclear.
Purpose: To evaluate the association of Ca, P and PTH status with biochemical and functional parameters in HF-REF patients in relation to patients without HF-REF.

Comparison of HF-REF and control groups

	HF-REF group -baseline (n = 124)	Control group (n = 21)	P value HF-REF baseline vs control baseline	HF-REF group - 6 months	P value HF-REF baseline vs HF-REF 6 months	P value HF-REF 6 months vs control baseline
Calcium, mmol/l	2.3 IQR: 2.2-2.4	2.4 IQR 2.3-2.5	0.017	2.4 IQR: 2.3-2.4	0.085	0.062
Phosphorus, mmol/l	3.4 IQR: 3.1-3.6	2.9 IQR 2.7-3.4	0.018	3.3 IQR: 2.8-3.6	0.274	0.135
Parathormone, pg/ml	34.9 IQR: 14.7-44.7	44.1 IQR 35.7-79.1	0.031	46.7 IQR 34.4-64.9	0.005	0.615
Calcium-phosphate product, mmol^2/l^2	7,8 IQR: 7.1-8.6	7 IQR: 6.5-8.4	0.108	7,8 IQR: 7-8.2	0.564	0.29

Methods: The study included 124 stable HF-REF patients with optimal pharmacotherapy, aged 64 ± 10 years (107 males) and 21 volunteers without HF-REF aged 64 ± 9 years (14 males), who had assessed calcium or phosphate or both of them at baseline.
Results: The analysis showed higher serum P, lower Ca and lower PTH levels in HF-REF patients compared to controls (Table). However, in both study groups the levels of Ca and PTH remained within the normal range, while the level of P was increased. After 6 months of the treatment there was an increase in PTH in HF-REF group (Table). Calcium-phosphate product did not differ between study groups at baseline and 6 months follow-up (Table).
The analysis of correlations in HF-REF group at baseline revealed that calcium inversely correlated with BNP (r = -0.21, p = 0.029), ventricular asynchrony (r = -0.21, p = 0.049) and directly with hemoglobin (r = 0.2, p = 0.032) and ejection fraction (r = 0.26, p = 0.014).
While phosphate correlated with urea (r = 0.25, p = 0.007) and maximal ventilatory equivalents for carbon dioxide measured in cardiopulmonary exercise test (r = 0.23, p = 0.042).
Conclusions: HF-REF patients at baseline present the altered mineral element profile compared to the control group, that reflect their worse general status. After 6 month of treatment calcium and phosphate levels were similar with those observed in control group.

P1670

Design of the EMPERIAL-reduced trial of empagliflozin in patients with chronic heart failure with reduced ejection fraction

W T Abraham[1]; P Ponikowski[2]; S D Anker[3]; A Salsali[4]; B Peil[5]; M Brun[6]; M Brueckmann[7]; J Lindenfeld[8]
[1]The Ohio State University, Columbus, United States of America; *[2]Wroclaw Medical University, Wroclaw, Poland*; *[3]Charité University, Berlin, Germany*; *[4]Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, Connecticut, United States of America*; *[5]Boehringer Ingelheim Pharma GmbH & Co. KG, Ingelheim, Germany*; *[6]Boehringer Ingelheim France, Reims cedex, France*; *[7]Boehringer Ingelheim GmbH & Co. KG, Ingelheim am Rhein, Germany*; *[8]Vanderbilt University Medical Center, Nashville, Tennessee, United States of America*

Background and Purpose: Besides increasing the risks of cardiovascular death and hospitalisation, chronic heart failure with reduced ejection fraction (HFrEF) is associated with a high symptom burden, and impaired functional capacity. Empagliflozin is a sodium-glucose cotransporter-2 inhibitor that was shown in the EMPA-REG OUTCOME trial to reduce the risk of cardiovascular events, hospitalisations and mortality in patients with type 2 diabetes and established cardiovascular disease. A Phase III trial, EMPERIAL–reduced, has been initiated to investigate the effects of empagliflozin on functional outcomes in patients with HFrEF.
Methods: EMPERIAL–reduced (Effect of EMPaglifozin on ExeRcise ability and heart failure symptoms, In patients with chronic heArt faiLure with reduced ejection fraction) is a randomised, double-blind, placebo-controlled trial designed to evaluate the effect of empagliflozin on exercise capacity and symptoms in patients with HFrEF (left ventricular ejection fraction = 40%). Inclusion criteria include 6-minute walk test (6MWT) distance of 100m to = 350 m and elevated N-terminal pro-brain natriuretic peptide (NT-proBNP) >600 pg/mL. Patients must be clinically stable and on appropriate medical therapy for heart failure consistent with current guidelines, with doses stable for = 4 weeks (or = 2 weeks for diuretics). Approximately 300 patients will be randomised 1:1 to receive empagliflozin 10 mg or placebo once daily

for 12 weeks. The primary endpoint is the change from baseline in 6MWT distance at week 12. Key secondary endpoints are changes from baseline in Kansas City Cardiomyopathy Questionnaire, total symptom score and in Chronic Heart Failure Questionnaire Self-Administered Standardized format dyspnoea score at week 12. Patient Global Impression of change questionnaires and change from baseline in NT-proBNP at week 12 are other secondary endpoints.
Results: Recruitment for this trial will begin in 2018.
Conclusion: The findings of the EMPERIAL−reduced trial, together with those of the EMPERIAL−preserved trial that will be conducted in patients with chronic heart failure with preserved ejection fraction (HFpEF), will determine the effects of empagliflozin on symptoms, exercise capacity and patient reported outcome in patients with heart failure. The effects of empagliflozin on cardiovascular death and hospitalisation for heart failure in patients with chronic heart failure are being investigated in the EMPEROR−reduced and EMPEROR−preserved trials.

P1671

Changes of arterial function in patients with reduced left ventricular systolic function

K-H Park[1]; WJ Park[1]; SJ Han[1]; HS Kim[1]; SH Jo[1]; S-A Kim[1]
[1]Hallym University Sacred Heart Hospital, Cardiology, Anyang-Si, Gyeonggi-Do, Korea Republic of

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Background: In patients with heart failure with reduced ejection fraction (HFrEF), there has been no report about serial changes of arterial function according to the changes of the left ventricular ejection fraction (LVEF).
Purpose: The current study was designed to access the association between serial changes of LVEF and changes in arterial endothelial function and arterial stiffness in patients with HFrEP (LVEF <45%).
Methods: We consecutively enrolled 50 patients with HFrEP (25 patients with non-ischemic heart failure [NIHF] and 25 with ischemic heart failure [IHF]). The echocardiography, B-type natriuretic peptide (BNP), flow-mediated dilation (FMD), and brachial ankle pulse wave velocity (baPWV) were evaluated at baseline and at 6-month follow-up, and the change values (?) were evaluated.
Results: Compared to the baseline measurements, the 6-month values were as follows: ?LVEF, 10.0 ± 11.5 (from 32.7 ± 10.7 to 42.9 ± 13.4, p <0.01); ?BNP, -178.1 ± 278.3 (from 315.7 ± 299.2 to 126.1 ± 157.7, p <0.01); FMD, 0.86 ± 1.43 (from 2.44 ± 2.27 to 3.16 ± 2.27, p <0.01); ?baPWV, -61 ± 224 (from 1545 ± 346 to 1488 ± 378, p = 0.07), respectively. There was no significant correlation between initial LVEF and initial FMD (r = 0.136, p = 0.35), but there were significant correlations between 6-month LVEF and 6-month FMD (r = 0.398, p <0.01) and ?LVEF and ?FMD (r = 0.522, p <0.01). However, there was no significant correlation between LVEF and FMD in patients with IHF during the study period. In patients with NIHF, there were significant correlations between initial EF and initial FMD, 6-month LVEF and 6-month FMD, and ?LVEF and ?FMD (r = 0.568, p <0.01; r = 0.694, p <0.01; and r = 0.787, p <0.01, respectively). In multivariate analysis, only ?FMD was significantly correlated with ?LVEF, and the association was independent of the other variables, ?BNP, ?baPWV, ?systolic blood pressure, and ?diastolic blood pressure in patients with NIHF. There was no significant correlation between LVEF and baPWV throughout the study.
Conclusions: In patients with NIHF, there was significant correlation between serial changes of endothelial function and left ventricular systolic function.

P1672

Statins in non-ischemic heart failure - friend or foe?

L Luis Puga[1]; R Teixeira[1]; L Reis[1]; J Gameiro[1]; J Sousa[1]; JM Ribeiro[1]; M Madeira[1]; P Dinis[1]; A Siserman[1]; A Goncalves[1]
[1]University Hospitals of Coimbra, Cardiology Department, Coimbra, Portugal

Background: The use of statins in patients with heart failure (HF) has generated controversy due to conflicting results of clinical trials.
Purpose: To identify the long-term prognosis associated with prescription of statins in patients with HF.
Methods: Retrospective study of 119 patients admitted to a cardiac intensive care unit due to acute HF of non-ischemic etiology. The sample was divided in two groups, A - statins prescribed at discharge from hospital (n = 59) and B - no statins prescribed at discharge from hospital (n = 60). The groups were compared for mortality, mean survival in months and readmissions for heart failure. It was performed a sub analysis dividing the groups in two subsets of age (= 75 or >75 years old).
Results: The sample had a mean age of 68 ± 15 years old and 75% of the patients were male. The prevalence of hypertension was 74% and diabetes mellitus was 31%. 56% of the patients were admitted in NYHA class IV, 40% in NYHA class III. The mean left ventricle ejection fraction was 33 ± 14%. Mean follow-up time was 17 ± 15 months.
No statistically significant differences were found between mortality rate during follow up in the groups (A 29% (17/58) vs B 41% (24/59), P = 0,198). The readmission rate and the mean survival time by the Kaplan Meier method were also similar in both groups.

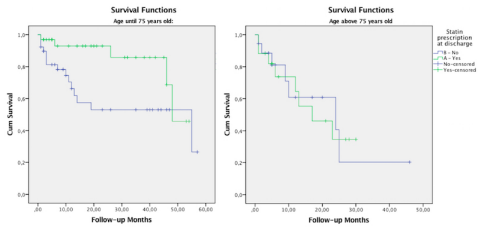

Figure 1 - Cumulative survival curves

In the sub analysis performed in two classes of age (Figure 1), group A showed a statistically significant increase in mean survival until 75 years old (A 46 months CI95%(39,6-51,8) vs B 34 months CI95%(24,7-42,6), log rank P = 0.028). This effect was not demonstrated in the subgroup of patients above 75 years old (A 18 months CI95%(11,9-23,6) vs B 22 months CI95%(11,8-31,7), log rank P = 0.955).
Conclusions: In our sample, the prescription of statins at discharge from hospital was associated with an increase in mean survival in the subgroup of patients = 75 years old. The decrease in the lipid levels associated with the progression of HF may explain the loss of the protective effect of statins in older ages.
Figure 1 - Cumulative survival curves by the Kaplan Meier method

P1673

Tolerance to the uptitration of the dose of sacubitril/valsartan is comparable to that of angiotensin converting enzyme inhibitors; single center experience

A Elasfar[1]; A Tharwat[1]; SA Elasfar[2]; I Alharbi[1]; OA Amoudi[1]
[1]Madina Cardiac Center, Madina, Saudi Arabia; *[2]CK secondary school, Chatham-kent, Canada*

Background: Sacubitril/valsartan is the first drug from a new class of angiotensin receptor neprilisin inhibitors (ARNIs) recommended to replace angiotensin converting enzyme inhibitors (ACE-Is) in heart failure with reduced ejection fraction (HFpEF).
Objective: We aimed to present our initial experience with regard to the tolerance to the uptitration to the recommended target dose of Sacubitril/ Valsartan (200 mg twice daily) to those of angiotensin converting enzyme inhibitors (ACE-Is) in a cohort of patients with HFpEF.
Methods: It's a single center cross sectional cohort study for patients with heart failure and reduced EF who were divided to 2x4 groups; group I includes patients on Sacubitril/ Valsartan and group II includes patients on ACE-Is plus standard background medical therapy. We tested both groups at 4 levels of tolerances: level 0 tolerance (patients who did not tolerate any dose); level I (patients only tolerated 25 of the target dose); level II (patients tolerated 50 % of the target dose); Level III (patients tolerated 100% of the target dose). Tolerance was mainly dependent on the assessment for symptomatic hypotension, worsening renal functions and rising serum potassium. The standard ACE-I used is enalapril with target daily dose of 20 mg. Average follow up was between 3 and 11 months. We used Chi Square software to test significance between groups with P value more than 0.05 was considered non-significant.
Results: One hundred and eighty five patients with heart failure and EF < 35, age of 48.7+/-11.9 years, 78.82% males were divided to 2 groups; group I (Sacubitril/valsartan) includes 105 patients and group II (ACE-Is) includes 80 patients. There were non-significant differences between both groups regarding the baseline demographic and clinical characteristics. The level of tolerance in group I/group II was 6.4/7.8%, 18.9/ 18.6, 57.5/ 55.8, and 17.2/17.8 for level 0, I, II, and III tolerance respectively with P value less than 0.05.
Conclusion: the level of tolerance to escalating to target doses for Sacubitril/valsartan was comparable to that of ACE-Is in ambulatory heart failure patients with reduced ejection fraction.

P1674

Effect of Low-Dose Dopamine on Depression of Patients with Heart Failure in Coronary Intensive Unit

T Kivrak[1]
[1]Firat University, Department of Cardiology, Elazig, Turkey

Objective: The aim of this trial is to assess the effects of low-dose dopamine on patients with depression in the intensive coronary unit.

Methods: Relatives of 43 ICU patients enrolled in the study. Sociodemographic characteristics of patients and their families recorded. Patients evaluated basal echocardiographic and biochemical values measured in the patient group. The Beck Anxiety and Depression Scale was used to assess anxiety and depression. The assessment performed first and the twenty-fourth hour by Beck scale.
Results: The final study population consisted of 42 patients hospitalized with heart failure. Median patient age was 67.5 ± 12.6 years. Average EF was 23.5 ± 8.7 and mean ProBNP was 6343.76 in our study population. Changes in depression score of HF patients before and after dopamine treatment was showed significantly(before value:18.95 ± 9.89; after value:17.29 ± 10.30;p <0.001) however systolic and diastolic pressure difference was not significant(Table 1).
Conclusion: We think that critical study because of low dose dopamine decreased depression degree in the intensive coronary unit, and low dose dopamine can be used for to increase renal perfusion in these patients.

TABLE 1

	Before	After	P value
Depression score	18.95±9.89	17.29±10.30	<0.001
Systolic blood pressure (mmhg)	115±20	117±17	0.342
Diastolic blood pressure mmhg)	70±11	69±10	0.279

Changes in parameters of HF patients before and after dopamine treatment

P1675

Prognostic impact of neurohormonal blockade in patients with an acute coronary syndrome and mid-range ejection fraction

PM Pedro Azevedo[1]; T Mota[1]; D Bento[1]; D Carvalho[1]; J Bispo[1]; J Guedes[1]; S Pereira[1]; W Santos[1]; J Mimoso[1]; N Marques[1]; I Jesus[1]
[1]*Faro Hospital, Cardiology, Faro, Portugal*

Introduction: In 2016, the European Society of Cardiology introduced the term heart failure (HF) with mid-range ejection fraction (HFmrEF) to represent patients with HF and left ventricular ejection fraction (LVEF) between 40% and 49%. This range of LVEF is less well studied compared with HFpEF and HFrEF. Whether these patients benefit from neurohormonal blockade, similarly to patients with HFrEF, requires further studies. After an acute coronary syndrome (ACS), beta-blockers (BB) and angiotensin-converting enzyme inhibitors (ACEi) are frequently prescribed, but their impact on long-term outcomes of patients without systolic dysfunction is controversial.
Purpose: Evaluate the impact of BB, ACEi and mineralocorticoid receptor antagonists (MRA) on long-term mortality and rehospitalization of patients with mid-range EF after an ACS.
Methods: Retrospective, descriptive and correlational study with all patients admitted to a Cardiology department with the diagnosis of ACS between the 1st of October 2010 and 31st September 2016. Patients were divided as followed: LVEF < 40% (rEF), LVEF between 40% and 49% (mrEF) and LVEF = 50% (pEF). Patients were followed for 1-year. Statistical analysis was performed in SPSS.
Results: 2860 patients were included, 309 (10.8%) had rEF, 460 (16.1%) had mrEF and 2091 (73.1%) had pEF. The mean age of patients with mrEF was 68.4 ± 13.7 years (versus 68.6 ± 13.7 in rEF and 64.6 ± 12.9 in pEF, p < 0.001). Patients with mrEF had more frequently STEMI (54.8% in mrEF, 49.8% in rEF and 45.2% in pEF, p < 0.001). Acute HF was present in 131 (28.5%) patients with mrEF (vs 49.5% in rEF and 7.2% in pEF, p < 0.001). Coronary angiography was performed in 310 (67.4%) patients with mrEF (vs 50.5% in rEF and 83.1% in pEF, p < 0.001) and PCI in 233(50.7%) (vs 41.4% in rEF and 64.7% in pEF, p < 0.001). The overall in-hospital mortality rate was 3.1% (16.5% in rEF, 3.7% in mrEF and 1.0% in pEF, p < 0.001).
After discharge, beta-blockers were prescribed to 74.3% of patients (75.6% in rEF, 71.7% in mrEF and 74.6% in pEF, p = 0.4), ACEi to 76% (82.2% in rEF, 79.3% in mrEF and 74.6% in pEF, p = 0.007) and MRA to 13.7% (60.7% in rEF, 34.8% in mrEF and 3.6% in pEF, p < 0.001).
At 1-year, mortality rate was 8.5% (26.3% in rEF, 15.8% in mrEF and 4.7% in pEF, p < 0.001) and rehospitalization rate was 21.4% (42.1% in rEF, 30.7% in mrEF and 16.8% in pEF, p < 0.001).
In patients with mrEF, after adjusting for covariates, neurohormonal blockade had no impact on 1-year mortality (BB OR 0.96, 95%CI 0.45-2.1; ACEi OR 0.36 95%CI 0.6-3.4 and MRA OR 0.74 95%CI 0.5-2.7) or 1-year rehospitalization (BB OR 1.1 95%CI 0.7-2.1; ACEi OR 0.74 95%CI 0.4-1.4 and MRA OR 0.7, 95%CI 0.4-1.4).
Conclusion: In this study, treatment with BB, ACEi or MRA had no impact on 1-year mortality or rehospitalization rate in patients with ACS a mid-range EF. Further studies, preferably randomized controlled trials, should be performed to assess the impact of neurohormonal blockage in this range of LVEF.

P1676

Urine biomarkers as determinants of poor outcomes in patients with acute kidney injury and heart failure with mid-range ejection fraction

A Klimenko[1]; S Villevalde[1]; Z Kobalava[1]
[1]*RUDN University, Moscow, Russian Federation*

Background: Decompensated heart failure (DHF) is one of the leading causes of hospitalization worldwide. The development of acute kidney injury (AKI) is associated with poor outcomes. There is a strong need to detect AKI before serum creatinine (SCr) rise. The aim of the study was to determine the AKI in patients with DHF in subpopulation with mid-range ejection fraction (DHFmrEF), to evaluate the association of urine neutrophil gelatinase associated lipocalin (uNGAL) and kidney injury molecule-1 (KIM-1) with changes in kidney function and outcomes.
Methods: In 65 patients with DHFmrFF (53 male, 69 ± 9 years (M ± SD), arterial hypertension 94%, ischemic heart disease 63%, myocardial infarction 51%, atrial fibrillation 49%, diabetes mellitus 26%, known chronic kidney disease 51%) levels of SCr, uNGAL and KIM-1 were determined on admission. AKI was defined using 2012 KDIGO Guidelines. Patients with AKI were classified into four groups on the basis of their levels of SCr, uNGAL and KIM-1. Mann-Whitney and multiple logistic regression analysis were performed. P < 0.05 was considered statistically significant.
Results: 32% of patients developed AKI. Patients with AKI compared with patients without AKI had higher SCr (227 ± 92 vs 109 ± 19 mkmol/l, p < 0.001), uNGAL (234 ± 74 vs 3,8 ± 1,5 ng/ml, p = 0.001). Levels of KIM-1 did not differ (0,48 ± 0,03 and 0,42 ± 0,03, p>0.05). Urine NGAL >184 ng/ml (odds ratio (OR) 3.85; 95% confidential interval (CI) 1.8-5.8) was determined to be significant and independent factor for development of AKI. Urine KIM-1 >0.41 ng/ml (OR 2.85; 95% 95% CI 1.4-4.6) was determined to be significant and independent factor for DHF rehospitalization after AKI. Of 21 patients with AKI 13% had two criteria of AKI [NGAL(+)/KIM-1(+)], 20% - isolated increase of SCr, 30% two criteria [Scr(+)/KIM-1(+)] and 37% - two criteria [SCr(+)/NGAL(+)]. Patients with NGAL(+)/KIM-1(+) and patients with SCr(+)/NGAL(+) compared with other groups demonstrated transient character of AKI and the higher risk of 30-days mortality: all patients with AKI and NGAL(+)/KIM-1(+), 50% of patients with AKI and NGAL(+)/SCr(+) died in 30 days. There were no deaths in 30 days in patients with AKI with isolated increase of SCr and patients with AKI and SCr(+)/KIM-1(+).
Conclusions: 32% of patients admitted to the hospital with DHFmrEF developed AKI. Elevation levels of urine biomarkers (uNGAL >184 ng/ml and KIM-1 >0.41 ng/ml) in patients with AKI is associated with persistent character of AKI and higher risk of 30-days mortality. The use of uNGAL together with KIM-1 might be useful for the clinician to suspect the subgroup with high risk of mortality in patient population with DHFmrEF and AKI.

P1677

Clinical characteristics and biomarkers in the patients with different phenotypes of heart failure

T Tatyana Kurchick[1]; S Tikhonova[1]; L Kholopov[1]
[1]*Odessa National Medical University, Internal Medicine #2, Odessa, Ukraine*

Background: The pts with mid-range ejection fraction (EF) 40-49% (HFmrEF) have a clinical profile and prognosis that are closer to those of pts with preserved EF >50% (HFpEF) than those of reduced EF < 40% (HFrEF), with certain distinctions.
Purpose: Evaluation of co-morbidities and some biomarkers that may point to a higher risk of developing HF and characterize pt's EF range.
Methods. The pts (N = 127, 54M:73F), hospitalized during 2017 to Internal Medicine Dept. with proved diagnosis of HF (NYHA I-IV) were classified according to EF by transthoracic echo (Simpson) into 3 groups: 1 (n = 12) - with HFrEF, 2 (n = 22) - HFmrEF, and 3 (n = 93) - HFpEF. Some clinical and laboratory markers and parameters as well as rate and types co-morbidities were estimated and compared between groups.
Results: The most pts (73.2%) were related to HfpEF. It was no gender differences between groups. Group 3 was significantly younger (69.3 ± 11.3 yrs) compared to group 2 (73.8 ± 10.2 yrs, p < 0.05). During analysis of comorbidity structure of groups we reveal that group 1 prevailed over the rest in the proportion of pts with stroke and/or transient ischemic attack (25.0%), arrhythmias (83.3%), c2 = 6.635, p < 0.01) and peripheral arteries disease (PAD) (33.3%, c2 = 6.422, p < 0.05). Group 2 prevailed in hypertension (45.5%), coronary artery disease (54.5%), encephalopathy (81.8%) and atrial fibrillation (AF) (63.6%, c2 = 6.635, p < 0.01). Group 3 prevailed only in diabetes mellitus rate (33.3%). We didn't find any significant difference in hypertension rate between groups, but blood pressure (BP) levels were significantly higher in groups 2 (systolic 201.0 ± 30.9 and diastolic 114.0 ± 5.5 mmHg) and group 3 (176.3 ± 18.0 and 108.8 ± 8.5) compared to group 1 (156.3 ± 9.5 and 91.3 ± 2.5 mmHg, p < 0.01 for all). These differences can be connected with more strict BP control in group 1 pts. We found increasing of uric acid levels with EF decreasing. Thus, uric acid level in group 3 (316.0 ± 132.8) was significantly lower compared to both other groups (442,3 ± 84,4 and 398.3 ± 81.0 mmol/l, p < 0.05). We noted

reducing the severity of dyslipidemia as the EF decreases. So, total and LDL cholesterol (CHL) were significantly higher in group 3 (6.5 ± 1.2 and 4.4 ± 0.6 mmol/l) versus group 1 (4.0 ± 1.0 and 2.3 ± 0.6 mmol/l, p < 0.05 for all). Moreover, there were light positive correlation for CHL and EF (r = 0.3, ? < 0.05). HDL-CHL in group 3 (1.6 ± 0.4) was higher compared to groups 1 (1.1 ± 0.2) and 2 (1.2 ± 0.4 mmol/l, p < 0.05 for all). Creatine phosphokinase levels tended to decrease with EF increasing. It can be connected with high rate of multifocal atherosclerosis clinical manifestations in groups 1 and 2.
Conclusion: Some concomitant factors of HF with different meaning of EF may be distinct. Significant difference demonstrated for BP, uric acid, CHL, HDL- and LDL-CHL levels, pts with PAD and arrhythmias, AF especially. We can characterize HFmrEF pts as separate clinical grope with specific metabolic and co-morbidity profile.

P1678
Characteristics of obese patients with heart failure with mid-range ejection fraction

A Alexandra Dadarlat[1]; A Sitar-Taut[1]; D Zdrenghea[1]; D Pop[1]; A Buzoianu[1]
[1]*University of Medicine and Pharmacy of Cluj Napoca, Cluj Napoca, Romania*

On behalf of: "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca, 4 Pasteur street, Romania

Background. Despite all complex therapeutic opportunities, heart failure remains a tremendous public health burden. Moreover, the diagnosis of chronic heart failure in obese population brings unique challenges. So, a comprehensive understanding of their paradoxical particularities is desirable.
Purpose: To investigate and improve the knowledge on the profile of obese patients with heart failure with mid range ejection fraction.
Material and methods. We retrospectively enrolled 126 overweight and obese (body mass index = 25 kg/m2) patients who were hospitalized for decompensated heart failure. Baseline characteristics, clinical presentation, laboratory data, echocardiographic parameters and in-hospital therapies were compared among obese heart failure patients divided into three groups: with reduced (< 40%), mid-range (40-49%) and preserved (= 50%) ejection fraction (EF). Heart failure was defined according to 2016 ESC criteria. A multivariable analysis was performed.
Results: The mean age of the analyzed study population was 70.45 ± 9.12 years and 54.8% were men. Among the patients, 26.4% had reduced ejection fraction (HFrEF) with a mean NT-proBNP value of 4355.76 ± 4312.08 pg/ml, 28.8% mid-range ejection fraction (HFmrEF)- NT-proBNP mean value of 2257.97 ± 2507.91 pg/ml, and 44.8% preserved ejection fraction (HFpEF)- NT-proBNP value of 1921.57 ± 1824.10 pg/ml. The 3 groups were similar in terms of age, sex, BMI and renal function. Patients with HFmrEF had a mean BMI of 35 ± 4.71 kg/m2. In HFmrEF obese patients the most frequent precipitating factor for admission was atrial fibrillation with rapid ventricular response. The main etiology of HF in our patients with mid-range EF was ischaemic (50%), followed by valvular heart disease. NT-proBNP values negatively correlated with BMI in patients with HFpEF (r= -0.307, p = 0.028), in the other groups NT-proBNP was not significantly influenced by BMI. An inverse relationship was found between NT-proBNP values and creatinine clearance estimated by Cockcroft-Gault equation in patients with HFmrEF (r=-0.355, p = 0.038) and HFpEF (r= -0.279, p = 0.042). NT-proBNP levels were not significantly influenced by the presence of atrial fibrillation, diabetes mellitus, age in neither of the three groups, regardless of sex. NT-proBNP levels were not significantly influenced by the presence of echocardiographic left ventricular hypertrophy or atrial dilatation.
In conclusion, obese individuals with HFmrEF presented particular characteristics, in terms of aetiology, precipitating factors, NT-proBNP values. In this group, NT-proBNP values were not significantly influenced by BMI, age, the presence of atrial fibrillation or diabetes mellitus. Despite all controversial data regarding the NT-proBNP diagnostic and prognostic value in patients with obesity and the lack of evidence in those with obesity and HFmrEF, this study showed they remain important biomarkers in this category of patients, too.

P1679
Profile and differential management of patients with a mid-range ejection fraction compared to patients with reduced ejection fraction

D Daniel Enriquez Vazquez[1]; C Perez Garcia[1]; TS Luque Diaz[1]; A Travieso Gonzalez[1]; V Ruiz Pizarro[1]; C Olmos Blanco[1]; D Vivas Balcones[1]; P Martinez Santos[1]; M Perez Serrano[1]; R Bover Freire[1]; I Vilacosta[1]; C Macaya[1]
[1]*Hospital Clinic San Carlos, Cardiovascular Institute, Madrid, Spain*

Background: In European Society of Cardiology guidelines on the diagnosis and management of patients with heart failure (HF), a new door opens to that gray area corresponding to patients with ejection fraction (EF) between 40-49%. These are framed within a new group known as mid-range ejection fraction (HFmrEF).
Purpose: The objective of this study is to characterize this type of patients and their comparison with heart failure with reduced EF (HFrEF).
Methods: Patients diagnosed with HF admitted to a Cardiology Service of a tertiary hospital between July 2016 and March 2017 were registered prospectively and consecutively for one year.
Results: Of the total of 341 patients, 90 patients had HFmrEF and 113 patients with HFrEF. Baseline characteristics of both groups of patients are shown in Table 1. Patients with HFmrEF have a generally poorer cardiovascular risk profile, and more often tachyarrhythmias or acute ischemic heart disease as triggers.
Beta-blockers were used at discharge in higher proportion in patients with HFrEF (83.8% vs 73.5%). The percentage of use of ACE inhibitors or ARA2 is similar between the two groups (65%), but in HFmrEF, ARA2 was used in a higher percentage (20, 4% vs 8.1%, p 0.027). MRAs are used in both groups, with greater use in patients with HFrEF (65% vs 30% at discharge, p < 0.001). The use of diuretics at discharge was higher in the group of patients with HFrEF than in the mid-range group (82% vs 69.4%, p 0.07).
Conclusion: HFmrEF patient presents higher cardiovascular risk, with admissions for heart failure mainly due to tachyarrhythmias or acute ischemic heart disease. They also have less right ventricular dysfunction. Diuretics are used in smaller quantities, as well as ARMs, and to a greater extent the ARA2.

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Mean age (yr)	77	71.7	0.002
Male sex	36%	23%	0.071
Hypertension	87.8%	75.2%	0.07
Alcohol consumption	4.1%	14.2%	0.06
NTproBNP at admission	8426	12005	0.06
Trigger: ICM	20.4%	10.6%	0.09
Trigger: TA	26.5%	15.2%	0.08
Mean EF	44.8%	27.6%	0.001
RVD	16.3%	43.2%	0.001

ICM ischaemic cardiomyopathy. TA tachyarrythmia. RVD right ventricle dysfunction.

P1680
Comparison of self-reported and accelerometer-assessed physical activity and sedentary time in patients with heart failure with preserved ejection fraction

C Cristine Schmidt[1]; L Bohn[1]; M Santos[2]; D Moreira-Goncalves[1]; J Oliveira[1]
[1]*Faculty of Sport University of Porto , CIAFEL, Porto, Portugal*; [2]*Faculty of Medicine University of Porto, Surgery and Physiology Department; Centro Hospitalar do Porto, Department of Cardiology, Porto, Portugal*

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Introduction: Pharmacological therapies have failed to improve clinical outcomes among patients with heart failure have preserved ejection fraction (HFpEF), who represent more than half of patients with HFpEF. High levels of physical activity and low sedentary time are associated with better quality of life and reduced risk of hospitalization and mortality in HFpEF patients. In order to effectively prescribe physical activity, recommendations need to be grounded in accurate measures of physical activity.
Purpose: To compare self-reported with accelerometer-assessed physical activity levels and sedentary time in HFpEF patients.
Methods: HFpEF patients (n = 24; stable and well-medicated) were recruited and assessed for physical activity levels through the IPAQ–Short Form and with accelerometers (ActiGraph GTX3). To be considered as valid data, a minimum of 4 days recorded with at least 10 wear-time hours/day was determined. Sedentary time and time spent in moderate to vigorous activity (MVPA) were compared according to gender. Time spent in MVPA derived from IPAQ were merged with self-reported walking and MVPA to compare with objectively measured MVPA (= 2752 cpm, derived from vector magnitude). Mean differences were examined using the Mann–Whitney test (non-parametric data) or the Student t test (parametric data).
Results: Validated data was obtained from twenty-two patients (age= 76 ± 6.1; 16 females, and 6 males). Mean accelerometer wearing time was 13.16 ± 1 h/day. IPAQ

underestimated sedentary time compared with the accelerometer (253 ± 156 vs 555 ± 78 min.d-1, p = 0.002), even when adjusted for gender. According to IPAQ, 68% of the patients accumulated at least 150 minutes of MVPA, in bouts = 10 minutes, as specified by the guidelines, while none met the recommendations when PA was objectively measured. However, if remove the bout length restriction, 77% of the patients would achieve the recommendations for MVPA objectively measured.
Conclusion: The study suggests that in patients HFpEF, IPAQ–Short Form may underestimate sedentary time and overestimate physical activity MVPA levels according to the guidelines (bouts = 10 minutes). This has important clinical implications as it limits IPAQ-based decisions targeting the management of both sedentary time and MVPA in HFpEF patients.

P1681

Genetic determination of myocardial mechanics: towards a deeper understanding of heart failure with preserved ejection fraction?

A Kovacs[1]; AA Molnar[1]; M Kolossvary[1]; B Szilveszter[1]; B Lakatos[1]; AD Tarnoki[2]; DL Tarnoki[2]; G Jermendy[3]; PP Sengupta[4]; P Maurovich-Horvat[1]; B Merkely[1]
[1]Semmelweis University Heart and Vascular Center, Cardiovascular Imaging Research Group, Budapest, Hungary; *[2]Semmelweis University, Department of Radiology and Oncotherapy, Budapest, Hungary*; *[3]Bajcsy-Zsilinszky Hospital, Budapest, Hungary*; *[4]Heart and Vascular Institute, Morgantown, United States of America*

Genetic effects in the determination of left ventricular (LV) mechanics are scarcely characterized. The present study was performed to assess heritability of LV function and to reveal possible common genetic background of different LV functional phenotypes as measured by advanced echocardiographic parameters in a cohort of Caucasian twins.
Ninety-two twin pairs were recruited (54 monozygotic and 38 same-sex dizygotic twin pairs, mean age 56 ± 9 years). Siblings with obstructive coronary artery stenosis assessed by coronary CT angiography or siblings with any cardiomyopathy or severe valvular disease were excluded. Beyond conventional echocardiographic parameters, global longitudinal (GLS), circumferential strain, apical counter-clockwise, basal clockwise rotation and longitudinal early diastolic strain rate were measured by speckle-tracking echocardiography.
The univariate genetic and environmental effects model showed high genetic component in the variance of LV systolic deformation (62-77%), however, heritability of LV diastolic functional parameters was low (31-46%), whilst unique environmental effects dominated. Cholesky decomposition was carried out to calculate the magnitude of covariation between the investigated phenotypes and to estimate the proportion of shared and unique genetic factors. Despite high heritability of LV systolic deformation parameters, no shared genetic background could be revealed between these parameters (p = 0.99). Even though LV diastolic parameters showed low genetic determination, we found a significant common latent phenotype responsible for the heritability of these parameters (p < 0.001). Furthermore, GLS and LV diastolic function showed also common heritability (p < 0.001).
Our work demonstrated high heritability of LV systolic deformation in Caucasian twins. These findings support further investigation of potential candidate genes determining LV systolic function. Different directions of LV deformation are inherited independently. However, GLS shares common genetic background with diastolic function. This points at the importance of systolo-diastolic coupling of myocardial mechanics and may provide further insights into the understanding of heart failure with preserved ejection fraction.

P1682

Differences in patient reported outcome in women and men with HFpEF

U Ulrika Ljung Faxen[1]; C Hage[1]; E Donal[2]; JC Daubert[2]; C Linde[1]; LH Lund[1]
[1]Karolinska Institute, Department of Medicine, Stockholm, Sweden; *[2]University Hospital of Rennes, Département de Cardiologi & CIC-IT U 804, Rennes, France*

On behalf of: KaRen investigators
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Aims: Heart failure with preserved ejection fraction (HFpEF) is associated with poor quality of life (QoL), or patient reported outcome (PRO). Despite female predominance in HFpEF, sex-specific differences in PROs remain poorly studied. We assessed PRO measures and their association with HF-severity and outcome in HFpEF by sex.
Methods and Results: In 387 patients with HFpEF from the KaRen study, EQ-5D-3L® and Minnesota Living with Heart Failure Questionnaire® (MLHFQ) were assessed. Characteristics and comorbidities were largely similar in women (n = 220, 57%) and men. Women expressed more problems in EQ-5D part 1 in all five dimensions, but significantly different from men regarding mobility (53 vs. 42%, p = 0.018), usual activities (47 vs. 34% p = 0.011), and anxiety and depression (51 vs. 38% p = 0.012). Women also expressed worse QoL in EQ-5D part 2 (EQ-VAS), independent of age and HF severity, mean (SD), 56(20) vs. 61(19), p = 0.010. There was no difference in MLHFQ, 31(20) vs. 29(21), p = 0.269.
Spearman's correlations with HF severity (NYHA class) were for MLHFQ in women r 0.35 vs. men 0.41, p for both < 0.001, and for EQ-VAS r -0.27, p = 0.001 vs. -0.45, p < 0.001. Correlations with natriuretic peptides were for MLHFQ r 0.22 in women vs. men 0.25, p = 0.002, and for EQ-VAS r -0.18, p = 0.012 vs. -0.26, p = 001.
Associations between PRO and the composite of HF hospitalisation or all-cause death were present in men only, adjusted HR per 5 units increase in MLHFQ 1.06, 95% confidence interval(CI) 1.01-1.11, p = 0.027 and EQ-VAS, HR 0.92, 95% CI 0.88-0.98, p = 0.010.
Conclusion: n HFpEF, women had worse general but similar disease specific QoL compared to men. QoL was more strongly associated with HF severity in men, and associated with outcomes in men only. In women with HFpEF, QoL appears less determined by HF itself and potentially more by other unknown factors. This might have implications for the magnitude of improvement of PRO in women from HF treatment.

P1683

Left atrial function, volume and compliance in patients with HFpEF

G Bajraktari[1]; I Bytyci[1]; MY Henein[2]
[1]University Clinical Centre of Kosova, Clinic of Cardiology, Pristina, Kosovo Republic of; *[2]Umea University, Department of Public Health and Clinical Medicine, Umea, Sweden*

Background and Aim: Left atrial (LA) structure and function indices; LA function index (LAFI), LA volume index, LA stroke volume and LA diameter have been shown to predict clinical outcome in patients with heart failure and preserved ejection fraction (HFpEF). The aim of this study was to assess the relationship between LAFI and LA structure and function in patients with HFpEF.

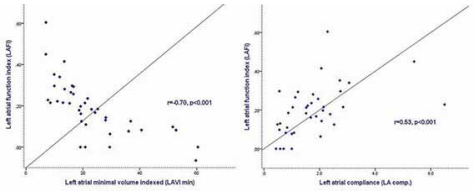

Figure 1. Correlation of LAFI with LAVI

Methods: In 53 consecutive patients with HFpEF (age 62 ± 7 years, NYHA class I - III, LV EF = 50) and 40 controls, a complete echocardiographic examination was performed. In addition to conventional volume measurements, LAFI was calculated using the formula (LAFI = LAEF x LVOT VTI/LAVI max) and LA compliance using the equation [LAV max - LAV min / LAV min x 100].
Results: Patients were older (p = 0.002), with higher LV mass index (p = 0.01), reduced septal and lateral MAPSE (p < 0.001, for both), reduced TAPSE (p = 0.01), larger LA volume (p < 0.001), raised LAVI max and LAVI min (p < 0.0001, for both) and impaired LA compliance index (p < 0.001), compared to controls. LAFI modestly correlated with LV EF (r = 0.39, p = 0.01), LA size (r=-0.47, p = 0.01), LA EF (r = 0.46, p = 0.003), LAVI max (r=-49, p = 0.01) and LA compliance (r = 0.53, p < 0.001) but correlated strongly with LAVI min (r=-0.70, p < 0.001, figure 1).
Conclusions: Patients with HFpEF have increased left atrial volume and reduced compliance. These measurements support the need for routine assessment of LA in heart failure clinics.

P1684

The dynamics of galectin-3 in patients with heart failure and preserved ejection fraction

Y Yulia Kushnir[1]
[1]Dnipropetrovsk State Medical Academy, Dnipropetrovsk, Ukraine

Nowadays galectin-3 is concidered as a myocardial firosis marker and the possibility of its applying in diagnostics and prognosis of chronic heart failure (CHF) is discussed. At the same time some authors presuppose the existence of antifibrotic effect of the torasemide - one of the loop diuretics which are the major drug group to reduce liquid retention in patients with CHF.
The aim of the study was to estimate the dynamics of galectin-3 in patients with CHF with preserved left ventricular ejection fraction during loop diuretics treatment.

Materials and methods. There were examined 31 patients (male - 23, female - 8) with the age limit 51-75 years (average M ± m - 66.9 ± 1.4) who suffered from CHF II-III functional class caused by coronary heart disease (CHD) with preserved ejection fraction. The control group consisted of 15 patients in age from 46 to 73 (average M ± m - 66.2 ± 2.2) with CHD without CHF manifestation. Twenty-six examined patients who needed prescription of diuretics were randomly divided into 2 groups. The fist one – 15 CHF patients who were treated with torasemide, the second one - 11 patients who were prescribed furosemide. Before the therapy was started groups were comparable in all investigated parameters (p>0,05 in all comparisons). In addition to diuretics, all patients received standard CHF therapy. Clinical efficiency and dynamics of galectin-3 was estimated in 2-3 month.
Results: The positive dynamics of the functional class (FC) was established in both groups after treatment. In group I the average FC decreased from 2.80 ± 0.11 (Me = 3) to 2.20 ± 0.17 (Me = 2) (p = 0.008), in the II group - from 2.73 ± 0.14 (Me = 3) to 2.27 ± 0.19 (Me = 2) (p = 0.043). The positive dynamics of the FC was associated with improving the health of patients. Thus, in the first group complaints of general weakness decreased by 46.6%; shortness of breath by 60.0%; swelling of the lower extremities by 93.3%; heart pain by 20.0%; in the second group 36.3%; 54.5%; 90.9%; 18.2%, respectively. The analysis of the dynamics of the galectin-3 levels on the background of treatment with loop diuretics is presented in the table.
Conclusion. Analysing the clinical comparability of loop diuretics in patients with CHF addition of torasemide to their therapy has advantages which are expressed by positive influence on the dynamics of galectin-3 level.

The dynamics of galectin-3 levels in pts

Period of observation	1 group, n = 15	2 group, n = 11	$?_1$
Before treatment, ng/ml	21,6±0,97 (20,4)	23,8±1,45 (23,8)	0,287
After 8-10 weeks of treatment, ng/ml	20,4±1,07 (18,9)	24,8±1,64 (25,3)	0,035
D (%), ?	-5,6% (? = 0,001)	+4,2% (? = 0,090)	? <0,01

P1685

Increased pulmonary capillary wedge pressure is the major hemodynamic abnormality during supine exercise in patients with heart failure with preserved ejection fraction

E Emil Wolsk[1]; D Kaye[2]; J Komtebedde[3]; SJ Shah[4]; D Burkhoff[5]; B Borlaug[6]; DW Kitzman[7]; C Lam[8]; D Van Veldhuisen[9]; P Ponikowski[10]; M Petrie[11]; C Hassager[12]; JE Moller[13]; F Gustafsson[12]
[1]Gentofte Hospital, Department of Cardiology, Copenhagen, Denmark; *[2]Baker IDI Heart and Diabetes Institute, Melbourne, Australia*; *[3]Corvia Medical, Andover, United States of America*; *[4]Northwestern University, Chicago, United States of America*; *[5]Cardiovascular Research Foundation, New York, United States of America*; *[6]Mayo Clinic, Rochester, United States of America*; *[7]Wake Forest University, Winston-Salem, United States of America*; *[8]Duke-NUS Graduate Medical School Singapore, Singapore, Singapore*; *[9]University Medical Center Groningen, Groningen, Netherlands*; *[10]4th Military Hospital, Wroclaw, Poland*; *[11]University of Glasgow, Glasgow, United Kingdom*; *[12]Rigshospitalet - Copenhagen University Hospital, Copenhagen, Denmark*; *[13]Odense University Hospital, Odense, Denmark*

Background: Severely reduced exercise capacity is a hallmark of heart failure with preserved ejection fraction (HFpEF), but its mechanisms are not fully understood.
Methods: We examined invasive hemodynamic variables during rest and peak supine cardiopulmonary exercise testing in HFpEF patients compared with healthy controls at matched workloads utilizing data from 3 large prospective trials: 108 HFpEF patients from REDUCE LAP-HF & REDUCE LAP-HF I (LVEF:52 ± 10%) and 42 healthy controls from the HemReX study (LVEF:62 ± 7%). Student's t-test and logistic regression with stepwise selection (p < 0.05) were used to assess hemodynamic variables associated with HFpEF vs. controls. Dominance analysis was used to obtain the proportion of fit metric attributable to each independent variable. A p value of < 0.05 was considered statistically significant.
Results: At matched workloads (HFpEF - peak workload: 45 ± 13 W vs. controls - matched workload: 45 ± 23 W, p = 0.85) in HFpEF patients compared to controls, the increase in cardiac index (+1.5 ± 0.9 vs. +2.9 ± 1.1 l/min/m2, p < 0.0001) and stroke volume index (SVi; +4 ± 10 vs. +19 ± 10 ml/m2, p < 0.0001) were substantially blunted, and pulmonary capillary wedge pressure [PCWP] was increased(+17 ± 7 vs +10 ± 6 mmHg, p < 0.0001), whereas changes in heart rate (29 ± 19 vs. 29 ± 16 bpm, p = 0.94) were similar (Table). Changes in arterial-venous O2 difference, a measure of peripheral function, tended to be lower in HFpEF compared to controls (+4.8 ± 0.8 vs. +5.1 ± 1.5 ml/dl, p = 0.08). In multivariate modeling, 2 exercise hemodynamic variables independently distinguished HFpEF from healthy controls (r2:0.75); SVi (OR: 0.89 [0.82, 0.96], p = 0.002) and PCWP (OR: 1.55 [1.30, 1.86], p < 0.0001), accounting for 17% (SVi) and 57% (PCWP) of the difference between HFpEF and controls.
Conclusion: Increased PCWP and blunted SVi account for the majority of hemodynamic differences between HFpEF patients and healthy controls during supine exercise.

Hemodynamics at matched workloads

	Controls	HFpEF	p-value
Heart rate (bpm)	93±18	99±20	0.04
MAP (mmHg)	99±14	111±23	0.0007
SVi (ml/m2)	60±13	44±12	<0.0001
CI (l/min/m2)	5.6±1.1	4.3±1.2	<0.0001
RAP (mmHg)	10±4	19±6	<0.0001
mPAP (mmHg)	30±8	46±11	<0.0001
PCWP (mmHg)	19±7	35±7	<0.0001
Ca-vO2 (ml/dl)	4.8±0.1	5.1±0.1	0.08

P1686

The level of uric acid in patients with heart failure with preserved ejection fraction depending on age

Y Kushnir[1]
[1]Dnipropetrovsk State Medical Academy, Dnipropetrovsk, Ukraine

Today there is numerous evidence of the importance of hyperuricemia in the progression of chronic heart failure (HF). Hyperuricemia considered as a marker of poor prognosis in patients with HF. According to the literature hyperuricemia can be observed in 60% of patients with CHF hospitalized with decompensation.
The aim was to estimate the level of uric acid in patients with heart failure with preserved ejection fraction (EF) depending on age.

Uric acid level in patients with HF

Measurement, units	Number of patients (abs.,%) or average level (M±m, ??)		
Patients under 59 years (n = 74)	Patients from 60 to 75 years (n = 73)	Patients over 76 years (n = 51)	
Uric acid, mcmol/l	349±6,4	356±8,5	377±7,2*
Hyperuricemia	12 (16,2%)	9 (12,3%)	11 (21,6%)

Materials and Methods: A retrospective analysis of clinical records of 198 patients with HF and preserved EF (EF more than 45 %, average (M ± m) - (63,8 ± 6,3) %) was enrolled. All patients were hospitalized in 2015-2016 and were older than 40 years (average age (M ± m) of 51.7 ± 9,4). All patients were divided into three groups according to age: the first group - patients aged 40 to 59 years (n = 74), the second group - patients aged 60 to 75 years (n = 73), the third group - patients older than 75 years (n = 51). HF was diagnosed in case of presence of objective and subjective features inherent to this clinical syndrome, collected anamnesis, physical examination, laboratory and instrumental analysis. The average level of uric acid in all patients with HF and preserved EF was estimated. According normative values were adopted following indicators: men - 200-420 mmol/l; women - 140-340 mmol/l. Statistic processing of materials research conducted using the methods of biostatistics implemented in the software package STATISTICA 6.0.
Results: The increased average level of uric acid was found in all age groups. However, the frequency of hyperuricemia registration was maximum (21.6%) in patients from 75 years, which may indicate poor prognosis in this age group (Table).
Conclusion. All patients with chronic heart failure have increased average level of uric acid. Determined that the average level of hyperuricemia increases with age.

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Role of vascular endothelial growth factor-A in left ventricle remodeling and diastolic dysfunction in patients with heart failure

D Dina Shorikova[1]; E Shorikov[1]
[1]Bucovinian State Medical University, Chernivtsy, Ukraine

At the last decades, the paradigm about exclusive role of renin-angiotensin-aldosterone system in target organs injuries during chronic heart failure (HF) is the basic conception in the most of clinical trials. But, it is also essential to provide

researchers about relating role of different biomarkers which could affect cardiovascular continuum. On our opinion, the superfamily of growth factors, especially vascular endothelial growth factor-A (VEGF-A), may keep definite position in the development of HF.

Material and methods: We have included 288 patients with diagnosis of non-ischemic HF with preserved ejection fraction (HFpEF) (mean of LVEF of patients was 53,8 ± 4,72%) in the study. All patients were inspected with echocardiographic and Doppler ultrasound and immunoassay detection of VEGF-165 (type ?).

Using unadjusted regression model we have analyzed interrelationship between the VEGF-165 concentration and parameters of LV remodeling in patients with HFpEF

We have set the reliable negative correlation between level of VEGF-A and LV mass (R=-0,61; ? = 0,007) and myocardium mass index (R=-0,54; ? = 0,004). Nevertheless, the observed data showed unreliable regression between the decrease of the VEGF-A level and the relative wall thickness as with VEGF-A level and index EDV/LV mass. In non-parametric ANOVA we have found the dependency of the distribution of medians of the VEGF-A level on the eccentric and concentric hypertrophy (? = 6,58; ? = 0,04).

However, we observed strong positive correlation between VEGF and ratio of early and late peak velocity (Ve/Va) and negative correlation with VEGF and isovolumetric relaxation time. The decrease of VEGF level also associated with the shortness of duration time of early peak of diastolic flow (DTe) (table).

Conclusion: in patients with HFpEF the decrease of VEGF-165 associated with the increase of left ventricle mass and the strongest link set in condition of eccentric and concentric hypertrophy. In addition, there is the direct dependency between the level of VEGF and the parameters of diastolic function of left ventricle.

Interrelationship between VEGF-A and som

Index	IVRT, ?	DT E, ?	Ve/Va
Level VEGF-165	r=-0,52 (? = 0,03)	r = 0,47 (? = 0,09)	r = 0,65 (? = 0,011)

P1688

Diastolic dysfunction grades stratify patients on chronic hemodialysis therapy

J Jan Malik[1]; A Valerianova[1]; J Lachmanova[1]; M Bartkova[1]
[1]*Charles University, 1st Faculty of Medicine , Prague, Czech Republic*

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Background: Heart failure is a frequent consequence of end-stage renal disease (ESRD). Among other involved mechanisms, left ventricular (LV) diastolic dysfunction is frequent. New echocardiographic guidelines for assessing diastolic function were published recently. They help in the diagnosis and severity stratification of HFpEF and have been studied in various populations. However, data in ESRD patients, typically affected by cyclic volume overload, is sparse. In this population, the diagnosis of heart failure is tricky since both echo findings and B-type natriuretic peptide (BNP) levels are related also to the actual volume status.

Purpose: We performed a single center study aimed at assessing the role of diastolic dysfunction grading in ESRD patients treated by hemodialysis.

Methods: We included a cohort of 46 ESRD patients treated by hemodialysis in our Institution if they fulfilled the following criteria: good echo visibility, ejection fraction >45%, lack of moderate-to-severe valvular disease. The Euro-American 2016 guidelines primary criteria for assessing diastolic function (mean E/e'>14, e' septal < 7cm/s or e' lateral < 10 cm/s, peak tricuspid regurgitation velocity > 2,8m/s, left atrial volume index >34 ml/m2) were applied. Examinations and blood drawing for BNP analysis was done just before hemodialysis.

Results: Included subjects were 62 ± 15 years old, their dialysis vintage lasted for 61 ± 52 months. Diastolic dysfunction as well as left atrial dilatation was present in 64% of them. BNP rose significanty with diastolic dysfunction grade and also with left ventricular mass index. Medial e' was more robust than lateral e'.

Conclusions: Diastolic dysfunction grades further differentiate ESRD patients according to their BNP levels. High frequency of diastolic dysfunction is affected mainly by the high prevalence of LV hypertrophy. The border between heart failure and water overload is not sharp in this population.

P1689

Hepatocardiac relations in patients with heart failure and diabetes mellitus.

I Kniazkova[1]; A Bilovol[1]; V Maziy[2]
[1]*Kharkov national medical university, Kharkov, Ukraine*; [2]*Institute therapy of L.T.Malay of AMS of Ukraine, Kharkov, Ukraine*

We aimed to investigate the association between the structural and functional state of the liver and the cardiac haemodynamics in patients (pts) with ischemic heart failure (HF) and diabetes mellitus (DM).

Materials and methods. The study included 82 pts with HF NYHA II-III after myocardial infarction, 42 of which (mean age 55.8 ± 2.6 years) had DM (1 group) and the other 40 (mean age 54.3 ± 2.9 years) - had not (group 2). The groups comparable to demographic and clinical characteristics. Central haemodynamics parameters was evaluated with echocardiography. Structural state of the liver was investigate with an ultrasound scanner and included assessment of the echogenicity of hepatic parenchyma, vascular pattern, the degree of fatty change and the stage of liver fibrosis. The parameters of the liver functional status and hepatocyte damage markers were determined (serum total protein and albumin, total bilirubin, prothrombin index, alanine aminotransferase (ALT) and aspartate aminotransferase (AST) alkaline phosphatase (AP) and gamma-glutamyltransferase (GGP)). The insulin resistance index of HOMA and the QUICKI test were calculated. The hepatic steatosis index (HSI), the fatty liver index (FLI) and nonalcoholic fatty liver disease fibrosis score (NFS) were calculated.

Results: It was found that the HSI and the FLI were significantly ($p < 0.05$) higher in group 1 (39.1% and 2.3-fold respectively) than in group 2. Patients with DM also had higher values of NFS (-0.51 ± 0.7) compared with non-DM patients (-1.5 ± 0.6; $p < 0.05$). The patients of group 1 characterized by higher blood levels of bilirubin 2.2-fold, GGTT 4-fold, ALT 5.3-fold and AST 1.7-fold and lower total protein levels (67.1 ± 3.2 vs. 72.9 ± 3.6 g/l) and albumin (36.1 ± 3.1 vs. 42.1 ± 3.3 g/l) in compare with group 2. Also, under comparable NYHA classes of heart failure the left ventricular myocardial mass index (LVMI) was 12.1% ($p < 0.05$) higher in group 1 in compare with group 2. In group 1 the following left ventricle (LV) remodeling patterns were noted: concentric hypertrophy and eccentric hypertrophy (54.8% and 45.2% respectively), which significantly differed from group 2, where 15% of patients had a normal geometry of LV, in 62,5% and 22.5% of patients - concentric hypertrophy and eccentric hypertrophy, respectively. We found a correlation between LVMI and the FLI ($r = 0.31$, $p < 0.05$) and LVMI and the NFS ($r = 0.33$, $p < 0.05$) in group 1. In addition, the NFS demonstrates correlation with the six minute walk test and NYHA classes (r=-0.33 and r = 0.31 respectively, all $p < 0.05$) in group 1.

Thus, in patients with CHF and DM showed more expressed structural and functional status changes of the liver, which included formation of steatosis and initial signs of hepatic fibrosis, laboratory syndromes of cytolysis and cholestasis. This corresponds to more pronounced structural changes in the heart, manifested by increasing LVMI and development of adverse types of LV remodeling.

P1690

Single centre audit of experience in tallaght hospital among patients with chronic heart failure and iron deficiency anemia (ida).

W Ashram[1]
[1]*Beaumont Hospital, cardiology, Dublin, Ireland*

Introduction: Chronic heart failure is a common condition and is significantly projected to increase in the coming years due to increased survival of patients with coronary artery disease.

Iron deficiency anemia is a commonly present co-morbidity in patient with heart failure and it has been associated with increased mortality and a poorer quality of life. Symptoms related to iron deficiency anemia are not specific and is considered as a major contributor to exercise intolerance even in the absence of anemia.

Purpose: The main purpose of this audit is to further characterize patients with chronic heart failure with iron deficiency anemia and normal iron storage irrespective of hemoglobin level in relation to the degree of kidney function, Pro BNP level and left ventricular systolic function.

Methods and Results: We reviewed 133 patients with chronic heart failure in our Hospital, in 12 months period of time from June 2016 until July 2017. The age range was between 39 and 94 with mean of 71 years. 88 patients were males and 45 patients were females.

94 patients (70%) out of 133 patients have iron profile. Interestingly, two groups were almost equal in number (46 patients with IDA and 48 patients with normal iron storage)

Comparing 2 groups in relation to kidney function, Pro BNP level and left ventricular systolic function showed significant difference in Pro BNP level between 2 groups (Pro BNP was elevated in 84.78% in IDA while only 12.5% in patients with normal iron storage). Both groups showed > 90% of patients have stage 2 to stage 5 CKD. In relation to left ventricular systolic function, 50% in each group showed severely reduced systolic function.

Conclusion: IDA is strongly associated with high level of Pro BNP and heart failure exacerbation in 85% of HF population studied (especially when LVEF is severely reduced) when compared to patients with normal iron storage. There is no much difference in both groups regarding kidney function and left ventricular systolic function as both group almost (half of them) have severe LVEF with CKD stage 2 to 5. Therefore, checking iron storage in patients with high level of Pro BNP and heart failure exacerbation will have an excellent impact on patients' wellbeing and eventually reducing the burden on health care system. Which can be easily corrected if approached appropriately.

P1691

Paulus criteria are valuable for predicting outcome in patients with asymptomatic diastolic dysfunction

A Anna Bobenko[1]; L Schleussner[1]; A Duvinage[2]; T Trippel[1]; C Herrmann-Lingen[3]; L Binder[4]; K Nolte[5]; V Holzendorf[6]; M Mende[7]; G Hasenfuss[5]; R Wachter[5]; B Pieske[1]; F Edelmann[1]

[1]Charite - Campus Virchow-Klinikum (CVK), Department of Cardiology, Berlin, Germany; *[2]Technical University of Munich, Depatment of Prevention, Rehabilitation and Sports Medicine, Munich, Germany*; *[3]University Medical Center Gottingen (UMG), Depatment of Psychosomatic Medicine and Psychotehrapy, Gottingen, Germany*; *[4]University Medical Center Gottingen (UMG), Clinical Chemistry, Gottingen, Germany*; *[5]University Medical Center Gottingen (UMG), Department of Cardiology and Pneumology, Gottingen, Germany*; *[6]University of Leipzig, Clinical Trial Centre, Leipzig, Germany*; *[7]University of Leipzig, Department of Informatics, Statistics and Biometry, Leipzig, Germany*

Background: High prevalence and lack of pharmacological treatment are making heart failure with preserved ejection fraction (HFpEF) a growing public health problem. Therefore, prevention of onset of HFpEF has become an important issue, but no algorithm for screening asymptomatic patients with risk factors for developing HFpEF exists to date.
Purpose: We assessed whether Paulus criteria are suitable for predicting cardiovascular outcome in asymptomatic patients with preserved left ventricular ejection fraction (LVEF) and diastolic dysfunction.
Methods: We performed a post-hoc analysis of the Diagnostic Trial on Prevalence and Clinical Course of Diastolic Dysfunction and Heart Failure (DIAST-CHF) investigating patients with cardiovascular risk factors. All patients underwent a comprehensive non-invasive diagnostic workup, including ECG, blood pressure measurement, detailed echocardiography and blood analysis at baseline and within a 5-year-follow-up. Asymptomatic patients with preserved LVEF (< 50%) were selected from all DIAST-CHF patients and classified according to Paulus criteria (tissue doppler derived E/e' > 15 or E/e' > 8 and presence of either NT-proBNP > 220 ng/l, BNP > 200 ng/l or atrial fibrillation) into "Paulus positive" and "Paulus negative". Outcome was assessed for both groups after 5 years of follow-up.
Results: 851 asymptomatic patients (age 65.5 ± 7.6 years, 44% female, mean BMI 28.1 kg/m2) were included in the analysis. Paulus positive patients were significantly older ($p < 0.001$), more often women ($p = 0.003$) and more often had a history of coronary artery disease, atrial fibrillation and renal dysfunction ($p < 0.001$) compared to Paulus negative. Incidence of death, cardiovascular hospitalization and onset of heart failure signs or symptoms was significantly higher in Paulus positive group after 5 years of follow-up ($p < 0.001$).
Conclusion: Asymptomatic patients with preserved LVEF that fulfill Paulus criteria on diastolic dysfunction have a worse 5-year-outcome than those who do not fulfill Paulus criteria. Therefore, Paulus criteria may be used for outcome assessment and prevention of HFpEF in asymptomatic patients with risk factors for heart failure.

Chronic Heart Failure - Epidemiology, Prognosis, Outcome

P1692

Impact of cardiometabolic syndrome on the incidence of heart failure; a nationwide, longitudinal cohort study in South Korea

S H Sung Hea Kim[1]; KH Ryu[2]; SW Han[2]; HJ Kim[1]; HS Kim[1]; JC Youn[2]; SW Choi[2]

[1]Konkuk University Hospital, Seoul, Korea Republic of; *[2]Hallym University, Cardiology, Dongtan, Korea Republic of*

Background: Although studies on association with HF (HF) and the cardiac CMS(CMS) have been conducted in Swedish study (ULSAM cohort) and the Finnish study, these studies were conducted only in middle aged men with 50 years old or old age over 70. But there is few data on the association between HF and CMS in young age group or women, furthermore in Asian.
Methods: In this study, 7,830,602 study subjects who were aged between 30 and 70 years and had received national health checkups in 2009 were retrospectively included and followed up for 7 years. Participants excluded were those with cardiovascular disease and cancer. Based on revised National Cholesterol Education Program-Adult Treatment Panel III criteria, subjects were divided into three groups according to their number of MS factors: the control group (0), Pre-MS Group (1-2), and MS group (3-5). The occurrence of HF was defined by the ICD-10 coding system after considering medication history and admission to a tertiary hospital. The incidence of HF was presented as the rate per 100,000 person-years, and the risk of HF with respect to MS was analyzed through Cox proportional hazard regression analysis. Confounding variables were gender, age, health behavior (e.g., smoking and exercise), family history (e.g., stroke, hypertension, heart disease, and diabetes), body mass index, and blood creatinine and hemoglobin values. The results are presented as hazard ratio (HR) and 95% confidence interval (95% CI).
Results : A total of 1,251,138 (15.9%) of the 7,830,602 subjects were assessed as having MS. Of the total 57 million person-years, the incidence rate per 100,000 person-years was 27.7 for HF. The incidence of HF increased significantly in both men and women over the age of 40 with respect to the stage of MS. The risk of HF in the Pre-MS and MS groups was 1.661 and 2.456 times higher, respectively, than that in the control group, even after adjustment for all confounding variables.
Conclusion : MS was associated with a higher risk of HF in young and women group in addition to old and men in Korea.

HF incidence according to age and sex

Rate per 100,000 person-years	30's	40's	50's	60's	
Male	control	4.54	7.82	19.20	48.33
	preMS	7.38	14.24	35.88	79.00
	MS	*19.57	*28.10	*55.05	*111.1
Female	control	5.23	7.10	13.38	26.48
	preMS	6.87	13.47	19.42	40.98
	MS	*19.51	*22.12	*34.91	*64.82

*p value < 0.001 among 3 groups

		Model1	Model 2	Model 3	Model 4
MS stage	Control	1	1	1	1
	pre-MS	2.39 (2.257, 2.53)	1.694 (1.598, 1.795)	1.691 (1.596, 1.793)	1.661 (1.566, 1.763)
	MS	4.549 (4.28, 4.835)	2.58 (2.423, 2.748)	2.571 (2.413, 2.738)	2.456 (2.289, 2.634)
sex	female		1	1	1
	male		1.311 (1.239, 1.388)	1.321 (1.247, 1.398)	1.643 (1.538, 1.756)
age	30-39		1	1	1
	40-49		1.626 (1.471, 1.798)	1.614 (1.46, 1.784)	1.529 (1.382, 1.691)
	50-59		3.564 (3.247, 3.912)	3.528 (3.213, 3.873)	3.269 (2.975, 3.592)
	≥60		7.732 (7.053, 8.477)	7.7 (7.023, 8.443)	7.09 (6.461, 7.781
smoke	Non-smoker		1	1	1
	Ex-smoker		1.021 (0.954, 1.092)	1.013 (0.947, 1.084)	1.046 (0.991, 1.104)
	Smoker		1.662 (1.572, 1.757)	1.655 (1.565, 1.749)	1.688 (1.596, 1.785)

Hazard ratio for HF according to CMS

P1693

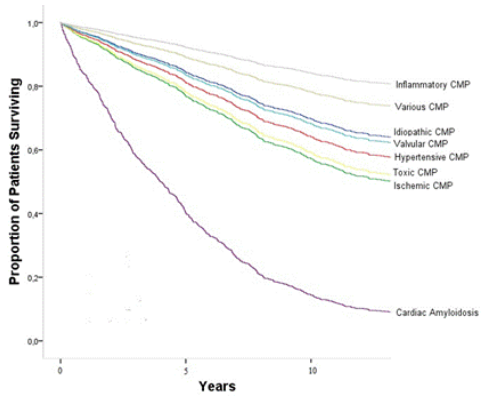
Long-term outcome in cardiomyopathies according to etiology: survival is best in inflammatory CMP and worst in cardiac amyloidosis

P Pliger[1]; F Kocher[2]; S Dobner[3]; C Ensinger[4]; J Doerler[1]; MM Zaruba[1]; G Poelzl[1]

[1]Innsbruck Medical University, Department of Internal Medicine III, Cardiology and Angiology, Innsbruck, Austria; *[2]Innsbruck Medical University, Department of Internal Medicine V, Haematology and Oncology, Innsbruck, Austria*; *[3]Bern University Hospital, Department of Cardiology, Bern, Switzerland*; *[4]Innsbruck Medical University, Institute of Pathology, Innsbruck, Austria*

Introduction: Early studies have shown that etiology of underlying cardiomyopathy (CMP) predicts prognosis in heart failure. However, diagnostic work-up and goal-directed therapy have improved substantially over time. We were interested if advancements in diagnosis and therapy have changed the impact of various etiologies on prognosis.
Methods: In this single-centre registry 2029 consecutive patients treated for heart failure according to prevailing guidelines between 2000 and 2016 were analysed. Underlying CMPs were classified into eight groups: idiopathic (25.9%), ischemic (24%), hypertensive (16.4%), inflammatory (15.0%), various (5.5%), toxic (4.5%), cardiac amyloidosis (4.4%), and valvular (2.9%). Patients were followed for a median of 80 (IQR 34-134) months. Primary endpoint was death of any cause. Kaplan-Meier estimator was used to calculate 5-year survival. A multivariate cox regression analysis was performed to compare survival between groups.
Results: Five year overall survival in the whole cohort was 81.9% (inflammatory 91.9%, various 90.4%, idiopathic 85.3%, hypertensive 81.1%, valvular 80.8%, toxic 77.7%, ischemic 76.3%, cardiac amyloidosis 48.4%). In multivariate analysis

adjusted for age, gender, LV-EF, and NYHA class, individuals with cardiac amyloidosis were 6.5 time (95% CI 3.0-14.0; p < 0.01) more likely to die of any reason than were individuals with inflammatory CMP. In this model, mortality was also higher in ischemic (HR 3.0, 95% CI 1.8-5.2; p < 0.01), valvular (HR 2.5, 95% CI 1.2- 5.4; p = 0.02) and toxic CMP (HR 2.4; 95% CI 1.3 - 4.4; p < 0.01).
Conclusion: Comparing long-term outcome according to CMP etiology survival is worst in patients with cardiac amyloidosis and best in patients with inflammatory CMP. From this perspective, thorough etiologic evaluation and targeted therapy is mandatory in the management of patients with heart failure.



Overall surivival according to etiology

P1694
Prevalence of bendopnea in elderly patients with heart failure

VN Larina[1]; Il Chukaeva[1]; DG Karpenko[1]; OM Kulbachinskaya[1]
[1]The Russian National Research Medical University named after N.I. Pirogov, Moscow, Russian Federation

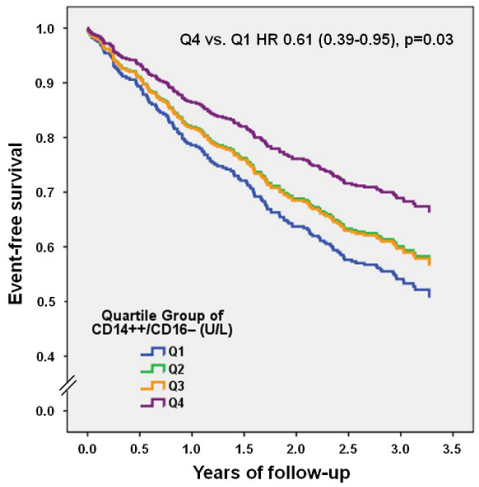
Recently, a symptom of heart failure (HF) called bendopnea or flexodyspnea was described by J. Thibodeau. We conducted the present study to evaluate the prevalence and characteristic of bendopnea in elderly ambulatory patients with heart failure. There was a a single-center prospective observational study of a convenience sample of 80 outpatients aged 60-89 years with HF, which was reviewed by the institutional review board. All patients had clinical examination, laboratory collection, ECG and echocardiography examination during the outpatient clinic visit. All patients were under optimal HF therapy. HF duration was 24 (12-48) months. To determine the presence of bendopnea, each subject sat in a chair and bent forward at the waist as if putting on their shoes or socks. The subject was classified as having bendopnea if they reported shortness of breath within 30 seconds of bending. If there was no shortness of breath at 30 seconds, the patient was classified as not having bendopnea.
Results: The prevalence of bendopnea in ambulatory elderly patients with heart failure is 39% and it increases to 90% in those with LVEF <45%. 31 (38,8%) patients (7F/24?, ? <0,001), aged 73,2 ± 6,7 years, had bendopnea. All patients had advanced NYHA functional class and 14 (45,2%) - orthopnea. In addition, bendopnea had 90% patients with LVEF <45% and 21,6% - with LVEF = 45% (? <0,001). The relationship of bendopnea with male gender (? <0,001, ?R 11,8, 95% CI 4,04 - 34,8), symptoms of advanced HF (? <0,001, ?R 1,78, 95% CI 1,29-2,38), ischemic heart disease (? = 0,002, ?R 26,6, 95% CI 3,3-21,3), LV aneurysm (? = 0,002, OR 13,3, 95% CI 2,7-65,9), LV EDDi (? = 0,008, ?R 4,9, 95% CI 1,5-15,9), LV ESDi (? = 0,004, ?R 8,2, 95% CI 1,9-34,1), left atrium (? = 0,008, ?R 4,3, 95% CI 1,4-12,5), LV EDV (? = 0,012, ?R 1,12, 95% CI 1,03-1,2), LV ESV (? = 0,010, ?R 1,32, 95% CI 1,07-1,64), systolic pulmonary pressure (? = 0,002, ?R 1,26, 95% CI 1,03-1,45), serum NT-proBNP (? = 0,055, ?R 1,0, 95% CI 1,0-1,002), creatinine (? = 0,001, ?R 1,04, 95% CI 1,02-1,07) or uric acid (? = 0,004, ?R 1,006, 95% CI 1,002 - 1,011) was confirmed. In addition, patients with bendopnea had a greater rate of all hospitalizations (? = 0,003, ?R 7,61, 95% CI 2,04-28,4) and cardiovascular hospitalizations (? = 0,003, ?R 1,4, 95% CI 1,09-1,80). Conclusion. The prevalence of bendopnea in ambulatory elderly patients with heart failure is 39% and it increases to 90% in those with LVEF <45%. Our findings indicate that this symptom of heart failure may have a great interest in ambulatory clinical practice, indicating a group of patients with worse course of disease and hospitalization risk.

P1695
Prognostic value of monocyte subsets in patients with heart failure

E Elchinova[1]; J Lupon[2]; MA Fernandez-Sanmartin[2]; M De Antonio[2]; I Teubel[2]; M Domingo[2]; S Roura[2]; P Moliner[2]; E Zamora[2]; B Gonzalez[2]; C Rivas[2]; V Diaz[2]; J Santesmases[2]; MI Troya[2]; A Bayes-Genis[2]
[1]Inselspital, Berm, Switzerland; [2]Germans Trias i Pujol University Hospital, Badalona, Spain

Background: Circulating monocytes can be distinguished by flow cytometry. Three distinct human monocyte subsets are identified. The distribution and role of these monocyte subsets in heart failure (HF) is not established.

	Total N = 404	Alive N = 295	Dead N = 109	p-value
Percentage				
CD14++/CD16-	50.0 ± 17.2	50.4 ± 16.5	48.6 ± 19.0	0.36
CD14++/CD16+	42.0 ± 17.2	41.1 ± 16.6	44.3 ± 18.7	0.10
CD14-/CD16+	8.1 ± 4.2	8.5 ± 4.2	7.1 ± 4.1	0.003
U/mL				
CD14++/CD16-	890 ± 437	916 ± 423	820 ± 468	0.05
CD14++/CD16+	732 ± 368	736 ± 362	721 ± 383	0.73
CD14-/CD16+	146 ± 89	155 ± 90	119 ± 81	<0.001



Purpose: To evaluate the prognostic role of monocyte subsets in HF outpatients.
Methods: Monocyte subsets were classified as CD14+/CD16– (classical), CD14++/CD16+ (intermediate), and non-classical CD14–/CD16+ (also described as CD14+/CD16++). We assessed the percentage of each monocyte subset and also we determined quantitatively the absolute cell count of each subset, expressed by units/mLitter (U/mL).
Results: Four-hundred four patients were consecutively included (73% male, age 69.5 ± 12.2 years, LVEF 41.6% ± 14.5). During a mean follow-up of 2.6 ± 0.9 years, 109 patients died, 101 had a HF hospitalization and 162 suffered the composite end-point of all-cause death or HF hospitalization. Table 1 shows percentage and U/mL of monocyte subsets in alive and dead patients at the end of the study. In multivariable analysis percentage of monocyte subsets did not remain related to any of the end-points. In contrast, when U/mL were considered, non-classical subset remained associated with all-cause death (p = 0.03) and classical subset whit HF-related hospitalization (p = 0.04) and the composite end-point (p = 0.01). Figure 1 shows free-event survival curves for quartiles (U/mL) of classical monocyte subset.
Conclusions: The quantitative determination of the absolute cell count of each monocyte subset was superior from the prognostic viewpoint than the percentage of these monocyte subsets in HF outpatients. Classical subset was independently associated with HF-related hospitalization and the composite end-point and non-classical subset with all-cause mortality.

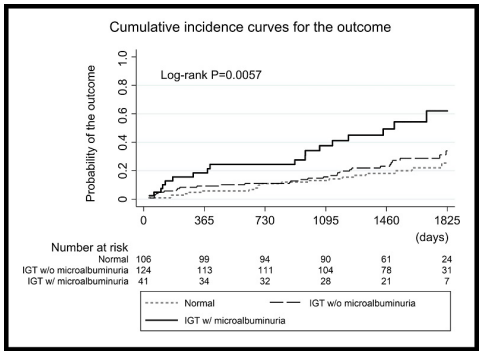
P1696

Association between impaired glucose tolerance and prognosis according to presence of microalbuminuria in patients with chronic heart failure

K Kotaro Nochioka[1]; YS Sakata[1]; RA Abe[1]; TO Oikawa[1]; SK Kasahara[1]; MS Sato[1]; HA Aoyanagi[1]; MM Miura[1]; TS Shiroto[1]; JT Takahashi[1]; MS Miyata[2]; HS Shimokawa[1]
[1]Tohoku University Graduate School of Medicine, Department of Cardiovascular Medicine, Sendai, Japan; *[2]Tohoku University Graduate School of Medicine, Departments of Evidence-based Cardiovascular Medicine, Sendai, Japan*

On behalf of: The SUPPORT Trial Investigators
Funding Acknowledgements: The Ministry of Health, Labour, and Welfare and from the Ministry of Education, Culture, Sports

Background: Previous studies have shown that diabetes mellitus (DM) is a strong predictor in patients with chronic heart failure (CHF), especially when complicated with microalbuminuria. However, it is unclear whether the association of impaired glucose tolerance (IGT), a prediabetic status and microalbuminuria also has a prognostic impact in CHF patients.
Purpose: To examine the prognostic impact of the association of IGT and microalbuminuria in CHF patients.
Methods: We studied 554 CHF patients (mean 66 yrs., women 25%, HbA1c 6.4%) from the control arm of our intervention trial, the SUPPORT (SUPPlemental benefit of an angiotensin receptor blocker in hypertensive patients with stable heart failure using OlmesaRTan), which examined whether an additive treatment with an ARB (olmesartan) reduces the mortality and morbidity in CHF patients with history of hypertension. In patients without known DM (n = 280), we performed 75g oral glucose tolerance test (OGTT). Microalbuminuria was defined as a spot urine albumin = 30 mg/L. We examined the prognostic impact of the association of IGT and microalbuminuria on the composite endpoint of all-cause death, myocardial infarction, stroke, and HF hospitalization for 5 years.



FIgure

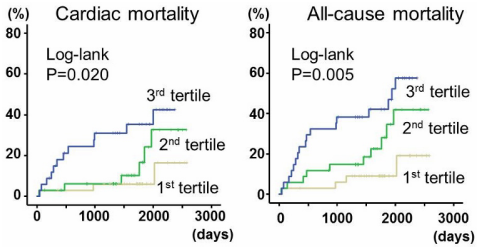
Results: We identified 158 (57.7%) normal glucose tolerance (NGT; 64 yrs., women 27%) and 113 (41.2%) IGT (mean 67 yrs., women 30%) patients, after excluding 3 newly diagnosed DM (mean 70 yrs., all men). As compared with NGT patients, IGT patients had comparable prevalence of microalbuminuria (IGT, 36% vs. NGT, 33%, P = 0.56), estimated glomerular filtration rate (75.9 ± 33.7 vs. 79.1 ± 39.2 mL/min/1.73 m^2, P = 0.48), and the use of angiotensin converting enzyme inhibitors (85 vs. 80%, P = 0.27). After adjustment for age, sex, systolic blood pressure, heart rate, body-mass index, ischemic etiology, NYHA functional class, history of HF hospitalization, left ventricular ejection fraction, and B-type natriuretic peptide levels, the multivariable Cox hazard models showed that IGT itself was not associated with increased risk of the composite endpoint (hazard ratio (HR) 1.03, 95% confidence interval (CI) 0.63-1.68, P = 0.90). However, when stratified by the presence of microalbuminuria, IGT was a risk in the presence of (HR 2.20, 95%CI 1.13-4.28, P = 0.02), but not in the absence of microalbuminuria (HR 0.77, 95%CI 0.37-1.54, P = 0.21) (P for interaction = 0.045). (Figure)
Conclusions: These results indicate that although IGT itself is not a risk factor in CHF patients, it is associated with poor prognosis when complicated by microalbuminuria. Thus, combined assessment of OGTT and urinalysis may be useful for risk stratification for CHF patients.

P1697

Urinary N-terminal fragment of titin to predict mortality in dilated cardiomyopathy

Y Yasuchika Takeishi[1]; A Yoshihisa[1]
[1]Fukushima Medical University, Fukushima, Japan

Titin is associated with myocardial stiffness and hypertrophy, and mutations in its gene have been identified in cardiac myopathies such as dilated cardiomyopathy (DC). It has recently been reported that in damaged muscle, the N-terminal fragment of titin (Titin-N) is cleaved by calpain-3, and urinary Titin-N could be a marker of sarcomere damage. We aimed to investigate the impact of urinary Titin-N on prognosis of DC. We measured urinary levels of Titin-N/creatinine ratio (U-TN/Cr; pmol/mg/dl) in 102 DC patients, and followed up all the patients (mean 1,167 days). The patients were divided into three groups based on the U-TN/Cr: 1st (U-TN/Cr < 3.35, n = 34), 2nd (3.35 = U-TN/Cr < 7.26, n = 34) and 3rd (7.26 = U-TN/Cr, n = 34) tertiles. In the Kaplan-Meier analysis, cardiac and all-cause mortality progressively increased from the 1st to 2nd and 3rd groups (P < 0.05, respectively). In the Cox proportional hazard analyses, U-TN/Cr was a predictor of cardiac and all-cause mortality in DC patients (P < 0.05, respectively). Urinary Titin-N, a novel marker of sarcomere damage, can identify high risk DC patients.



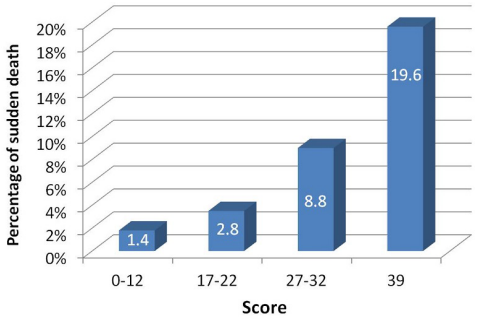
P1698

Sudden death prediction in outpatients with heart failure

P Moliner[1]; J Josep Lupon[1]; G Cediel[1]; M De Antonio[1]; M Domingo[1]; J Nunez[2]; E Zamora[1]; E Santiago[1]; B Gonzalez[1]; C Rivas[1]; V Diaz[1]; J Santesmases[1]; C Diez-Quevedo[1]; M Boldo[1]; A Bayes-Genis[1]
[1]Germans Trias i Pujol University Hospital, Badalona, Spain; *[2]University Hospital Clinic of Valencia, Valencia, Spain*

Background: Although prevalence of sudden death (SD) has declined during last decade in patients with chronic heart failure (HF) its prediction remains a difficult challenge, not only for the diversity of parameters possibly associated with it and the difficulty of selecting the most influent but also the need of threshing from other causes of death, currently more frequent in HF patients.
Purpose: To assess the prevalence of SD at 5 years in a real-life cohort of patients managed according to international guidelines and closely followed and to find a simple prognostic predictive model of SD.
Methods: Competing risk strategy using the Gray method was adopted in Cox regressions analyses, considering non-cardiovascular and other cardiovascular causes of death as the competing event. Statistics-C were also calculated taking into account competitive risk and time-to-event outcome. SD was considered any unexpected death, witnessed or not, occurring in a previously stable patient with no evidence of worsening HF or any other cause of death. Ambulatory patients treated at a multidisciplinary HF unit were consecutively included in the study in an outpatient setting from May 2006 to July 2010. All patients have been followed until death or completion of 5 years of follow-up.
Results: After excluding 27 patients who died from unknown causes 837 consecutive outpatients (72% men, mean age 67.9 ± 12.2 years, LVEF 36% ± 14, 65.6% NYHA class II and 25.9% class III) were included. During follow-up 336 deaths occurred; causes of death were: HF 100 patients, sudden death 43, AMI 18, stroke 10, cardiovascular procedure 8, other cardiovascular 25 and non-cardiovascular 132. Variables associated with SD in univariate analyses were age (p = 0.04), hemoglobin (p = 0.02), eGFR (p = 0.001), HF duration (p = 0.02), hs-TnT (p < 0.001), NTproBNP (p = 0.004) and ST2 (p = 0.001). In a multivariable analysis (backward stepwise) that included all these variables and also other considered clinically relevant such as sex (p = 0.16), NYHA class (p = 0.06), LVEF < 45% (p = 0.07), ischemic etiology (p = 0.18), beta-blocker treatment (p = 0.28), loop diuretic dose (p = 0.08) and ICD (p = 0.38), only HF duration (p = 0.01), eGFR (p = 0.009), LVEF < 45% (p = 0.04) and ST2 (p = 0.005) remained in the model. The obtained model achieved an AUC of 0.75 (0.68-0.82) for the prediction of 5-year risk of SD. The constructed

score including such variables in a dichotomous manner (ST2 >45), LVEF < 45%, HF duration > 3 years and eGFR < 55) obtained an AUC of 0.76 (0.69-0.83).
Conclusions: In a current HF real-life cohort managed according to a structured HF clinic and international recomendations, SD accounted only for the 12% of all deaths at 5 years, affecting only to the 5.1% of the cohort. Of the 3 studied biomarkers, only ST2 remained indepenently associated with SD. A simple model containing ST2, eGFR, LVEF and HF duration allowed to predict the risk of SD at 5 years with an AUC of 0.76.



P1699

Elevated cystatin C predicts higher mortality in chronic heart failure independently of creatinine clearance based on 24h urine collection

P Lourenco[1]; J Pereira[1]; A Ribeiro[1]; P Marques[1]; S Silva[2]; JP Araujo[3]; P Bettencourt[4]
[1]Sao Joao Hospital, Department of Internal Medicine, Porto, Portugal; [2]Hospital CUF, Department of Internal Medicine, Porto, Portugal; [3]Sao Joao Hospital, Department of Internal Medicine - University of Porto Medical School, Porto, Portugal; [4]Hospital CUF, Department of Internal Medicine - University of Porto Medical School, Porto, Portugal

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Background: Cystatin C is a biomarker mainly used to assess kidney function. It can be also used as a prognostic marker in cardiovascular diseases. Its role in acute heart failure (HF) has been widely documented. The prognostic value of cystatin C in chronic HF is less well established with some, but not all, reports suggesting added value beyond estimated glomerular filtration rate.
Purpose: We aimed to assess the prognostic value of Cystatin C in a cohort of real-world chronic stable HF patients taking into consideration the creatinine clearance based on 24h urine.
Methods: We prospectively recruited HF patients followed in a HF clinic. To be eligible patients had to have HF diagnosed for at least 6 months and be under optimized and stable evidence-based therapy. Only patients with ejection fraction < 40% were included in the analysis. Patients were excluded if they were on renal replacement therapy and if they had hospitalizations or therapeutic adjustments in the previous 2 months. Patients' comorbidities and medications in use were recorded; a venous blood sample and 24h urine were collected in all patients. Follow-up was 5 years and all-cause mortality was the outcome under analysis. Cystatin C was measured and creatinine clearance was calculated using (Urinary creatinine x Urinary volume)/(Serum creatinine x 1440). A receiver-operating characteristic curve was used to assess the association of Cystatin C with 5-year mortality. The area under the curve (AUC) was calculated and the best cut-off for death prediction chosen. The prognostic role of cystatin C was determined using a Cox-regression analysis. Multivariate model was built including creatinine clearance based on 24h urine collection.
Results: We studied 215 chronic stable HF patients with ejection fraction < 40%. Mean age was 68 years and 72.1% were male. Median cystatin C 1.15 (0.89-1.54)mg/dL, creatinine 1.20 (1.00-1.50) mg/dL, and creatinine clearance (24h urine) 63.6 (40.6-98.0) ml/min. During the 5-year follow up 103 (47.9%) patients died. The AUC under the ROC curve for cystatin C in predicting mortality was of 0.77 (0.70-0.83), p < 0.001. The best cut-off value for 5-year death prediction was approximately 1.00mg/dL with a Sensitivity of 83.5%, a specificity of 56.2% a 63.7% positive predictive value and a 78.7% negative predictive value. The multivariate-adjusted (age-, BNP-, beta blocker-, ACEi or ARB-, NYHA class- and creatinine clearance-) HR of 5-year mortality was of 2.46 (95% CI: 1.28-4.73), p = 0.007 for patients with cystatin C = 1.00mg/dL.
CONSLUSIONS: Patients with Cystatin C < 1.00mg/dL have an almost 80% probability of being alive at 5 years. Patients with Cystatin C = 1.00mg/dL have almost 2.5-fold higher death risk independently of BNP and creatinine clearance based on 24h urine collection.

P1700

Atrial fibrillation and heart failure: double trouble for hospitalized patients with acute decompensated heart failure

U Kocabas[1]; UY Sinan[2]; E Arugaslan[3]; M Kursun[4]; A Coner[5]; O Ozcan Celebi[6]; C Ozturk[7]; O Dalgic[8]; I Turkoglu[9]; HS Kemal[10]; E Gazi[11]; C Altin[12]; M Zoghi[13]
[1]Soma State Hospital, Department of Cardiology, Manisa, Turkey; [2]Istanbul University Cardiology Institute, Department of Cardiology, Istanbul, Turkey; [3]Marmara University, Department of Cardiology, Istanbul, Turkey; [4]Tepecik Training and Research Hospital, Department of Cardiology, Izmir, Turkey; [5]Baskent University, Medical and Research Center of Alanya, Department of Cardiology, Antalya, Turkey; [6]Turkiye Yuksek Ihtisas Hospital, Department of Cardiology, Ankara, Turkey; [7]Gulhane Military Medical Academy and Faculty, Department of Cardiology, Ankara, Turkey; [8]Karsiyaka State Hospital, Department of Cardiology, Izmir, Turkey; [9]Kemalpasa State Hospital, Department of Cardiology, Izmir, Turkey; [10]Near East University Hospital, Department of Cardiology, Nicosia, Cyprus; [11]Canakkale 18 March University, Department of Cardiology, Canakkale, Turkey; [12]Baskent Univesity, Department of Cardiology, Izmir, Turkey; [13]Ege University, Department of Cardiology, Izmir, Turkey

On behalf of: JOURNEY HF-TR Study Investigators

Background: Atrial fibrillation (AF) is common among patients with acute decompensated heart failure (ADHF).
Purpose: The aim of this study was to determine AF prevalence and impact of AF in patients hospitalized due to ADHF.
Methods: The Journey HF-TR study is a cross-sectional, multicenter and observational trial that was conducted in 37 intensive/coronary care units and cardiology. Patient's demographic and clinical characteristics, clinical history, symptoms and signs and their journey in hospital (using diagnostic methods, laboratory findings, medications, length of stay, mortality) were evaluated. The demographic, clinical and prognostic factors were compared between the patients with and without AF.

	HF with AF	HF without AF	P – value
Age (years)	71 ± 12	65 ± 13	<0.001
Female (%)	51	37.4	<0.001
De novo presentation (%)	15.6	21.3	0.007
NYHA class III – IV (%)	83.4	70.1	<0.001
Hypertension (%)	69.9	64.8	0.048
Diabetes mellitus (%)	37.3	44.7	0.002
Ischemic heart disease (%)	49.9	65.9	<0.001
Cerebrovascular disease (%)	16.6	7.3	<0.001
HFpEF (%)	23.2	11.5	<0.001
Pulmonary hypertension (%)	66.2	47.6	<0.001
Heart rate (bpm)	102 ± 26	88 ± 20	<0.001
LVEF (%)	33.9 ± 16.1	32.0 ± 12.6	0.017
NT-proBNP (pg/ml)	7895 ± 1103	8022 ± 2021	0.918
Length of stay for ICU (days)	4	4	0.405
In-hospital mortality (%)	8.9	6.8	0.069

Table

Results: Among 1604 patients (male 57.2%, mean age 67.8 ± 13 years) with ADHF, 39% had atrial fibrillation. Patients with AF were older (71 vs. 65 years, p < 0.001) and the half of them were female (p < 0.001). The de novo clinical presentation was lower in patients with AF (p = 0.007). Patients with AF were more symptomatic and a greater proportion were NYHA III-IV (p < 0.001) than those without. The prevalence of hypertension, cerebrovascular disease, pulmonary hypertension and heart failure with preserved ejection fraction were higher in AF group (p = 0.04, p < 0.001, p < 0.001, p < 0.001 respectively). However, the ischemic heart disease was more common in patients without AF. Heart valve diseases were more prevalent in AF group (p = 0.007 and p < 0.001, respectively). The rate of the patients who have taken digoxin and diuretic was higher in AF group. Compared to those without AF, patients with AF had a higher mean ventricular rate on admission (102 vs. 88 bpm, p < 0.001). The NT-proBNP levels on admission were similar between patients with and without AF.
Conclusion: Atrial fibrillation was frequent in patients hospitalized with ADHF and they were more likely elderly and female. The concomitant diseases were higher in this group and nearly quarter of patients with AF had a preserved ejection fraction. However the length of hospitalization was similar in patients with and without AF, the in-hospital mortality rate was higher in patients with AF.

P1701

Concerns about the ESC heart failure guidelines

C Claudia Stoellberger[1]; B Schneider[2]
[1]*Rudolfstiftung Hospital, Department of Internal Medicine II, Vienna, Austria*; [2]*Sana Kliniken, Luebeck, Germany*

Background: In 2011, the Institute of Medicine (IOM) published standards for developing trustworthy clinical practice guidelines (CPGs) recommending that "Whenever possible guideline development group members should not have conflicts of interest (COIs)… Members with COIs should represent not more than a minority of the guideline development group members. The chair or cochair should not be a person with COIs."
Purpose: Aim of the study was to assess if the standards of the IOM have influenced the development of the heart failure guidelines of the European Society of Cardiology (ESC).
Methods: From the ESC homepage, the declarations of COIs of task force members (TFM) and reviewers of the 2012 and 2016 guidelines for the diagnosis and treatment of acute and chronic heart failure were retrieved. The number of COIs was assessed for each version of the guideline.
Results: Of the 2012 guidelines, 24 TFMs (92%) indicated any COI (range 1-36). The mean number of direct personal payments was 6.7 per TFM with COIs. Among the TFMs, the chairperson had the 14th most COIs (8). Among the reviewers 32 (84%) indicated any COI (range 1-29). The mean number of direct personal payments was 5.2 per reviewer with COI.
Of the 2016 guidelines, 19 TFMs (90%) indicated any COI (range 1-35). The mean number of direct personal payments was 9.3 per TFM with COI. Among the TFMs, the chairperson had the second most COIs (33) and the co-chairperson the fourth most COIs (21). Among the reviewers 67 (77%) indicated any COI (range 1-31). The mean number of direct personal payments was 5.4 per reviewer with COI.
Conclusion: Despite the recommendations from the IOM, the COIs among TFM and reviewers for heart failure guidelines, especially personal payments, have increased from 2012 to 2016. Additionally, there was an increase in COIs among the chairs and cochairs from 2012 to 2016. Since we are interested in CPGs in whom we can trust, we suggest that the ESC follows the standards of the IOM when developing guidelines including the choice for appropriate experts for the task force and as reviewers.

P1702

The economic burden of heart failure: findings from a systematic literature review

CL Freeman[1]; L Giles[1]; P Field[1]; G Osei-Assibey[2]; E Sorstadius[3]; B Kartman[3]
[1]*PharmaGenesis Oxford Central, Oxford, United Kingdom*; [2]*Oxford PharmaGenesis, Oxford, United Kingdom*; [3]*AstraZeneca Gothenburg, Mölndal, Sweden*

Funding Acknowledgements: Systematic review and medical writing support were provided by PharmaGenesis Oxford Central, Oxford, UK, and funded by AstraZeneca.

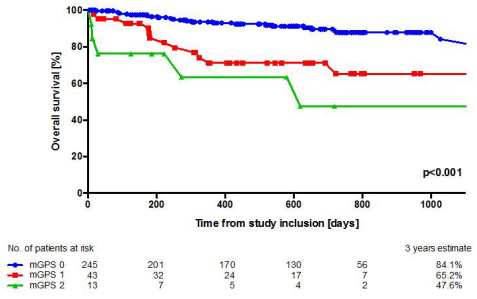
Background: Heart failure (HF) represents a growing economic burden owing to various factors, including the ageing population worldwide and the rising prevalence of cardiovascular disease, diabetes mellitus (DM) and obesity.
Purpose: To assess the impact of HF with preserved, mid-range or reduced ejection fraction on costs and resource use, using findings from a systematic literature review (SLR).
Methods: Electronic databases (Embase, MEDLINE and the Cochrane Library) were searched in May 2017 for observational studies published between 2012 and 2017 reporting costs in 100 patients or more.
Results: In total, 70 papers were identified (Europe: 15; North America: 49; rest of the world/multinational: 6). The total annual costs associated with HF varied widely across studies and geographies owing to differences in study settings and patient populations (n = 208-88 195). In Germany, Spain, and Sweden the annual cost of HF per patient was estimated at 3150 EUR, 6571 EUR and 5700 EUR, respectively. In two Italian studies this cost was 11 864 EUR and 11 100 EUR, respectively. In other countries the annual cost of HF per patient was estimated at 27 809 CAD (Canada) and 28 974 RMB (China), and in the range of 13 897-36 426 USD (USA). Hospitalization and inpatient care were identified as cost drivers in HF, accounting for 48-90% of overall spending in multiple studies. Several US studies, but none in any other region, compared costs for patients with HF with those incurred by individuals without HF, and the results indicated that HF is associated with significant additional expenditure. One of these studies reported that overall total costs were more than four times higher for individuals with HF than for those without HF. A US study compared annual healthcare costs for individuals with HF and those with DM and found that HF was associated with a comparatively higher cost. Another US study reported costs associated with various chronic conditions, and showed that annual costs were higher for HF than for asthma, coronary artery disease, chronic obstructive pulmonary disease, DM, hyperlipidaemia, and hypertension. There was a very limited evidence base for costs of HF relative to disease severity. Only one study, conducted in Japan, reported costs for patients with HF of different NYHA classes; hospitalization costs increased significantly for patients with HF at NYHA class III or IV compared with those at class II.
Conclusions: The evidence identified in this SLR indicates that patients with HF incur considerable health care costs. Inpatient care and hospitalization are key cost drivers in HF, contributing up to 90% of total costs in some studies. Furthermore, HF is associated with higher costs compared with both individuals without HF and those with other chronic diseases. Limited evidence indicates that hospitalization costs are likely to be higher in patients with more severe HF than in those at earlier disease stages.

P1703

The inflammation based prognostic score mGPS predicts survival in stable heart failure patients.

A Anna Cho[1]; N Pavo[1]; H Arfsten[1]; G Goliasch[1]; PE Bartko[1]; R Wurm[1]; G Strunk[1]; M Huelsmann[1]
[1]*Medical University of Vienna, Vienna, Austria*

Background: The progression of heart failure is presumed to be linked to inflammatory host response. The combination of the inflammatory markers albumin and C-reactive protein (CRP), termed modified Glasgow Prognostic Score (mGPS), has been derived from cancer patients and validated in multiple cohorts. This study aimed to investigate the impact of the easily available mGPS on survival of stable patients with heart failure with reduced ejection fraction (HFrEF).
Methods: HFrEF patients under routine ambulatory care at the heart failure unit of the Medical University of Vienna between January 2011 and November 2017 were retrospectively identified. Comorbidities and laboratory data at baseline were assessed. All-cause mortality was defined as the primary study endpoint. The mGPS score and its impact on overall survival were determined.
Results: Data was complete and analyzed for a total of 301 patients. The mGPS score was 0 for 245 (81%), 1 for 43 (14%) and 2 for 13 (4%) patients, respectively. The three groups showed significant differences in other routine laboratory parameters associated with survival, especially NT-proBNP [1895pg/ml (IQR 834-3462) vs. 3852pg/ml (IQR 2312-7232) vs. 9935pg/ml (IQR 4082-19821) for mGPS score 0, 1 and 2 respectively; $p < 0.001$]. In the Cox regression analysis, increasing mGPS was associated with adverse outcome in the univariate analysis [crude HR 2.43 (95%CI 1.60-3.69), $p < 0.001$] and after adjustment for age and NT-proBNP [adj. HR 1.79 (95%CI 1.02-3.12), $p = 0.042$]. Kaplan-Meier analysis confirmed the high discriminatory power of the mGPS score ($p < 0.001$) (Figure1).
Conclusions: The inflammation based score mGPS predicts survival in HFrEF patients. The association underlines the age independent impact of the inflammatory response in heart failure. Inflammatory response appears to be most relevant in patients with advanced heart failure.



P1704

Left ventricular ejection fraction and prognosis in chronic heart failure

A Alberto Aimo[1]; JL Januzzi[2]; G Vergaro[3]; V Siciliano[4]; S Molinaro[4]; C Passino[1]; M Emdin[1]
[1]*Sant'Anna School of Advanced Studies, Pisa, Italy*; [2]*Massachusetts General Hospital, Boston, United States of America*; [3]*Gabriele Monasterio Foundation, Pisa, Italy*; [4]*Institute of Clinical Physiology, CNR, Pisa, Italy*

Background: The recent introduction of a new heart failure (HF) category defined by a left ventricular ejection fraction (LVEF) interval (40-49%) has attracted great criticism, and led to a reappraisal of the meaning of LVEF in HF. The prognostic value

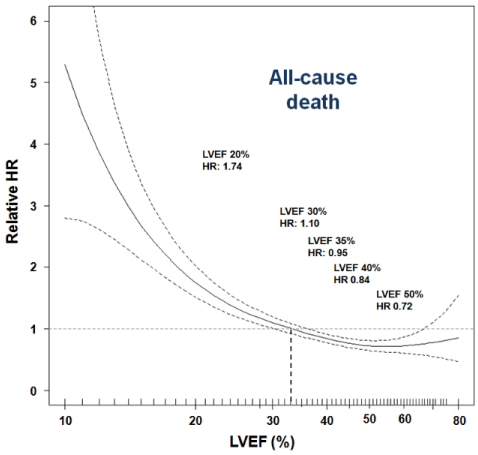
of LVEF and LVEF-based patient categorization has been basically overlooked in this debate.

Methods: Data from patients with stable chronic HF assessed at a tertiary referral center from 1999 to 2017 were analyzed. Baseline characterization and follow-up were considered. The endpoints were all-cause and cardiovascular death.

Results: 2583 patients were evaluated (69 ± 12 years, 70% men, LVEF < 50% in 84% of patients). Over 3.2 years (interquartile interval 1.3-6.7), all-cause death occurred in 872 patients (34%), and cardiovascular death in 513 (20%). Patients with LVEF < 50% had shorter survival than those with = 50% (all-cause death: log-rank 17.9, p < 0.001; cardiovascular death: log-rank 42.1, p < 0.001), because of patients with LVEF < 40% (n = 1539).

In the LVEF < 50% subgroup, LVEF retained an independent association with both all-cause and cardiovascular death. The 35% cut-off displayed a more balanced combination of sensitivity and specificity than the 40% cut-off. At spline curve analysis, considering the whole LVEF spectrum, the risk of death increased slowly with decreasing LVEF until 35%, which was very close to the inflection points of the curves (33% for all-cause death, and between 35 and 36% for cardiovascular death). Patients with very severe depression of systolic function (LVEF < 20%) had a particularly high risk for all-cause and cardiovascular death, though representing only a small minority of patients (n = 122, 5%). This accounted for the prognostic relevance of higher LVEF cut-offs, including 40%.

Conclusions: Patients with chronic HF and LVEF = 50% have worse prognosis than those with LVEF < 50%, although the risk increases gradually until LVEF values around 35%. In systolic HF, defined as LVEF < 50%, LVEF is an independent predictor of all-cause and cardiovascular mortality. The 40% LVEF cut-off has independent prognostic significance, which is driven mostly by patients with severely depressed systolic function. For this reason, lower LVEF cut-offs, such as 35%, display a better combination of sensitivity and specificity than 40% for risk stratification.



P1705

Long-term clinical impact of permanent pacemaker after Transcatheter Aortic Valve Replacement

E Munoz-Garcia[1]; M Munoz-Garcia[1]; A J Antonio Jesus Munoz Garcia[1]; A Ruiz-Salas[1]; A Barrera-Cordero[1]; JM Garcia-Pinilla[1]; JH Alonso-Briales[1]; JM Hernandez-Garcia[1]; MF Jimenez-Navarro[1]; E De Teresa-Galvan[1]
[1]*University Hospital Virgen de la Victoria, Department of Cardiology, Malaga, Spain*

Very few data exist on the clinical impact of permanent pacemaker implantation (PPI) after Transcatheter Aortic Valve Replacement (TAVR) at the long-term follow-up. The aim of this study was to assess the impact of PPI after TAVR on late outcomes in a large cohort of patients in terms of all-cause mortality and morbidity.

Methods and Results: A total of 561 consecutive patients without prior PPI undergoing transcatheter aortic valve replacement were included. Of them, 145 patients (25.8%) required a PPI within the first 30 days after TAVR, median time 2 days (1.9-2.4 days) and 16 patients required a PPI in the follow-up. At a mean follow-up of 37 ± 25 months, there was a tend more mortality in patients with PPI (42.1% vs. 34.4% p= 0.061), but no association was observed between the need for PPI and all-cause mortality (hazard ratio, 1.385; 95% confidence interval, 0.940-2.041; P = 0.100), cardiovascular mortality (hazard ratio, 1.122; 95% confidence interval, 0.466-2.699; P = 0.797), and it was associated with more rehospitalisation for heart failure (hazard ratio, 2.352; 95% confidence interval, 1.172-4.718; P = 0.016).

There were 8 cases of unexpected (sudden or unknown) death and was observed in 7 patients without PPI. Patients with new PPI showed a poorer evolution of left ventricular ejection fraction over time. Mean left ventricular ejection fraction increased from 59.6 ± 14 % to 62.7 ± 11% after TAVI and decreased to 60.9 ± 10% at 1 years and 59.7 ± 6 at 4 years (p for post-TAVI trend 0.04).

Conclusions: The need for PPI was a frequent complication of TAVR and it was associated with increased admission for heart failure, A new PPI did have a little negative effect on left ventricular function over time. However, but not associated with any increase in overall or cardiovascular death, a mean follow-up of 3.06 years.

P1706

Evolution of mortality and mode of death in chronic heart failure outpatients

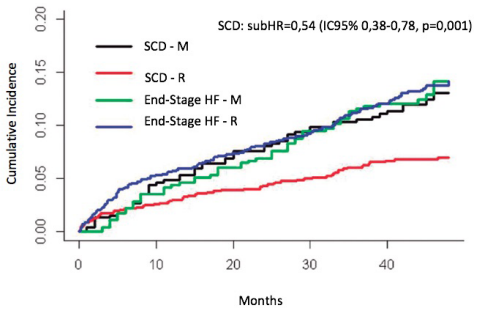
D David Fernandez Vazquez[1]; E Cabrera Romero[1]; DJ Vazquez Andres[1]; A Ferrero-Gregori[2]; I Gomez-Otero[3]; R Vazquez[4]; J Delgado Jimenez[5]; J Alvarez-Garcia[2]; F Worner Diz[6]; A Badarji[7]; P Garcia-Pavia[8]; JR Gonzalez-Juanatey[3]; J Cinca[2]; D Pascual Figal[1]
[1]*Hospital Clínico Univeristario Virgen de la Arrixaca, Servicio de Cardiología, Murcia, Spain*; [2]*Hospital de la Santa Creu i Sant Pau, Servicio de Cardiologia, Barcelona, Spain*; [3]*University Hospital of Santiago de Compostela, Servicio de Cardiologia, Santiago de Compostela, Spain*; [4]*University Hospital Puerta del Mar, Servicio de Cardiologia, Cadiz, Spain*; [5]*University Hospital 12 de Octubre, Servicio de Cardiologia, Madrid, Spain*; [6]*Hospital Arnau de Vilanova, Servicio de Cardiologia, Lleida, Spain*; [7]*Hospital Universitario Joan XXIII, Servicio de Cardiologia, Tarragona, Spain*; [8]*University Hospital Puerta de Hierro Majadahonda, Servicio de Cardiologia, Madrid, Spain*

On behalf of: MUSIC and REDINSCOR I research groups

Introduction: Optimal medical therapy (OMT) and the use of implantable cardioverter-defibrillator (ICD) had improved global survival of patients with heart failure (HF) with reduced ejection fraction. Nevertheless, there are few data available regarding the evolution of mortality before and after the implementation of these therapies. MUSIC register (2004-2004) studied HF outpatients before widespread use of ICD as prevention of sudden cardiac death (SCD) and OMT. On the other hand, REDINSCOR register (2007-2011) has a OMT and ICD rate similar to nowadays.

Purpose: To describe variations in cumulative incidence of death and its causes related to implementation of ICD therapy and medical treatment.

METHODS. Retrospective study of clinical, analytical and imaging variables of 2307 patients with < 45% ejection fraction (EF) and NYHA Class II/III taken out of the MUSIC and REDINSCOR registers. Mortality and way of death analysis by using cumulative incidence curves.



Cumulative incidence function for EF < 35%

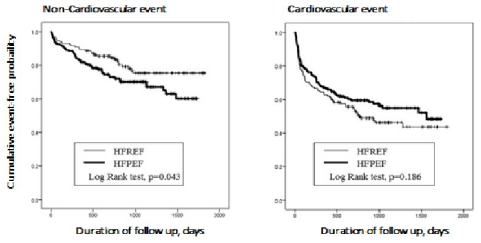
Results: There were no significant differences between both cohorts in age (64 ± 11 vs. 64 ± 12 years, p = NS), male gender (77% vs. 77%, p = NS), previous myocardial infraction (47% vs 43%; p = NS), atrial fibrillation (17% vs 18%; p = NS) or dilated cardiomyopathy (26% vs 24%; p = NS). However, patients from REDINSCOR register had a significant higher prevalence in hypertension (52% vs 63%; p < 0.001), diabetes (36% vs 42%; p = 0.012), mitral regurgitation III-IV (13% vs 20%; p < 0.001), higher levels of N-terminal pro-B type natriuretic peptide (median 921 vs. 1809 pg/mL; p < 0.001) as well as worse functional status (NYHA III) (23% vs 48%; p < 0.001). In spite of, patients from REDINSCOR register had a significant higher rate of ICD (1.6% vs 20.2%; p < 0.001) and use of angiotensin-converting enzyme inhibitors or angiotensin receptor blockers (90% vs 100%; p < 0.001), beta-blockers (71% vs 86%; p < 0.001) and mineralocorticoid receptor antagonists (43% vs 63%; p < 0.001). After 48 months follow-up, there were no significant differences in total mortality (28% vs 27 %; p = NS). We analyzed mortality causes and found a significant decrease in sudden cardiac death (SCD) in REDINSCOR cohort (10.6% vs 6.3%; p < 0.001), without significant differences in end-stage heart failure death (10.1% vs 11.5%; p = NS). Cumulative incidence curves showed a decrease in SCD

for REDINSCOR group without differences in end-stage heart failure death. In the sub-group analysis, patients with < 35% EF show a significant decrease in SCD (13.1 vs 7.0%; p < 0.001) without changes in end-stage heart failure death (14.1 vs 14.2%; p = 0.79) (Fig. 1). Besides, we found similar results in the sub-group analysis by NYHA Class.
CONCLUSIONS: Optimal medical therapy and ICD had shown a decrease in sudden cardiac death in patients with heart failure with reduced ejection fraction, while not having implication in avoiding disease progression.

P1707
Difference in pattern of mortality between heart failure with reduced ejection fraction and heart failure with preserved ejection fraction after hospitalization for acute decompensated heart failure

M Mitsutaka Nakashima[1]; S Sakuragi[1]
[1]*Iwakuni Clinical Center, Cardiology, Iwakuni, Japan*

Background/Introduction : Prevalence of heart failure (HF) is increasing rapidly in the community. HF with preserved ejection fraction (HFpEF) currently represents almost one-half of all HF patients. It is still unknown whether long term prognosis is different between HFpEF and heart failure with reduced ejection fraction (HFrEF).
Purpose: In this study, we investigated the difference in clinical features and pattern of mortality between HFpEF and HFrEF.
Methods: Two hundred and ninety-seven patients with acute decompensated HF were enrolled (158 males, 76 years). Patients were classified into two groups according to LVEF: HFrEF (LVEF <50%, n = 165) and HFpEF (LVEF ?50%, n = 132). We followed cardiovascular event, such as cardiovascular death, coronary artery disease, heart failure and stroke and non-cardiovascular event. Clinical outcomes were compared between the two groups.
Results: HEpEF had higher age, higher proportion of female. Prevalence of non-cardiac comorbidities, such as anemia and pulmonary dysfunction, were significantly higher in HEpEF. With regards to long term mortality, the incidence of non-cardiovascular events was significantly higher in HFpEF group (p = 0.043), whereas incidence of all cardiovascular event (p = 0.186) as well as heart failure admission (p = 0.234) were comparable between the two group. In Cox regression analysis, HFpEF was associated with higher incidence of non-cardiovascular event compared with HFrEF after adjustment for confounding factors, including age, gender, and cardiovascular risk factors (HR 1.648, 95%CI 1.009, 2.691, p = 0.046).
Conclusion(s): HFpEF tend to be associated with non-cardiovascular event more than HFrEF.



long term events

P1708
Disparate risk for heart failure in immigrants compared to residents Results from the STAAB cohort study

C Morbach[1]; G Gelbrich[2]; T Tiffe[2]; F Eichner[2]; M Breunig[1]; M Wagner[2]; PU Heuschmann[2]; S Stoerk[1]
[1]*University Hospital Wuerzburg, Comprehensive Heart Failure Center and Dept. of Medicine I, Wuerzburg, Germany*; [2]*University of Wuerzburg, Institute of Clinical Epidemiology and Biometry and Comprehensive Heart Failure Center, Wuerzburg, Germany*

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Introduction: About 20% of the German population are immigrants. Different cultural backgrounds may influence health/health behaviour, and health status can be affected by a migration background.
Purpose: We here compare the profile of risk factors for heart failure (HF) in immigrants against German residents.
Methods: We report data of a planned interim analysis of the prospective Characteristics and Course of Heart Failure Stages A-B and Determinants of Progression (STAAB) cohort study investigating a representative sample of inhabitants of the City of Würzburg, Germany, aged 30 to 79 years, free of self-reported HF. Residents: individuals speaking German as native language, who had no other native language and/or were born in Germany. Immigrants: non-residents. Risk factors for HF were hypertension, obesity, atherosclerotic disease, diabetes mellitus, and metabolic syndrome, defined according to current guidelines. Differences between groups were adjusted for age and sex, and reported as odds ratio (OR) with 95% confidence interval (CI). If p < 0.05, mean effects were displayed separately for subgroups (EU vs Russia vs other countries).
Results: Of 2,473 subjects, 291 (12%) were immigrants, 2,168 (88%) were residents, and 14 did not provide this information. The origin of 107 (37%) immigrants was from an EU country, 117 (40%) from Russia, 67 (23%) from another country. Of both immigrants and residents, 51% were female, but immigrants were younger: mean age 51 ± 11 vs. 55 ± 12 years, p < 0.001. Risk factors of residents and immigrants (table) were similar with respect to hypertension, atherosclerotic disease, and diabetes mellitus, and also smoking and alcohol consumption (data not shown). By contrast, prevalence of obesity and metabolic syndrome was significantly higher in immigrants.
Conclusion: Immigrants exhibited a higher risk factor burden predisposing to accelerated development of HF compared to residents. Differences were predominantly carried by higher frequency of obesity and metabolic syndrome with the least favourable profile apparent in immigrants from Russia. Strategies for primary prevention of HF may benefit from deliberately considering the migration background.

Risk factors for heart failure

Risk factor - n (%)	Residents	Immigrants	OR (95% CI)	EU	Russia	OC
Hypertension	995 (46)	121 (42)	1.2 (0.9-1.5)			
Atherosclerotic disease	149 (7)	19 (7)	1.3 (0.8-2.2)			
Diabetes mellitus	214 (10)	24 (8)	1.1 (0.7-1.7)			
Obesity	413 (19)	70 (24)	1.5 (1.1-2.1)	1.6	2.2*	0.6
Metabolic syndrome	401 (18)	61 (21)	1.5 (1.1-2.0)	1.2	1.7*	1.5

* p = 0.05 compared with residents. EU= European Union, OC= other country

P1709
The prognostic power of cardiopulmonary exercise testing in patients with Chagas heart disease

P Pedro Schwartzmann[1]; HT Moreira[1]; D Mayumi[1]; JC Crescencio[1]; LFL Oliveira[1]; EEV Carvalho[2]; R Arena[3]; A Schmidt[1]; LFL Gallo-Junior[1]; MV Simoes[1]
[1]*Medical School of Ribeirao Preto, University of Sao Paulo, Internal Medicine, Ribeirao Preto, Brazil*; [2]*Uberaba's University, Uberaba, Brazil*; [3]*University of Illinois at Chicago, Physical Therapy, Chicago, United States of America*

Introduction: Cardiopulmonary exercise testing (CPX) has demonstrated a strong prognostic value in patients with ischemic and non-ischemic heart failure (HF). Increased minute ventilation/carbon dioxide production (VE/VCO2) slope, presence of exercise oscillatory ventilation (EOV), and low peak oxygen consumption (VO2) are markers of adverse outcomes in patients with HF. However, the prognostic role of these CPX-derived parameters in patients with Chagas disease is unknown.
Purpose: We aimed to examine the prognostic performance of CPX in a cohort of patients with Chagas heart disease.
Methods: This longitudinal retrospective study included 93 patients with Chagas disease and HF who underwent a symptom-limited CPX. The patients were classified according to VO2: >18, between 10-18 and < 10 mlO2.kg-1.min-1; according to EOV: presence or absence; and according to VE/VCO2 slope < 35 and = 35. The primary outcome was a composite of cardiovascular death or heart transplantation. Survival analysis was performed using Kaplan-Meier curves, log-rank test, and Cox regression analysis. Age, sex and left ventricular ejection fraction (LVEF) were included in the multivariable model. Harrell's C statistics was used to verify discrimination of risk prediction models. P < 0.05 was considered significant.
Results: Mean age was 56 ± 14 years, 51 (55%) were men, with mean LVEF of 43 ± 18. NYHA functional class I, II, III and IV were detected in 39% 29% 29% and 3% of the participants, respectively. Mean VE/VCO2 slope and mean VO2 were 36 ± 11 and 16 ± 6 mlO2.kg-1.min-1, respectively. EOV was present in 11 (12%) patients. During a follow-up of 1.87 ± 1.32 years, 30 events of interest (26 cardiovascular deaths and 4 heart transplants) were recorded. In the univariate analysis, all the CPX-derived parameters studied were predictors of the combined outcome (logrank p < 0.001 for both VO2 and VE/VCO2 slope, and logrank p = 0.030 for EOV), figure 1. In the multivariable analysis, VO2 < 10 mlO2.kg-1.min-1 and presence of EOV were associated with the combined outcome independently

of age, sex and LVEF (Hazard Ratio [HR] = 5.72; 95% confidence interval [95%CI] = 1.17-27.76, p = 0.03, and HR = 3.32, 95%CI = 1.35-8.15, p = 0,009, respectively).

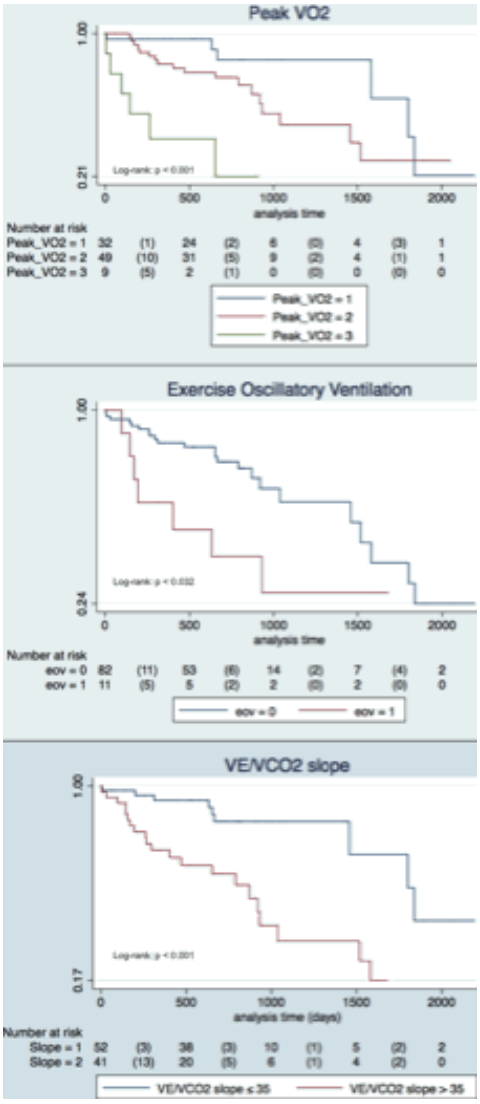


Figure 1

No association of VE/VCO2 slope and the combined outcome in the multivariable analysis was found. Harrell's C statistics of the VO2 adjusted model and of the EOV adjusted model were 0.815 and 0.819, respectively.
Conclusion: In a cohort of patients with Chagas heart disease, CPX demonstrated prognostic power for cardiovascular death and heart transplant. Lower VO2 and the presence of EOV showed prognostic value independently of sex, age or LVEF.

P1710

Clinical value of the Geriatric Nutritional Risk Index in Patients Aged >80 Years With heart failure with preserved ejection fraction

Y Mitsuke[1]; Y Suzuki[1]; N Ootsuki[1]; H Tsutani[1]
[1]NHO Awara Hospital, Fukui, Japan

Background: Malnutrition has been identified as an important predictor of poor clinical outcomes in patients with heart failure with preserved ejection fraction (HFpEF). The clinical significance of nutritional risk assessment in HFpEF patients aged >80 years is less well defined.
Methods: We studied consecutive 122 Japanese HFpEF patients (58 males, older than 80 years of age (84.1 +/- 3.2 years) who were hospitalized with HFpEF at the authors' institution. The impact of nutrition, assessed using Geriatric Nutritional Risk Index (GNRI) on admission was calculated as follows:14.89 × serum albumin (g/dl) + 41.7 × body mass index/22. None had evidence of unstable angina, chronic inflammatory disease, collagen disease, or cancer at the time of evaluation. Patients were followed up for an average of 24.1 months, and 23 of 122 patients had all death.
Results: Patients in the low-GNRI group (GNRI < 92) had higher cystatin C, interleukin-6, and B-type natriuretic peptide (BNP), noradrenalin, and uric acid compared to those in the high-GNRI (GNRI = 92) group (P < 0.05, respectively). By multivariate Cox proportional hazard analysis, GNRI, cystatin C, and IL-6 were significant predictors for all death in those patients.
Conclusions: These findings indicate that GNRI measurement provides additional prognostic information in those elderly patients with HFpEF.

P1711

The prognostic value of B-natriuretic peptide is more evident in first diagnosed Acute Coronary Syndrome patients, with heart failure and preserved ejection fraction, irrespectively of renal function;

C Christina Chrysohoou[1]; H Kosyfa[1]; M Kouvari[2]; G Georgiopoulos[1]; P Aggelopoulos[1]; G Metallinos[1]; C Pitsavos[1]; D Tousoulis[1]
[1]University of Athens, Athens, Greece; [2]Harokopio University, Nutrition Science - Dietetics, Athens, Greece

Background/Introduction: The prognosis stratification in case of heart failure management remains a challenge, despite the undeniable advances performed in the interpretation of the pathophysiology behind this chronic disease. Among the predictors of much interest renal function and B-natriuretic peptide (BNP) are on the short list.
Purpose: the role of glomerular filtration rate (GFR) and BNP on the 10y ACS mortality of coronary patients with heart failure was evaluated.
Methods: from May 2006 to March 2009, 1,000 consecutive patients who were hospitalized at a Cardiologic Clinic in Athens with ACS diagnosis were enrolled in the study. In 2016, the 10y follow-up (2006-2016) was performed in 745 participants. GFR was evaluated through the MDRD formula. Heart failure phenotype was defined according to baseline ejection fraction (EF); heart failure with reduced EF (i.e. <40%) (HFrEF), preserved EF (i.e = 50%) (HFpEF) and mid range EF (i.e. 40-49%) (HFmrEF).
Results: 10y ACS incidence was 55% with fatal events being 21%. Patients who suffered from a new fatal episode within the decade had significantly lower GFR and higher BNP values at baseline, compared with their alive counterparts (all ps <0.001). In multivariate logistic regression analysis, GFR remained an independent predictor for the 10y ACS event, after adjusting for potential confounders (OR = 0.98 95%CI (0.97, 1.00), p = 0.04). Moreover, since BNP levels were strongly associated with both the primary outcome and the GFR (p <0.001 from Spearman's correlation test), BNP was forced included in the multivariable model as a covariate with potential mediating effect. After adjusting for baseline BNP, GFR lost its significance whilst BNP levels (expressed per 2 fold increase) independently predicted ACS mortality (OR = 1.39 95%CI (1.15, 1.67), p = 0.001). What is more significant interactions of BNP with EF and baseline ACS history on the tested outcome were highlighted (p for interaction = 0.002 and p for interaction <0.001, respectively). In analysis with HF phenotype as strata, the aforementioned significant predictive value of BNP retained only in HFmrEF (OR = 1.43 95%CI (1.01, 2.03), p = 0.04) and in HFpEF (OR = 1.80 95%CI (1.15, 2.82), p = 0.01). Additionally, in case of baseline ACS history, subgroup analysis revealed a similar outcome only in first diagnosed ACS patients OR = 1.53 95%CI (1.21, 1.94), p <0.001).
Conclusion: BNP level was highlighted as a significant predictor in long term prognosis of coronary patients with heart failure, namely in case of first diagnosed ACS patients and most importantly, in those subjects with preserved performance of left ventricle.

P1712

Implementation of diagnostic strategy for heart failure in frail elderly with reduced exercise tolerance or shortness of breath

F H Frans Hendrik Rutten[1]; Y Van Mourik[1]; LCM Bertens[2]; MJM Cramer[3]; JWJ Lammers[4]; A Gohar[1]; JB Reitsma[1]; KG Moons[1]; AW Hoes[1]
[1]University Medical Center Utrecht, Julius Centre for Health Sciences and Primary Care, Utrecht, Netherlands; [2]Erasmus Medical Center, Rotterdam, Netherlands; [3]University Medical Center Utrecht, Cardiology, Utrecht, Netherlands; [4]University Medical Center Utrecht, Pulmonology, Utrecht, Netherlands

On behalf of: Utrecht Heart Failure Organization
Funding Acknowledgements: Research grant from the "Netherlands Organization for Health Research and Development" (ZonMw grant 311040302).

Background: Heart failure often remains undiagnosed in older individuals, while it inhibits functionality and impair health. We wanted to assess the effectiveness of a case-finding strategy.

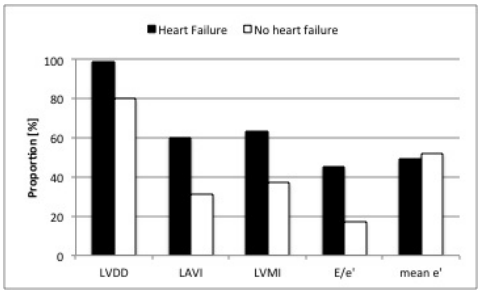
Methods: A cluster randomized trial with general practices randomly allocated to a case-finding strategy or usual care. Frail (pragmatically defined by the number of comorbidities and drugs prescribed) community-dwelling subjects aged 65 years or over with shortness of breath or reduced exercise tolerance were eligible for inclusion. The case-finding strategy consisted of history taking, physical examination, blood tests, electrocardiography, spirometry and echocardiography. Subsequent treatment decisions were at the discretion of the general practitioner. Outcomes: Changes in medication and health care use during the six months follow-up.
Results: In total, 18 general practices were randomized resulting in 829 participants; 389 in the screening strategy group (8 practices) and 440 in the usual care group (10 practices). More patients in the screening group received a new diagnosis of heart failure than the usual care group (cumulative incidence 34% vs. 2%, respectively). After six months of follow-up, the scores for health status, functionality, and health care use were similar between the two strategies.
Conclusion: A screening strategy applied in primary care to frail older people with shortness of breath or reduced exercise tolerance resulted in a number of new diagnoses of heart failure, but did not result in short-term improvement of health status compared to usual care.

P1713

Left ventricular dysfunction and heart failure in general population

M Lainscak[1]; A Zupan Meznar[2]; D Crncic[1]; I Nikolajevic[1]; D Omersa[3]; J Farkas[1]
[1]General Hospital Murska Sobota, Murska Sobota, Slovenia; *[2]General Hospital Celje, Celje, Slovenia*; *[3]General Hospital Jesenice, Jesenice, Slovenia*

Background: Heart failure (HF) prevalence in general population is estimated at 1-2% with about even distribution between reduced and preserved left ventricular systolic function. According to 2016 European Society of Cardiology guidelines, evidence of left ventricular diastolic dysfunction is needed for diagnosis of HF with mid regional or preserved ejection fraction. To best of our knowledge, there are no studies to investigate left ventricular dysfunction and heart failure in general population.



Left ventricular diastolic dysfunction

Purpose: To investigate prevalence and characteristics of left ventricular dysfunction in general population with emphasis on left ventricular diastolic dysfunction.
Methods: The Screening Of adult urBan pOpulation To diAgnose Heart Failure (SOBOTA-HF) study is an ongoing cross sectional epidemiological study in Murska Sobota city residents aged 55 years or more. This interim report presents data for 702 participants of NT-proBNP screening; those with concentration = 125 pg/mL were invited for a detailed diagnostic visit that included echocardiography. HF diagnosis and left ventricular dysfunction were evaluated according to 2016 European Society of Cardiology guidelines.
Results: Overall, 339 participants completed diagnostic visit (age 70 ± 8 years, 35% men, NTproBNP 481 ± 936 pg/mL) and 92 were diagnosed with HF. Left ventricular diastolic dysfunction was detected in 289 participants and prevalence was higher in HF (99% vs 80%). Most HF patients met two criteria (37%), followed by three (34%), single (24%) and all four criteria (4%). More patients with HF also met individual criteria for left ventricular diastolic dysfunction except for mean e' septal and lateral wall (Figure). Presence of left ventricular diastolic dysfunction did not correlate with age, gender or NT-proBNP.
Conclusions: Left ventricular diastolic dysfunction is common in general population aged 55 years or more and is present in almost all patients with HF.

P1714

Clinical PrOfile, ManagemEnt and In-Hospital Outcome of Patients AdmittEd with Acute Heart Failure Syndromes (COME HOPE HF)

N W Neil Wayne Salces[1]; A Junia[1]; E Gallardo[1]; L Noval[1]
[1]Chong Hua Hospital - Heart Institute, Section of Adult Cardiology, Department of Internal Medicine, Cebu City, Philippines

Background: Acute heart failure syndrome usually results in hospitalization and this has become a costly global health care epidemic that carries a high burden of morbidity and mortality. There is no national database on heart failure.
Purpose: This study aims to describe the heart institute's epidemiology of acute heart failure syndromes (AHFS) for a period of one year.
METHODOLOGY: This is a retrospective cross-sectional chart review study design.
Results: A total of 140 patients were identified from the hospital's database with a final diagnosis of heart failure based on the ICD 10 classification. Eighty four (84) patients with acute heart failure syndromes were included in the final analysis. The mean age of patients with AHFS was 66 years (range, 32-91 years old), and over one-half of the population were males (64%). Hypertension was most commonly seen in these patients in 70%. At presentation, 37% were hypertensive (SBP >140 mm Hg) and the mean blood pressure was 139/80 mmHg. Blood urea nitrogen, natriuretic peptides, and troponins were underutilized. Overall, 95% of patients were receiving diuretics, 56% on ACEi or ARB and 49% on beta blockers. Heart failure patients with reduced ejection fraction are seen in majority of cases (58%). There was no significant difference with the in-hospital outcome of patients in both groups in terms of the length of hospital stay and all-cause mortality. Male sex ($p = 0.011$), prior history of heart failure ($p = 0.001$) and the use of RAS inhibitors ($p = 0.034$) and aldosterone antagonists ($p = 0.002$) were associated with HFrEF while female sex ($p = 0.011$) and the use of CCBs ($p = 0.002$) were associated with HFpEF.
Conclusions: In Chong Hua Hospital, acute heart failure syndromes were commonly seen in the elderly males who are hypertensive. They were usually normotensive on clinical presentation. Diuretics, renin-angiotensin system (RAS) inhibitors and beta-blockers were most commonly used during the hospital phase. Majority of heart failure patients had reduced ejection fraction.

P1715

Quality of life and mortality on 1 year follow up in Manipal Heart Failure Registry [MHFR]

A Singh[1]; T Devasia[1]; H Kareem[1]; YR Karkala[2]; S Chauhan[2]; PN Shetty[1]; S Rao[1]
[1]Kasturba Medical College and Hospital, Cardiology, Manipal, India; *[2]Melaka Manipal Medical College, Pharmacology, Manipal, India*

Background/Introduction: Health-related quality of life in heart failure (HF) patients is an imperative indicator of mortality and re-admissions. Treatment policies are targeted to improve the quality of life. There are various parameters to know the physical and psychological condition of the HF patients.
Purpose: To assess the health-related quality of life in HF patients and to study 1-year mortality and re-admissions
Methods: The Manipal Heart Failure Registry (MHFR) study is an observational cohort study. It analyses the health-related quality of life (secondary objective) for recruited patients. The patient's data is collected on admission, discharge and at 1 month, 6 month and 12 month follow up. Mobility, self-care, routine activities, pain and anxiety, were the different parameters analysed to assess the quality of life.
Results: A total of 532 patients were studied. The mean age was 59 years and 61% were male. In-hospital mortality was 9.02% during an average of 5.2 days hospitalization. One month, 6 month and 12-month mortality were 4.9%, 13.2% and 16.9% respectively. HF with preserved ejection fraction (HFpEF), HF with mid-range ejection fraction (HFmid-rangeEF) and HF with reduced ejection fraction (HFrEF) was diagnosed in 17%, 28% and 55% patients respectively.
The incremental changes in quality related parameters after index hospitalization show the therapeutic success. Significant decrement compared to 1 month follow up was seen at 6 month and 12 month follows up. A score of wellness was calculated. There was clinical and statistical significance at admission and discharge. Mean wellness score at index admission, discharge, 1 month, 6 month and 12 month follow-up were 53.5%, 83.2%, 78.8%, 74.3% and 70.1% respectively. Wellness score < 50% at admission was significantly associated with in-hospital and 12-month mortality. Wellness score < 50% at discharge was significantly associated with 1 month and 6 month mortality and frequent re-admissions. Factors contributing to decreased mobility, self-care and barrier in usual activities were also analysed. Psychological status improved after extensive counselling and treatment; though it did not decrease at different follow up.
Conclusion(s): The decrement in wellness score is significantly associated with mortality and can be used as an indicator for aggressive HF management and frequent monitoring.
MHFR Clinical Trials Registry of India no.: CTRI/2017/11/010395
MHFR NIH clinical trial no.:- NCT03157219

P1716

Improved heart failure awareness over a period of three years in an European population

V Vlad Damian Vintila[1]; A Vintila[2]; M Cinteza[1]; M Lainscak[3]; S Stork[4]; D Vinereanu[1]
[1]*University of Medicine and Pharmacy Carol Davila, University and Emergency Hospital Bucharest, Cardiology Department, Bucharest, Romania*; [2]*University of Medicine and Pharmacy Carol Davila, Coltea Clinical Hospital, Internal Medicine Department, Bucharest, Romania*; [3]*Faculty of Medicine, University of Ljubljana, , General Hospital Murska Sobota, Murska Sobota, Slovenia*; [4]*Comprehensive Heart Failure Center (CHFC), University of Wurzburg, Wurzburg, Germany*

Background: Heart failure (HF) is a common pathological condition with high impact on prognosis. The objective of the HF Awareness Day, which represents an European annual event, is to increase the knowledge and awareness regarding this condition, using various educational approaches.
Aim. To demonstrate that exposure to general medical information and a better access to this information over time improve awareness of HF, irrespective of specific medical or personal experience to disease.
Method: We compared two cohorts of subjects (200 and 221 respectively) who were questioned about HF using the standard awareness questionnaires approved by the specific Working group of the European Society of Cardiology. Data from 2013 & 2016 campaigns were used. A score of awareness was computed and measured for each cohort.
Results: The global awareness score between the two years improved significantly from 4.7+/- 3.9 to 6.0 +/- 3.4 ($p < 0.001$). This was achieved by similar populations in relation to professional exposure (3.6 vs.7.2%, p = NS). The clinical picture was better presented in the latter cohort, tiredness (39.0 vs 79.6%, $p < 0.001$), weight gain (6.5 vs. 18.1%, $p < 0.0001$) and shortness of breath (45.0 vs. 55.7%, $p = 0.029$)being reported as most frequent presentation for HF. Depression (13 vs 34.9% $p = 0.002$) and memory disturbances (10.5 vs. 25.8%, $p < 0.001$) were reported as worsening conditions for HF. In terms of treatment a better recognition for diet (24.0 vs. 43.4%, $p < 0.001$), sport (20.0 vs. 38.5% $p < 0.001$) and pharmacotherapy (47.0 vs. 57.0% $p = 0.004$) was noted.
Conclusions: A better exposure of general population to general medical information improves both the knowledge and treatment of heart failure. Special educational programs are needed to further improve the general awareness.

P1717

Management of heart failure patients in a Slovenian General hospital: What has changed in 15 years?

B Mahne[1]; S Kariz[1]; L Jeraj[1]
[1]*Izola General Hospital, Department of Cardiology, Izola, Slovenia*

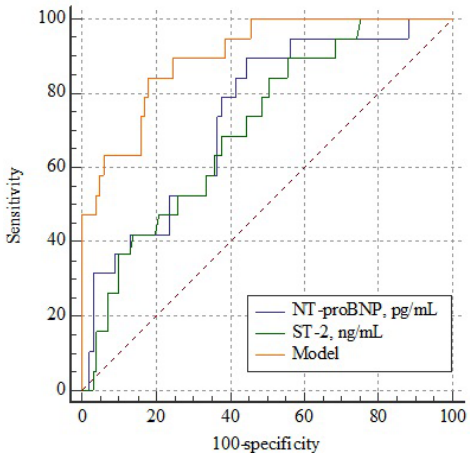
Background. Epidemiology trends in developed countries show that despite the decrease in the incidence of heart failure (HF) its prevalence is increasing. The population of HF patients is becoming older with a growing proportion of HF with preserved ejection fraction (pEF).
Purpose: The aim of the study was to investigate demographic trends, clinical characteristics and changes in management of patients hospitalized for HF in a Slovenian General Hospital in years 2001 and 2016.
Methods: We retrospectively analyzed medical records of all patients discharged from hospital with the diagnosis of HF between January and June 2016. Demographic data, clinical characteristics, comorbidities, pharmacological treatment and in-hospital mortality data were collected and analyzed. The results were compared with similar data collected in the period from January to June 2001.
Results: 198 patients in 2016 and 187 patients in 2001 were included in the study. Within a period of 15 years the median age increased from 76 to 81 years ($p < 0.001$) and the proportion of patients older than 80 years from 31% to 57% ($p < 0.001$). The median length of stay decreased from 10 to 7 days ($p < 0.001$). Patients hospitalized in 2016 had higher in-hospital mortality (18% vs 13%), however, the difference was not statistically significant. The proportion of patients with HFpEF increased from 43% to 54% ($p = 0.045$). However, no difference in etiology of heart failure was observed - ischemic heart disease was the most frequent cause of HF in both groups (33% vs 30%, $p = 0.495$), followed by hypertensive and valvular heart disease. Arterial hypertension and atrial fibrillation were more frequent in patients hospitalized in 2016 (76% vs 49%, $p < 0.001$ and 61% vs 48%, $p < 0.004$, respectively). COPD was less frequent (10% vs 27%, $p < 0.001$), while there was no significant difference in the prevalence of diabetes (32% vs 31%). More than half of patients treated in 2016 had anemia and chronic kidney disease (59% and 62 %, respectively). At hospital discharge, beta blockers were prescribed more frequently in 2016 (70% vs 16%, $p < 0.001$). On the contrary, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers (61% vs 77%, $p < 0.001$) and mineralocorticoid antagonists (35% vs. 54%, $p < 0.001$) were prescribed less frequently. Several additional types of treatment were also introduced in this period.
Conclusions. Our data confirm that HF has become primarily a condition of the older population characterized by an increased prevalence of HFpEF, and a greater burden of cardiac and non-cardiac comorbidities. No pharmacological intervention has so far demonstrated any convincing benefit on the outcome of HFpEF, therefore management of HF is increasingly challenging. However, the length of stay is decreasing and several new types of HF treatment were introduced or made more easily available.

P1718

Biomarkers of myocardial stress and fibrosis in determining clinical outcomes in patients with heart failure and previous myocardial infarction

N Shilyaeva[1]; E Medvedeva[2]; A Shpigel'[1]; Y Shchukin[1]
[1]*Samara State Medical University, Cardiology, Samara, Russian Federation*; [2]*Almazov National Medical Research Centre, Saint-Petersburg, Russian Federation*

Purpose: To evaluate the prognostic value of suppression of tumorigenicity 2 (ST2) and N-terminal prohormone of brain natriuretic peptide (NT-proBNP) levels in patients with chronic heart failure (HF) and previous myocardial infarction (MI).



ROC curves of biomarkers and model

Methods: The study included 127 patients with HF and the duration of MI with percutaneous coronary intervention (PCI) between 4 and 6 weeks (median age, 57 years; left ventricular ejection fraction (LVEF), 54%). The patients underwent clinical examination and echocardiography. Levels of biomarkers reflecting myocardial stretch (NT-proBNP) and ventricular fibrosis and remodeling (ST2) were determined by immunoassay analysis. The primary endpoint was the composite of all-cause mortality and rehospitalization due to HF and unstable angina, stroke and new MI with 9-month follow-up. Descriptive data are presented as frequencies (percent), median. Comparison between patients with adverse outcomes and without of them was performed using Mann-Whitney test. Receiver operating characteristics (ROC) curve was drawn to evaluate the potential roles of NT-proBNP and ST2 in predicting adverse clinical events. Logistic regression analysis was conducted to identify the independent risk factors for negative outcomes in this cohort. $P < 0.05$ was considered statistically significant.
Results: More than half of patients had I or II NYHA FC and cardiovascular risk factors. Most patients in both groups underwent primary PCI. During the 9-month follow-up period, communication was lost with 7 patients, adverse cardiovascular events occurred in 19 patients. Differences in age and sex between patients with adverse outcomes and without of them were not revealed. Enrolled patients were characterized by following levels of ST2 and NT-proBNP: 41,05 ng/ml and 245,99 pg/ml, respectively. Biomarkers concentrations were higher in patients with adverse outcomes compared with patients without recurrent cardiovascular events (? < 0,01, for both). Follow-up ROC analyses for outcome prediction showed similar areas under the curve (AUC) of biomarkers (? = 0,659): 0,709 for ST2 and 0,738 for NT-proBNP. Biomarkers yielded cut-off values 43,6 ng/mL for ST2 and 285 pg/mL for NT-proBNP. The odds ratio (OR) for cut-offs of the study biomarkers were 2,84 for ST2 and 2,97 for NT-proBNP. In the binary regression model, ST2, NT-proBNP and established risk factors (NYHA FC, aneurysm of the LV, a history of stroke, estimated glomerular filtration rate < 90 ml/min per 1,73m2) were statistically significant predictors for the combined endpoint. Model led to an AUC of 0.900 ($p < 0,001$), which better the AUC value for ST2 and NT-proBNP separately.

Conclusion. ST2 and NT-proBNP were independent predictors of adverse clinical outcomes in HF and previous MI patients.

P1719

Clinical and sociodemographic profile of patients with cardiac insufficiency admitted in a reference hospital in Fortaleza-Ce, Brazil

V L Vera Lucia Pessoa[1]; BJ Souza[1]; DL Salles[1]; MS Gama[1]; LC Souza[1]; MGV Sobral[1]; RS Florencio[1]; JD Souza Neto[1]; G G Vasconcelos[1]
[1]HOSPITAL DE MESSEJANA DR CARLOS ALBERTO STUDART GOMES, Fortaleza, Brazil

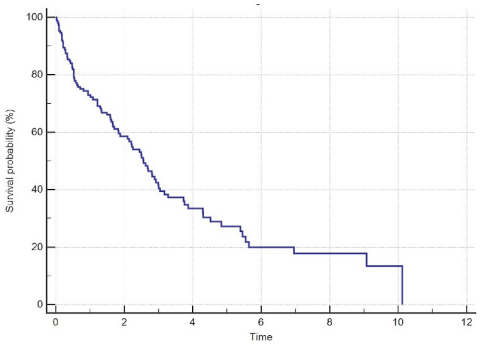
Introduction: Cardiac Insufficiency (CI) is a chronic disease considered as the final stage of most of cardiac illnesses. The causes are variable, being responsible for generating systemic impairment. It is known that socioeconomic characteristics are factors that can interfere in the prognosis as well as contribute to hospital readmission.
Objective: To describe the clinical and socioeconomic profile of patients admitted in a reference hospital.
Methods: It is a cross-sectional study with a quantitative approach conducted in adult patients, from both sexes, admitted in a hospital reference in treating cardiac illness, during April 2016 to October 2017, in Fortaleza-Ceará-Brazil. Such research is fruit of a conjunct project of Brazilian hospitals, by the Supporting Program for the Institutional Development of the Health System (from the Portuguese PROADI-SUS) of the Health Ministry, in partnership with the American Heart Association (AHA) and the Brazilian Cardiology Society. The clinical diagnosis of cardiac insufficiency was established by laboratory and echocardiographic tests as well as clinical information. It was used formularies and questionnaires to data collection. Data analysis was performed by the software SPSS 22.0 and statistic evaluation involved the calculation of frequencies and means. The results were discussed according the pertinent literature.
Results: from the 144 patients hospitalized by CI, it was verified that 59.9% were male, 95.8% considered "pardo", 35.7% did not finished elementary school and 22.5% did finished elementary school, 57.9% have a family income more than one minimal salary or less or equal to two minimal wages, 56.4% smoke, 57.4% drink alcohol and 82.9% do not exercise. Relating the clinical aspects of CI, 29.5% from the people have ischemic etiology, 17.3% idiopathic etiology, 12.7% valvar etiology, 10.1% Chagas disease etiology and 6.5% hypertensive etiology. Regarding the knowledge of CI before admission, 76.3% have already done treatment and 26.4% have been admitted in less than 6 months and 25.9% were diagnosed with NYHA of IV and had a mean ejection fraction of 37 ± 16.01.
Conclusion: cardiac insufficiency represents a challenge to health team, being configured as one of the major causes of hospitalization globally. Among them, it highlights the lack of knowledge about non-pharmacological methods, inadequate treatment adhesion and lack of capacity to identify signs and symptoms that are predictive to decompensation of the disease.

P1720

Prognosis and determinants of survival in patients with severe heart failure disqualified from heart transplantation due to contraindications

P Paula Polaska[1]; G Jerzak-Wodzynska[1]; P Leszek[1]; W Smigielski[1]; J Gajda[1]; P Rozentryt[2]; J Korewicki[1]; T Zielinski[1]; T Rywik[1]
[1]Institute of Cardiology, Warsaw, Poland; *[2]Silesian Center for Heart Diseases (SCHD), Zabrze, Poland*

Introduction: Heart failure is a common problem worldwide and despite some progress in treatment survival still leaves much to be desired. In patients with severe heart failure (SHF) the prognosis is particularly ominous. For these patients heart transplantation (HT) remains one of treatment options. However, presence of contraindications precludes acceptance for HT. There is a limited data on clinical characteristics and survival determinants of such patients.
Purpose: We intended to evaluate clinical characteristics and survival determinants of patients disqualified from HT due to contraindications.
Methods: It was a retrospective analysis, based on medical documentation of patients with SHF considered for HT, from a single transplantology center (Institute of Cardiology), between 01.2006 and 12.2016. There were 151 patients who constituted study population. All subjects were divided into two groups based on survival status: alive (AG) and deceased (DG).
Results: There were 57 in AG and 94 patients in DG. The mean age in both groups (AG/DG) was 56.3 ± 9 vs 55.7 ± 8.9 years ($p = 0,7$), percentages of males 82.4% vs 90.4% ($p = 0.2$). There was also no significant difference between groups in terms of occurrence of renal failure (RF) (33.3% vs 32.9%, $p = 1$), COPD (15.8% vs 24.5%, $p = 0.2$). The predominant etiology of SHF was ischaemic (61.4% vs 69.1% $p = 0.08$). There were borderline differences between groups in: EF (25.7% vs 22.4% $p = 0.06$), percentage of pts with liver failure (3.5% vs 7% $p = 0.08$), right ventricle failure (56.1% vs 47.3% $p = 0.09$), pulmonary hypertension (PH) (42.1% vs 50% $p = 0.08$), stroke (17.5% vs 10.6% $p = 0.098$), peripheral atherosclerosis (8.8% vs 11.7% $p = 0.05$), diabetes (40.4% vs 32.98% $p = 0.07$) and staying under the ambulatory care from specialist cardiological center (33.3% vs 26.6% $p = 0.07$). Median FU time for this population was 1.67 yrs. 2.1 yrs in AG group and 1.34 yrs in DG ($p = 0.0009$). At 1 year, there were 72% of subjects alive, whereas at 5 years only 25%. After excluding first 30 days of FU (to eliminate in-hospital mortality) in Cox regression model, supervision by specialist ambulatory cardiological center (HR 0.6, $p = 0.05$) was a negative predictor of death, whereas RF (HR 1.59; $p = 0.05$), PH (HR 1.5; $p = 0.06$) were positively associated with unfavorable prognosis.
Conclusions: The prognosis of patients with SHF disqualified from HT due to contraindications is poor. The ambulatory supervision by cardiology specialist center is beneficial in this population.



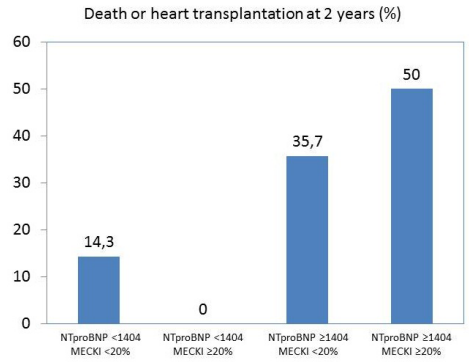
Survival probability

P1721

Prognostic evaluation of HF-rEF using the MECKI score can be improved by adding natriuretic peptide levels

F Francisco Gama[1]; P Freitas[1]; C Aguiar[1]; D Matos[1]; A Tralhao[1]; J Ferreira[1]; A Ventosa[1]; MJ Rebocho[1]; M Mendes[1]
[1]Hospital de Santa Cruz, Lisbon, Portugal

Background: Heart transplantation guidelines recommend the Seattle Heart Failure Model and the Heart Failure Survival Score when deciding on the timing of listing for transplantation, but recent studies have shown that the Metabolic Exercise Cardiac Kidney Index (MECKI) score has superior predictive accuracy. The aim of this study was to determine whether the NT-proBNP level adds prognostic value to the MECKI score.
Methods: Retrospective analysis of 129 patients with HF-rEF who underwent cardiopulmonary exercise test (CPET). The MECKI score was calculated for each patient using data at the time of the CPET, and NT-proBNP levels were measured before the test. The study endpoint was heart transplantation or death (any cause), whichever occurred first within 2 years after the CPET. ROC curve analyses were performed to determine the best discriminatory level of NT-proBNP.
Results: Mean age was 55 ± 11 years and 80% were male. The most common heart failure etiology was ischemic (50%). Peak VO2 was £14 mL/kg/min in 34 patients (26.4%). Over the 2-year follow-up period, 7 patients died and 8 underwent heart transplantation (study endpoint rate 10.9%). The MECKI showed good discrimination ability (c-statistic 0.85; 95% CI, 0.74-0.95). A NT-proBNP level >1404 pg/mL showed the best discriminatory accuracy (26% positive predictive value, 98% negative predictive value), and predicted the study endpoint independently of the MECKI score in Cox regression analyses (adjusted HR 5.9; 95% CI, 1.2-29) (see figure).
Conclusion: In patients with HF-rEF, the level of NT-proBNP added significant prognostic information to the MECKI score.



Figure

P1722

Perceptions of heart failure symptoms and disease severity by patients and cardiologists: a multinational survey in the real-world cardiology setting

S Bruce Wirta[1]; B Balas[2]; CC Proenca[3]; H Bailey[4]; Z Phillips[4]; J Jackson[4]; S Cotton[4]
[1]Novartis Sweden AB, Stockholm, Sweden; [2]Novartis Pharma AG, Basel, Switzerland; [3]Wellmera AG, Basel, Switzerland; [4]Adelphi Real World, Bollington, United Kingdom

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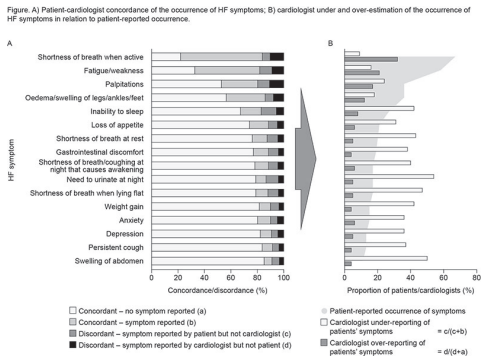
Background and Purpose: This study aimed to explore the extent to which symptoms experienced by patients with heart failure (HF) are recognized by their cardiologist and the level of concordance between patient and cardiologist perceptions of associated severity of HF.
Methods: A cross-sectional survey of cardiologists and their consulting patients with HF was conducted in 10 countries (Argentina, Brazil, China, Colombia, France, Japan, Mexico, Russia, Saudi Arabia and Turkey). Patient record forms (PRFs) were completed by cardiologists for consecutively consulting patients with HF, who were then invited to complete a patient self-completion questionnaire (PSC). Only responses from PRFs with an associated PSC were analyzed. Patient- and cardiologist-reported occurrences of individual HF symptoms were compared, and concordance was calculated as the number of response agreements by PSC and PRF for the total number of matched pairs. The over- or under-reporting of symptom occurrence by cardiologists relative to patient-reported occurrence was also calculated by taking the patient perspective and evaluating how often a patient-reported symptom was not recognized in the PRF (cardiologist under-reporting) and vice versa (cardiologist over-reporting). Patients' perceived severity of HF was also compared to their cardiologists' perceived risk of death within 12 months.



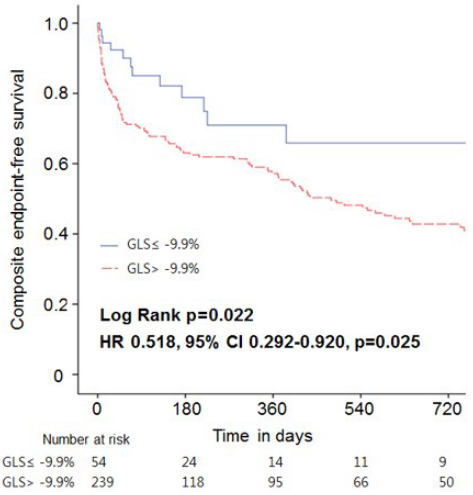
Results: Overall, a very high level of concordance was reported for the occurrence of symptoms experienced between matched patient and cardiologist pairs (n = 2379); 93% of matched cardiologists and patients described similar occurrences of any HF symptom. High concordance was also observed for the occurrence of individual HF symptoms reported by patients with HF and their cardiologists (range 80-92%) (Figure). For symptoms reported by >50% of patients, cardiologists more frequently over- than under-reported their occurrence, whereas for symptoms reported by < 50% of patients, it was more common for cardiologists to under-report than over-report their occurrence (Figure). The overall concordance of patient- and cardiologist-perceived severity of HF was 54% (n = 2260). Of the patients reporting their HF as mild, 28% were perceived by their cardiologist to have a moderate to high or very high risk of death within 12 months, which increased to 50% in patients that reported their HF as moderate and 75% in patients reporting their HF as severe.
Conclusions: This study shows that cardiologists are aware of the most common HF symptoms, but have a tendency to under-report less common HF symptoms. Results also show that patients often underestimate the severity of their HF. A better dialogue between cardiologists and patients may result in increased awareness of HF-associated risks and lead to improved treatment and outcomes.

P1723

The association of global longitudinal strain with clinical outcomes in heart failure patients with severe left ventricular systolic dysfunction

H W Lee[1]; JC Choi[1]; JY Shin[1]; SH Lee[1]; JH Ahn[1]; JS Park[1]; JH Oh[1]; JH Choi[1]; HC Lee[1]; KS Cha[1]; TJ Hong[1]
[1]Pusan National University Hospital, Department of Cardiology, Busan, Korea Republic of

Purpose: The heart failure (HF) patients with severe left ventricular (LV) systolic dysfunction still have unfavorable prognosis.We aimed to investigate if better global longitudinal strain (GLS) predicts improved clinical outcomes in these patients.



Severe LV dysfunction and GLS

Methods: Among 293 consecutive HF patients with severe LV systolic dysfunction, defined as LV ejection fraction (LVEF) = 30% at baseline echocardiogram, in an urban tertiary center (October 2013-September 2017), the predictive ability of GLS by speckle-tracking echocardiography for the subsequent occurrence of clinical outcomes was evaluated. The primary outcome was composite endpoint of cardiac death and HF readmission.
Results: Composite endpoint occurred in 140 patients (47.8%) during a mean 367 days of follow-up. GLS was independently predictive of composite endpoint, but LVEF was not. In the receiver operating characteristic curve analyses of GLS, the cutoff values for predicting composite endpoint were -9.9 % (sensitivity: 0.90; specificity: 0.28; area under the curve: 0.598). Better GLS group (defined as GLS =-9.9%, n = 54), compared to worse GLS group (defined as GLS >-9.9%, n = 239), had significantly lower rate of composite endpoint (24.1% vs. 53.1%, p < 0.001). Composite endpoint-free survival rate was significantly higher in better GLS group than worse GLS group (75.9% vs. 46.9%, log rank p = 0.022).Conclusion: GLS may provide the additive information for clinical outcomes in patient with severe LV systolic dysfunction.

P1724

Who will progress to advanced heart failure? Predictors from within a multidisciplinary disease management program.

RM Murphy[1]; LH Healy[1]; JG Gallagher[1]; S MCC Mc Cleland[1]; ML Ledwidge[1]; SZ Zhou[1]; K MCD Mc Donald[1]
[1]*St Vincent's University Hospital, Cardiology, Dublin, Ireland*

Background: Recurrent hospitalisation for acute decompensated heart failure (ADHF) is a concerning prognostic sign and usually underlines the need to consider advanced heart failure (HF) therapy or palliative care. Multidisciplinary disease management programs (DMP) are now recognised as the optimal method to deliver state of art HF care to those surviving an ADHF admission. What is unclear are the characteristics of those managed in a DMP likely to display a downward course in disease trajectory and thereby in need of a change in management strategy.
Methods: We recruited patients entering our DMP following an admission for ADHF. Patients were followed over time to determine what percentage of them defined features of disease progression (defined as 2 subsequent ADHF admission within a 6-month period) compared with those demonstrating a more stable course.
Results: 1984 patients were followed for an average of 3.6 years in our DMP post admission with ADHF. Mean age was 73 years old. 58% were male. Of these 493 had heart failure with a preserved ejection fraction (HFpEF) and 1239 had heart failure with a reduced ejection fraction (HFrEF). 264 patients demonstrated heart failure disease progression at an annual incidence of 3.7% per year.
On multivariate analysis the strongest indicators of progression to refractory heart failure were B-type natriuretic peptide (BNP) and renal function as estimated by creatinine, with stable raised BNP being the strongest predictor of disease progression. The optimal stable BNP to differentiate high and low risks was approximately 440 pg/ml.
Conclusion: Patients managed in a multidisciplinary disease management program showed a low rate of annual progression of HF syndrome as defined by recurrent hospitalisations. This highlights the importance of referring patients at risk of recurrent hospitalizations to a DMP to help improve patient outcomes. Persistently high stable BNP and impaired renal function were the strongest predictors of disease progression.

Chronic Heart Failure - Diagnostic Methods

P1725

Lung ultrasound in the diagnosis of cardiogenic dyspnea

T Valova[1]; ID Daskalov[1]
[1]*Military Medical Academy of Sofia, Cardiology and intensive therapy, Sofia, Bulgaria*

Introduction: Dyspnea is a common challenge in the routine clinical practice, especially arising in intensive care units, where the therapeutic modality has to be approved upon medical examination.
Objectives: Verifying the subtype of cardiogenic or non-cardiogenic dyspnea with reliable, safe, time-saving and non-expensive diagnostic method that can be performed anytime, at the patient's bench.
Method: Lung ultrasound differentiating B-lines score in 51 patients with non-cardiogenic dyspnea, 52 - with cardiogenic dyspnea and 49 - healthy controls was tested against conventional X-ray and FOCUS.
Results: All patients with cardiogenic dyspnea (class III-IV NYHA) showed B-lines score over 15 (16,85). The result from the performed lung ultrasound in this group strongly correlated with the chest X-ray (r- 0,86, $p < 0,001$). A moderate correlation with FOCUS (r- 0,68, $p < 0,001$) was also detected. No B-lines were shown in patients with non-cardiogenic dyspnea. A moderate correlation between the presented diagnostic modalities was found in the non-cardiogenic group (r-o,567, $p < 0,0001$). The estimated single B-lines in a definite lung zone was not a sign of cardiogenic dyspnea. It was accepted as an indirect criterion for inflammation or vessel damage in the observed lung zone. The absence of B-lines detected with lung ultrasound supposed non-cardiogenic cause for dyspnea such as chronic obstructive pulmonary disease, bronchial asthma, pneumothorax, pulmonary fibrosis or hysteria. It correlated with negative for pulmonary congestion chest X-ray and normal or low left ventricle filling pressure. No typical B-lines were identified in healthy controls.
Conclusions: B-lines seem to be an easy-to-perform and reliable non-invasive diagnostic tool for dyspnea pathogenetic differentiation. The method advantages include safe and bed lung ultrasound application, multiple use and precise control of the administrated therapy.

P1726

Changes in circulating miRNAs as a prognostic tool for heart failure related morbidity and mortality in patients suffering from stable HFpEF: A subgroup analysis of the ALDO-DHF trial

J Johannes Petutschnigg[1]; MWJ De Ronde[2]; TD Trippel[1]; L Schleussner[1]; F Baehr[1]; D Hashemi[1]; V Holzendorf[3]; JJ Leenders[4]; YM Pinto[5]; R Wachter[6]; G Hasenfuss[7]; C Hermann-Lingen[8]; B Pieske[1]; F Edelmann[1]
[1]*Charite - Campus Virchow-Klinikum (CVK), Department of Medicine and Cardiology, Berlin, Germany*; [2]*Academic Medical Center of Amsterdam, Amsterdam, Netherlands*; [3]*University of Leipzig, Faculty of Medicine, Leipzig, Germany*; [4]*Academic Medical Center of Amsterdam, ACS Biomarker BV, Amsterdam, Netherlands*; [5]*Academic Medical Center of Amsterdam, Heart Failure Research Center, Amsterdam, Netherlands*; [6]*Leipzig University Hospital, Department of Cardiology, Leipzig, Germany*; [7]*University Medical Center Gottingen (UMG), Department of Cardiology, Gottingen, Germany*; [8]*University Medical Center Gottingen (UMG), Department of Psychosomatic Medicine and Psychotherapy, Gottingen, Germany*

Background/ Introduction: Heart failure with preserved ejection fraction (HFpEF) is increasingly common as a major health burden in the western world. The underlying cellular mechanisms remain hardly explored and solid treatment opportunities as well as tools for risk prediction are desperately needed. Therefore, we investigated 14 selected microRNAs (miRNAs) regarding their potential to add prognostic information in patients with HFpEF.
Methods: We examined 14 miRNAs in the ALDO-DHF cohort in which the benefit of spironolactone 25 mg once daily vs. placebo for 12 months in 422 HFpEF patients with NYHA class II–III, LVEF = 50%, and peakVO2 = 25 mL/kg/min was investigated. MiRNA levels together with one technical normalization miRNA (cel-miR-39) were measured in plasma samples by standard Q-PCR at baseline, and after 6 and 12 months follow-up. Multivariable Cox proportional hazard regression analyses were performed to assess the association of the miRNAs with cardiovascular (CV) death and hospitalization rate during follow-up in comparison to established risk factors (in this case: age, sex, diabetes, creatinine, hemoglobin and sodium) with and without miRNAs and in conjunction with NT-proBNP.
Results: The panel that turned out to be predictive for worsening of the HFpEF related disorder (expressed by CV death and hospitalization rate) comprises the following 7 miRNAs: miR-22-3p, miR-142-5p, miR-320a, miR-378a-3p, miR-423-5p, miR-499 and miR-1254. We compared c-stats (Table 1) of established risk factors alone [0.54 (95% CI 0.48-0.61)] and in conjunction with NT-proBNP [0.60 (95% CI 0.54-0.66)] or the panel of miRNAs [0.66 (95% CI 0.60-0.72)]. Finally, we also used all of them [0.68 (95% CI 0.63-0.74)] and compared it with the prognostic value for HFpEF patients of solely this panel of miRNAs [0.67 (95% CI 0.60-0.74)].
Conclusion: Our findings suggest that a baseline model for risk prediction, using only established risk factors, performs poorly in the prediction of CV death and hospitalization rate. Adding NT-pro-BNP to this model increases the capacity of the model to predict risk, but the strongest contributor to the prediction model appeared to be the panel of 7 miRNAs.

Table 1

Analyzed models	c-stat (95% CI)
Established rik factors	0.54 (95% CI 0.48-0.61)
+ NT-proBNP	0.60 (95% CI 0.54-0.66)
+ panel of 7 miRNAs	0.66 (95% CI 0.60-0.72)
+ NT-proBNP and panel of 7 miRNAs	0.68 (95% CI 0.63-0.74)
panel of 7 miRNAs only	0.67 (95% CI 0.60-0.74)

P1727

Biomarker role of relaxins in myocardial fibrosis and left ventricular diastolic function in ischemic heart failure with reduced ejection fraction

E Edit Gara[1]; J Simon[1]; GY Csiko[1]; J Skopal[1]; T Radovits[1]; G Foldes[1]; B Merkely[1]
[1]*Semmelweis University, Heart Center, Budapest, Hungary*

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Background and Purpose: Relaxin is a pleiotropic hormone with well characterised effects in pregnancy and labor. Furthermore, preclinical and clinical studies are evaluating its possible therapeutic role in decompensated heart failure. Relaxin may also act as a novel biomarker in chronic heart failure. Here we aimed at investigating the value of endogenous, circulating relaxins (RLX-1 and RLX-2) in cardiac remodelling and fibrosis, as well as on left and right ventricular function.

Methods: Human myocardial samples were collected from consented patients with ischemic end-stage heart failure (HF) (n = 55). Serum and explanted myocardial tissue were biobanked during heart transplantation surgery. Medical history, laboratory findings, hemodynamical (cardiac output, PVR, PCWP) and echocardiographic measurements were assessed. Circulating RLX-1 and RLX-2 was measured by ELISA from serum. To assess collagen and connective tissue left and right ventricular wall segments were stained for Picrosirius red and Massons' trichrome. The amount of myocardial fibrosis was quantified with Image J density analyses. For statistical analyses, t-tests and Spearman's correlation tests were used.
Results: Mean levels of RLX-1 from end-stage HF were comparable with those measured in pregnant women (702 ± 283 pg/ml in vs. 560-1060 pg/ml, respectively). RLX-1 proved to be independent from age, gender, hypertension, diabetes mellitus, BMI or BSA. We found a moderate inverse correlation between serum RLX-1 levels and the extent of ventricular fibrosis (r=-0.493, p = 0.0005 in the right ventricle and r=-0.487, p = 0.0006 in the left ventricle). In parallel with this, a moderate correlation was found in left ventricular diastolic function parameters (E/A r = 0.456, p = 0.0025, n = 55). There were no significant differences in the laboratory results, hemodynamics, and other echocardiography parameters. RLX-1 levels showed moderate correlation with RLX-2 levels (r = 0.453, p = 0.0003).
Conclusion: In this population of end-stage heart failure patients with ischemic etiology higher endogenous RLX-1 levels were accompanied by significantly lower extent of myocardial fibrosis. This finding suggests the specified biomarker role for RLX-1 and emphasizes its therapeutic use of RLX-1 as an anti-fibrotic drug. Further studies are warranted to fully understand its role in myocardial function and detailed intracellular mechanisms of action.

P1728

Eyes on amyloidosis: Severe microvascular retinal dysfunction in cardiac amyloidosis.

E Zampiccoli[1]; J Barthelmes[1]; M Naegele[1]; R Schwotzer[1]; I Sudano[1]; F Ruschitzka[1]; AJ Flammer[1]
[1]University Heart Center, Cardiology, Zurich, Switzerland

Funding Acknowledgements: Swiss Heart Foundation, LHW Foundation, University Hospital Zurich

INTRODUCTION: Endothelial dysfunction is crucial in the development, progression, and prognosis of cardiovascular diseases. Cardiac amyloidosis is a particular form of heart failure with typical sings and symptoms and a devastating prognosis. Amyloid deposits are found both in the heart muscle as well as in the vasculature, limiting the ability of the vessel to adapt blood flow according to the need of the organs. Whether retinal endothelial function is impaired in these patients is still unclear. Therefore, it was the aim of this study to evaluate retinal vessel endothelial function - an easily assessable vasculature - in patients with amyloidosis.
OBJECTIVE: To investigate vascular function in chronic heart failure patients with cardiac amyloidosis.
MATERIALS & **Methods:** 22 patients with amyloidosis (15 AL, 7 TTR mean age 64 ± 9.2 years) were included. 82 healthy individuals (HC) without any cardiovascular risk factors served as controls (mean age 54.2 ± 15.8 years). Microvascular retinal endothelial function was measured via dynamic retinal vessel analysis (RVA). This non-invasive technique measures mainly NO-dependenr flicker light-induced dilatation of retinal arteries (FIDart). Other vascular measures included flow-mediated dilatation (FMD), retinal arteriovenous ratio (AVR) and pulse-wave velocity (PWV). To account for imbalanced possible confounders (age, sex, BMI, blood pressure, glucose and cholesterol levels), an inverse probability weighted analysis (propensity score) was employed.
Results: Arterial retinal vascular function (FIDart) was significantly impaired in patients with amyloidosis compared to HC (mean FIDart 3.7 ± 1.9 % vs. 1.0 ± 1.3 %, p < 0.001). CHF patients with AL (n = 15) and TTR (n = 7) amyloidosis both showed significantly impaired vascular function (mean FIDart = 1.5 ± 2.1 % for AL and mean FIDart = 0.5 ± 1.4 % for TTR) to a similar degree (p = 0.33). PWV was significantly faster in patients with amyloidosis than in HC (mean PWV 9.1 ± 2.6 ms-1 vs. 7.5 ± 1.3 ms-1, p = 0.005). There was no significant difference in FMD between the two groups (HC vs. amyloidosis; mean FMD 6.6 ± 3.4 % vs. 6.1 ± 3.4 %, p = 0.11). Balance for potential confounders was achieved.
Conclusions: Our results demonstrate profound alterations in microvascular function of patients with cardiac amyloidosis. Whether these results have clinical or prognostic impact needs to be carefully evaluated in further clinical studies.

P1729

Derivation and validation of a conversion equation between B-type natriuretic peptide and N-terminal pro BNP levels

S Kasahara[1]; Y Sakata[1]; K Nochioka[1]; R Abe[1]; T Oikawa[1]; M Sato[1]; H Aoyanagi[1]; M Miura[1]; T Shiroto[1]; J Takahashi[1]; S Miyata[2]; H Shimokawa[3]
[1]Tohoku University Graduate School of Medicine, Department of Cardiovascular Medicine, Sendai, Japan; [2]Tohoku University Graduate School of Medicine, Department of Evidence-based Cardiovascular Medicine, Sendai, Japan; [3]Tohoku University Graduate School of Medicine, Department of Cardiovascular Medicine and Department of Evidence-based Cardiovascular Medicine, Sendai, Japan

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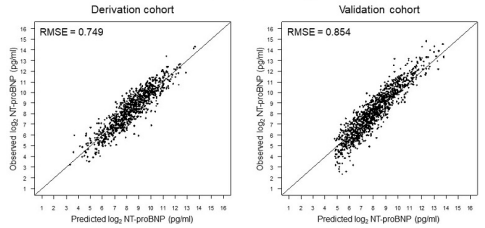
Background: The ESC guidelines recommend measurement of natriuretic peptides for diagnosis of Heart Failure (HF) as a Class I indication. Among natriuretic peptides, biologically active B-type natriuretic peptide (BNP) and inactive N-terminal pro B-type natriuretic peptide (NT-proBNP) are the most widely used diagnostic tools for HF. Although both molecules are released in equimolar proportions, their levels differ depending on clinical conditions, such as age, sex, body weight, renal function, anemia and so on. However, a reliable conversion equation between BNP and NT-proBNP remains to be developed in the daily clinical practice.
Purpose: To develop a conversion equation between BNP and NT-proBNP.
Methods: The derivation cohort included 928 patients (mean 66 yrs., female 26%) from our Supplemental Benefit of Angiotensin Receptor Blocker in Hypertensive Patients with Stable Heart Failure using Olmesartan (SUPPORT) Trial, in which we examined whether an additive treatment with olmesartan reduces the mortality and morbidity in hypertensive HF patients treated with evidence-based medications. The validation cohort included 1,163 consecutive cardiovascular patients aged = 20 yrs., in whom both BNP and NT-proBNP levels were measured simultaneously at a university hospital between April 2017 and October 2017 (mean 66 yrs., female 41%). To develop the conversion equation, we regressed log2 NT-proBNP onto log2 BNP and other covariates. In the multivariable models, all possible combinations of log2 BNP and the variables including age, sex, creatinine, hemoglobin, body weight, and height were examined as independent variables. For the best conversion equation, we selected the set of the covariates that maximized the adjusted R^2 in the derivation cohort first. Then, the root mean squared error (RMSE) was obtained in the validation cohort to examine the predictive accuracy of the selected model.
Results: Mean log2 BNP and log2 NT-proBNP levels were 6.2 pg/ml and 8.4 pg/ml, respectively, in the derivation cohort, while they were 5.8 pg/ml and 8.1 pg/ml, respectively, in the validation cohort. In the derivation cohort, the model with the highest adjusted R^2 consisted of log2 BNP, age, creatinine, hemoglobin, body weight, height, and sex. We developed the conversion equation as follows; log2 NT-proBNP (pg/ml) = 0.957*log2 BNP(pg/ml) - 0.00655*age(yrs.) + 0.731*creatinine(mg/dl) - 0.0184*hemoglobin(g/dl) - 0.00554*weight(kg) + 0.00880*height(cm) + 0.238(if female sex) + 1.34 (Figure). In the validation cohort, RMSE of this conversion equation was 0.854, which was smaller than that of previously reported conversion equations, demonstrating that this equation excellently converts BNP levels to NT-proBNP levels.
Conclusion: An excellent and reliable conversion equation between BNP and NT-proBNP levels has been developed with age, creatinine, hemoglobin, body weight, height and sex.

Figure. Predicted vs. Observed NT-proBNP levels



P1730

Prevalence of heart failure with preserved and reduced left ventricular ejection fraction and diagnostic value of MR-proANP in 803 outpatients with type 2 diabetes

J Jensen[1]; M Schou[1]; C Kistorp[2]; J Faber[2]; TW Hansen[3]; MT Jensen[4]; HU Andersen[3]; P Rossing[5]; T Vilsboll[5]; JS Jensen[1]; PG Jorgensen[4]
[1]Herlev and Gentofte Hospital, Faculty of Health and Medical Sciences, Copenhagen University, Department of Cardiology, Copenhagen, Denmark; [2]Herlev and Gentofte Hospital, Faculty of Health and Medical Sciences, Copenhagen University, Department of Endocrinology, Copenhagen, Denmark; [3]Steno Diabetes Center Copenhagen, Copenhagen, Denmark; [4]Herlev and Gentofte Hospital, Department of Cardiology, Copenhagen, Denmark; [5]Steno Diabetes Center Copenhagen, Faculty of Health and Medical Sciences, Copenhagen University, Copenhagen, Denmark

Background/Introduction: Type 2 diabetes (T2D) is associated with diastolic dysfunction and an increased risk of heart failure (HF). Overt HF may be difficult to acknowledge in T2D patients due to coexisting factors such as obesity. Also, the prevalence of HF with preserved (HFpEF) and reduced (HFrEF) left ventricular ejection fraction (LVEF) in T2D patients is debatable due to several ways of defining diastolic dysfunction. Further, in the outpatient setting, no data exist on the diagnostic value of the new natriuretic peptide, mid-region pro-atrial natriuretic peptide (MR-proANP), to rule out HFrEF or to diagnose HFpEF and HFrEF in T2D patients.
Purpose: To identify the prevalence of HFpEF and HFrEF and evaluate the diagnostic value of MR-proANP in a cohort of patients with T2D, consecutively followed in two specialized diabetes outpatient clinics.
Methods: The MR-proANP level was measured and a comprehensive echocardiography was performed in N = 803 T2D patients with sinus rhythm followed in two specialized diabetes outpatient clinics. HFrEF was defined regardless of presence of dyspnea as a LVEF = 40% and HFpEF defined as presence of dyspnea and at least one of the following present: LVEF > 40% and = 50%, E/e'medial = 15, increased LV mass or a left atrial volume index >34 ml/m2. Univariate and multivariate logistic regression analyses were applied.
Results: Of the patients (median [interquartile range] age of 65 [58, 71] years, 35% female), 38% complained of dyspnea, 17% had HFpEF and 2% had HFrEF. MR-proANP levels were respectively 61 [40, 88], 105 [68, 190] and 125 [95, 208] pmol/l in patients with normal echocardiography, in HFpEF and in HFrEF patients. Receiver operating characteristic (ROC) curves showed an optimal cut-off level for MR-proANP of 60 pmol/l to rule out HFrEF (N = 19) in all patients (sensitivity 94.7%, specificity 39.4%, negative predictive value (NPV) 99.7%, positive predictive value (PPV) 3.7%) (Figure A) and in patients with dyspnea (N = 309) (sensitivity 87.5%, specificity 32.9%, NPV 99.0%, PPV 3.3%) (Figure B). Adding MR-proANP to a multivariate model (including age, sex, T2D duration, albuminuria, systolic blood pressure above 170 mmHg, abnormal ECG and ischemic heart disease) in order to identify either HFpEF or HFrEF patients as a group, increased area under the curve (AUC) from 0.689 to 0.784 ($p < 0.001$) in patients with dyspnea (Figure C).
Conclusion(s): HFpEF (17%) is frequent and HFrEF (2%) is rare in outpatients with T2D. An MR-proANP level of less than 60 pmol/l effectively rules out HFrEF in T2D outpatients regardless of the presence of dyspnea and adds independent information in diagnosing either HFpEF or HFrEF in patients with dyspnea. Since HFpEF is frequent in T2D, a diagnostic rather than a rule out strategy is preferable in a specialized diabetes clinic setting.

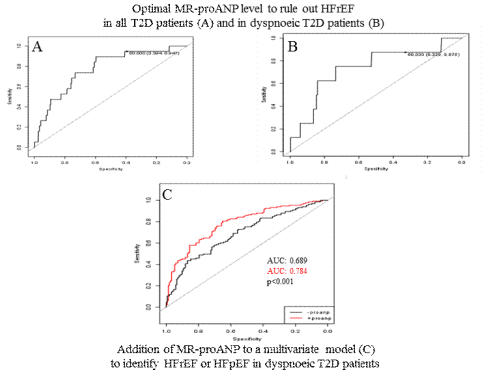


Figure A-C

P1731

Prognostic impact of copeptin and mid-regional pro-adrenomedullin in chronic heart failure with regard to comorbidities

L Lenka Spinarova[1]; J Parenica[2]; J Spinar[2]; M Spinarova[1]; K Labr[1]; F Malek[3]; P Ostadal[3]; O Ludka[2]; M Goldbergova-Pavkova[4]; J Tomandl[5]; K Benesova[6]; J Jarkovsky[6]
[1]Masaryk University,St. Anne's Faculty Hospital,1st Department of Internal Medicine-Cardioangiology, Brno, Czech Republic; [2]University Hospital and Masaryk university, Internal Cardiologic Dpt, Brno, Czech Republic; [3]Homolka Hospital, Cardiologic Dpt, Praha, Czech Republic; [4]Medical Faculty of Masaryk University, Pathophysiologic Dept, Brno, Czech Republic; [5]Masaryk University, Biochemistry Dept, Medical Faculty of Masaryk University, Brno, Czech Republic; [6]Masaryk University, Faculty of Medicine, Institute for Biostatistics and Analysis, Brno, Czech Republic

The aim of the study is to evaluate the impact of new humoral substances: copeptin and mid- regional pro-adrenomedullin (MR-proADM) on one year survival of patients with stable systolic chronic heart failure (CHF) and to compare them with AHEAD score assessing the comorbidities. The FAR NHL (FARmacology and NeuroHumoraL activation) registry is a database of patients treated in departments with specialized HF care in three University hospitals. The patients should have been treated for systolic HF: EF < 50% and stable for at least 1 month, follow up was 1 year. Primary endpoint after 1 year follow-up was: death or hospitalization for decompensation of HF or heart transplantation (HTX) or LVAD implantation. This endpoint was related to the levels of copeptin and MR-proADM and was caluculated for separate AHEAD scores. AHEAD score is a simple bed-side mortality predictive model for a wide population of AHF patients based on age and basic comorbidities. To whole FAR NHL registry a total amount of 1076 patients were included, in 552 of them the levels of copeptin and MR-proADM were available. Mean age was 65 +12 years, the etiology of CHF was ischemic heart disease in 53.5%, dilated CMP in 40.2% and 6.3% were classified as other. Mean EF was 31+9%. Patients without primary endpoint were assigned as group A (469 pts), those with the primary endpoint group B (83 pts). There were statistically significant differences between the groups in the levels of copeptin: group A median 15.9 pmol/l(3.4-50.9) vs group B 23.7 pmol/l(5.0-89.44) ($p < 0.001$),MR-proADM: group A median 0.63 nmol/l(0.32-1.34) vs group B 0.74 nmol/l(0.4-1.94) ($p < 0.001$)
Patients were then divided according the AHEAD score into three groups: AHEAD score 0-1, AHEAD score 2-3, AHEAD score 4-5. Relationship of AHEAD score to primary endpoint in the first year of follow-up was not significant, but within 24th month it reached statistical significance: p= 0.017. Patients with higher AHEAD score (more comorbidities) reached more often the primary end-point
The cutt-off value = 23.7 for copeptin had 50.6% sensitivity and 73.3% specificity to predict primary outcome at the first year of follow -up, $p < 0.001$. The cut –off value for MR-proADM= 0.58 had higher sensitivity 79.5% and lower specificity 42.0% for one year follow- up with $p < 0.001$. For both humoral substances there was statistical significant difference for discrimination of patients with primary endpoint in lower AHEAD score groups: copeptin ($p < 0.006$ and $p < 0.004$), MR-proADM ($p < 0.008$ and $p < 0.002$). However, in the highest AHEAD score the level of these substances lost their predictive value. Higher levels of copeptin, MR-proADM might identify HF patients with higher risk of adverse outcome. Our study is the first which evaluates the predictive value of copeptin and MR-proADM over the comorbidities of patients with HF assessed by AHEAD score.

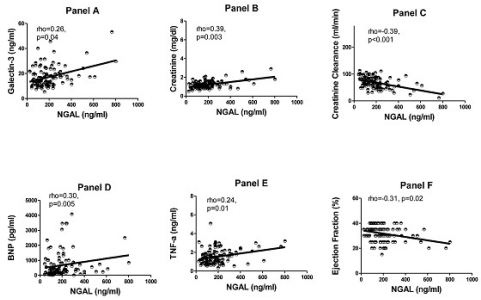
P1732

Interaction between renal and heart function in patients with heart failure: The role of NGAL

E Evagelos Oikonomou[1]; D Karlis[1]; S Tsalamandris[1]; G Siasos[1]; C Chrysohoou[1]; G Vogiatzi[1]; S Dimitropoulos[1]; G Charalambous[1]; E Kouskouni[1]; D Tousoulis[1]
[1]Hippokration Hospital, University of Athens, 1st Department of Cardiology, Athens, Greece

Background: Neutrophil gelatinase-associated lipocalin (NGAL) is a biomarker of renal injury associated with the progression of heart failure (HF). Galectin-3 is expressed in several tissues by inflammatory cells and may be used as an additive diagnostic and prognostic biomarker in patients with HF.
Purpose: To examine how NGAL levels are interrelated to Galectin-3 levels in patients with chronc HF of ischemic etiology.
Methods: We consecutive enrolled 115 subjects with stable ischemic HF of reduce ejection fraction. Serum levels of Galectin-3, b-type natriuretic peptide (BNP), NGAL and tumor necrosis factor alpha (TNFa) were measured.
Results: NGAL levels were positive correlated with Galectin-3 levels (rho = 0.26, p = 0.04), with BNP levels (rho = 0.30, p = 0.005), with TNF-a levels (rho = 0.24, p = 0.01) and inversely correlated with left ventricle ejection fraction (rho=-0.31, p = 0.02). NGAL levels were also positively correlated with Creatinine levels (rho = 0.39, p = 0.003) and inversely associated with CrCl (rho=-0.39, $p < 0.001$). After adjustment

for many confounders including age, gender, diabetes mellitus, hypertension, CrCl and BNP; logNGAL was independently associated with Galectin-3 levels [b = 0.05 95%CI (0.001 = 0.36), p = 0.04].



Figure

Conclusions: In the present study we found a positive correlation between NGAL and Galectin-3 in patients with heart failure. These findings reveal the potential association between renal injury and myocardial fibrosis and remodeling in heart failure and highlight a potential role of NGAL in the crosstalk between kidney and heart.

P1733

The importance of the NTproBNP rule-in criteria in the early diagnosis of HFmrEF and HFpEF

M Marta Szabo[1]; B Muk[1]; ZS Majoros[1]; D Vagany[1]; K Kosa[1]; T Borsanyi[1]; M Dekany[1]; RG Kiss[1]; N Nyolczas[1]
[1]*Medical Centre, Hungarian Defence Forces, Cardiology, Budapest, Hungary*

Background: In patients with acute dyspnoea, early diagnosis may reduce the duration of hospitalization, the probability of rehospitalization, and costs. In patients with left ventricular ejection fraction (LVEF) < 40% the diagnosis of heart failure (HF) can be accepted as proven. In case of LVEF = 40%, further examinations are necessary to confirm or exclude HF. In the current ESC guideline for HF, diagnostic criteria for HF with mid-range EF (HFmrEF; 40% = EF < 50%) and HF with preserved EF (HFpEF; EF = 50%) are the typical clinical signs and symptoms, specific values of LVEF, elevated natriuretic peptide levels, and structural heart disease (left ventricular hypertrophy and/or left atrial enlargement) and/or diastolic dysfunction (SHD/DD). In the ESC guideline the 300 pg/ml value of NTproBNP is the diagnostic cut-off value for rule-out in acute HF. The guideline of the Canadian Cardiovascular Society for HF determines age specific diagnostic rule-in NTproBNP criteria, according to the results of the ICON study (under 50 years >450 pg/ml, between 50 and 75 years >900 pg/ml, over 75 years >1800 pg/ml).
Purpose: The aim of the study was to evaluate the diagnostic importance, sensitivity, specificity, negative and positive predictive value of the NTproBNP rule-in criteria in the early diagnosis of HFmrEF and HFpEF.
Patients and **Methods:** We assessed the data of 207 patients (mean age: 76.5 ± 0.7 years, men: 61.4%, NYHA: 3.25 ± 0.35, ischemic etiology: 48.6%) with signs and symptoms of HF who had not been treated for HF previously and were referred to our hospital between 01.12.2015. and 30.11.2017. Echocardiography and NTproBNP measurement were performed in every case. Patients with atrial fibrillation, renal failure (GFR < 60 ml/min/1,73m2) and obesity (BMI>30 kg/m2) were excluded.
Results: By using the ESC rule-out criteria, HF was excluded in 56 cases. In the remaining 151 patients (72.9%) SHD/DD could be proved in 131 patients and HF was excluded in 20 patients. NTproBNP rule-in criteria were not met in any of these 20 patients. In the 131 patients with SHD/DD, rule-in criteria were met in 75 patients. In the HFmrEF and HFpEF patients diagnosed by the ESC criteria, the sensitivity of the NTproBNP rule-in criteria was 57.3%, specificity was 100%, negative predictive value was 26.3% and positive predictive value was 100%. When using both rule-in and rule-out NTproBNP criteria, HF could be excluded in 27.1%, the diagnosis could be confirmed in 36.2% with an easy laboratory examination, and time-consuming echocardiography for SHD/DD assessment is needed only in 36.7% of the patients.
Conclusion: Based on our findings, it appears that NTproBNP rule-in criteria reliably select HF patients in the LVEF = 40% patient population. In addition to the NTproBNP rule-out criteria, the use of rule-in criteria can significantly reduce the need for time-consuming SHD/DD assessment and thus shorten the time until the appropriate diagnosis is established.

P1734

Biological markers of endothelial dysfunction in patients with heart failure.

G A Gayane Shakaryants[1]; MV Kozhevnikova[1]; VY Kaplunova[1]; IS Ilgisonis[1]; AO Iusupova[1]; EA Zheleznikh[1]; JA Danilogorskaya[1]; EV Babayan[1]; ES Koniaeva[1]; VA Shakaryants[1]; EV Privalova[1]; YUN Belenkov[1]; NV Khabarova[1]
[1]*I.M. Sechenov First Moscow Medical State University, Moscow, Russian Federation*

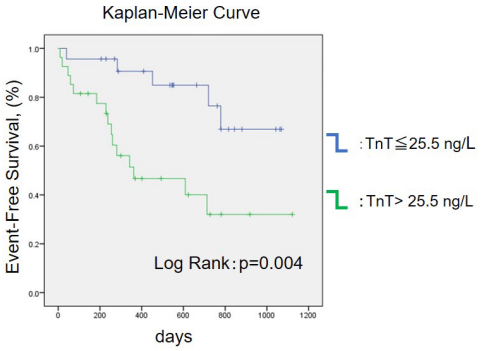
Background: the study was aimed to compare the level of biomarkers of endothelial dysfunction (endothelin-1 and E-selectin) in patients with heart failure (HF) as a result of ischemic heart disease and patients with coronary artery disease (CAD).
Patients and methods : We included 90 patients with CAD: 1) 40 patients with HF (the average 65,78 ± 8.79 years, women 16,EF 47,9 ± 7,16) 2) 50 patients without signs of HF (the average 65.31 ± 7.22 years, women 10, EF 59.23 ± 5.06). Among patients of the first group 17 persons (42,5%) have preserved ejection fraction (HFpEF), 16 persons (40%) with mid-range (HFmrEF) and 7 (17,5 %) - reduced ejection fraction (HFrEF). Diabetes mellitus type 2 (DM) was in 43 examined. The markers of endothelial dysfunction were assessed: E-selectin and endothelin-1 - by ELISA. We assessed endothelial function of large vessels (phase shear (PS, ms) and microcirculation (occlusion index (IO)).
Results: In patients with HF, the level of endothelin-1 was 0.86 fmol/L [0.41;1.3] significantly higher compared to the control group 0.87 [0.47; 1.28] p = 0.07. The same results were obtained for E-selectin: the level of the marker in the HF group was 48.37 ng/ml [40.77; 55.97] compared with the level 33.07 ng/ml [26.07, 40.06], p = 0.001 in the group with only CAD. There was a tendency for differences in the levels of E-selectin in subgroups of patients with HF (HFpEF 60.4 ng/ml [47.29, 73.51] HFmrEF 40.21 ng/ml [27.1, 53.32], HFrEF 39.51 ng/ml [19.69, 59.33] p = 0.066). Differences in endothelin-1 levels in patients with different variants of HF were not detected. There were not differences in levels of biomarkers in patients with and without DM. Strong positive correlation was revealed between the E-selectin level and the EF (r = 0.16, p <0.012), the negative correlation - endothelin-1 and EF (r = -0.35, p = 0.000). IO was decreased in both groups, perhaps in HF group it was significantly lower (1,45 ± 0,08) than in controls (1,6 ± 0.07) p = 0,003. Negative correlation was revealed between the E-selectin level and the IO (r = -0.4, p <0.05), and positive correlation between endothelin-1 and PS (r = 0.48, p = 0.05).
Conclusions: : 1) Significant increase in the levels of endothelin-1 and E-selectin in patients with CHF compared with the control group, which indicates an endothelial dysfunction, were found. 2) We obtained significant differences in the level of E-selectin in patients with HFpEF and HFrEF. 3) The levels of the endothelial dysfunction markers are interrelated with the ejection fraction.4) There was no significant difference in biological markers parameters between groups of patients with HF associated with diabetes mellitus type 2 and in patients with isolated HF

P1735

Prognostic significance of troponin t in patients with heart failure with preserved ejection fraction

S Suzuki[1]; H Motoki[1]; M Minamisawa[1]; Y Okuma[1]; W Shoin[1]; T Okano[1]; K Kimura[1]; S Ebisawa[1]; A Okada[1]; K Kuwahara[1]
[1]*Shinshu University Hospital, Matsumoto, Japan*

Background: Although several studies have demonstrated an association between elevated Troponin T (TnT) levels and risks of adverse clinical outcomes among patients with Heart Faliure with reduced Ejection Fraction (HFrEF), prognostic significance of TnT in Heart Failure with preserved Ejection Fraction (HFpEF) is not well established.
Purpose: To investigate the prognostic significance of TnT in patients hospitalized for decompensated HFpEF.
Methods: In consecutive 155 patients hospitalized for Heart Failure (HF), we evaluated TnT levels at discharge. All cause Death, non-fatal myocardial infarction, stroke, and HF hospitalization were prospectively followed up for median 449 [260-780] days.
Results: In our study cohort (age 76 [67-84] years, EF 45 ± 16%), major adverse cardiac events (MACE) were observed in 63 patients. TnT was significantly higher in patients with MACE in both HFpEF (36 [22, 66] ng/L vs 21 [14, 32] ng/L, p = 0.002, n = 64) and HFrEF (40 [29, 71] ng/L vs 27 [15, 56] ng/L, p = 0.021, n = 91) subgroups. TnT correlated with age, estimated glomerular filtration rate (eGFR), and B-type natriuretic peptide (BNP) levels. In Kaplan-Meier analysis, higher TnT group showed worse prognosis in both HFpEF (Figure, p = 0.004) and HFrEF (p = 0.010). In multiple Cox regression analysis, TnT level was an independent predictor for MACE (p = 0.004) after adjusting for age and eGFR (HR 1.018 [95% CI 1.005-1.032], p = 0.006), and age and BNP (HR 1.022 [95% CI 1.008-1.035], p = 0.001) in HFpEF population.
Conclusions: Elevated TnT levels were associated with MACE in patients not only with HFrEF but also HFpEF.



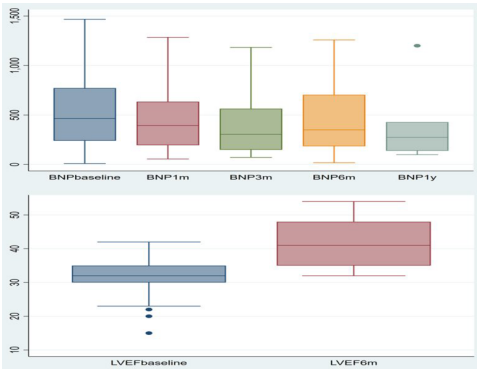
Kaplan Meier Curve (HFpEF)

P1736

Sacubitril-valsartan and BNP: Will they live happily ever after?

M Abellas-Sequeiros[1]; J M Vieitez Florez[1]; A Lorente[1]; G Alonso[1]; S Del Prado[1]; J M Del Rey[1]; J L Zamorano[1]
[1]*University Hospital Ramon y Cajal de Madrid, Madrid, Spain*

Introduction: After publication of the PARADIGM-HF trial, sacubitril/valsartan has been included in ESC Guidelines for the treatment of chronic heart failure. It is thought that sacubitril inhibits neprilysin, slowing down BNP degradation and rising its levels, but not NT-proBNP levels. That is the reason to recommend an NT-proBNP based monitoring. However, does this mean BNP is no longer useful during the follow-up of patients? Is it trustworthy in the acute setting?
Methods: To describe the evolution of BNP in that context, a series of patients with HFrEF who initiated LCZ696 was prospectively assessed. Clinical characteristics, aetiology, functional class and admissions were evaluated. BNP was analysed before treatment, in the first, third, sixth month and 1 year after treatment, just like in-hospital admission.
Results: Fifty-one patients with HFrEF receiving sacubitril/valsartan were included; mean age was 73 years old; 45 (88%) patients were men and 49% had ischaemic etiology. Mean LVEF was 32% and median estimated glomerular filtration rate was 60 ml/min. Regarding to OMT: 100% were on ACE-I, 89% beta-blocker and 81% MR antagonist; 33% had CRT and 35% an ICD. LCZ696 was discontinued in 9 patients (4 of them because of renal dysfunction; 1 hyperkalemia; 2 hypotension and the others because of economic trouble). One patient died during the follow up.
BNP levels were compared before and after the initiation of treatment with LCZ696 using nonparametric Wilcoxon signed-rank test. LCZ696 does not significantly rise BNP levels, as opposite, there was a tendency to lower levels in the long-term follow-up.
In acute decompensation BNP rises significantly in patients treated with a neprilysin inhibitor (p = 0,01), decreasing afterwards, resembling the biological response in the context of decompensation without sacubitril/valsartan.
Conclusions:
BNP could be still an applicable biomarker, not only in the acute setting, but also in clinically stable patients. We hypothesized that this tendency to lower BNP blood level, as NT-proBNP does, might be related to a decreased of parietal stress in context of heart failure improvement, as we described in that cohort, but more studies are needed to confirm it.

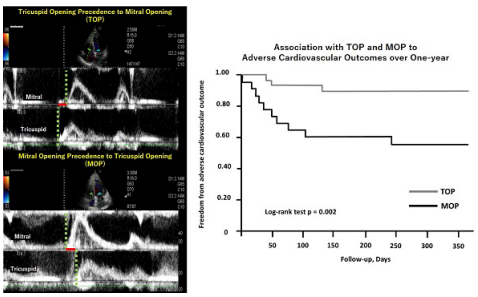


P1737

Time interval between mitral and tricuspid opening has prognostic value in patients with heart failure

M Sugahara[1]; M Asakura[1]; A Goda[1]; K Masai[1]; A Daimon[1]; T Masuyama[1]
[1]*Hyogo College of Medicine, Nishinomiya, Japan*

Background: There are no doubts about the values of comprehensive noninvasive assessment of LV and RV hemodynamics in the management of patients with heart failure (HF), the values have been hampered by methodological limitations. Dual Doppler echocardiography was used to overcome the limitations by measuring time interval between the mitral and tricuspid valve opening (MO-TO time) in a real-time fashion.
Purpose: We assessed hemodynamic correlates and prognostic value of MO-TO time in patients with HF.
Methods: We prospectively enrolled 60 patients with HF and sinus rhythm. MO-TO time was measured in addition to routine echo parameters, invasive hemodynamic parameters and plasma BNP level in all patients. Patients were divided into either of two groups based on the MO-TO time: MOP (MO precedence to TO), and TOP (TO precedence to MO) groups. We followed up the predefined adverse outcome, cardiovascular death and hospitalization due to worsening HF in all patients for a year.
Results: Pulmonary artery wedge pressure (PAWP) was higher in the MOP group than in the TOP group (21 ± 8.5 vs. 11 ± 4.5 mmHg, $p < 0.001$). PAWP correlated with MO-TO time ($r = -0.74$, $p < 0.001$). MOP had a high probability of adverse cardiovascular outcome (Log-rank test; $p = 0.002$). In univariate Cox analysis, mitral E/A ratio, BNP, and MO-TO time were significant predictors ($p = 0.044$, $p = 0.019$, and $p = 0.012$), respectively. An addition of MOP improved the predictive power of univariate predictors (mitral E/A ratio, BNP) in the bivariate Cox analysis.
Conclusions: MOP reflects pulmonary hypertension due to left heart disease and has a prognostic value in predicting adverse cardiovascular events in patients with HF.



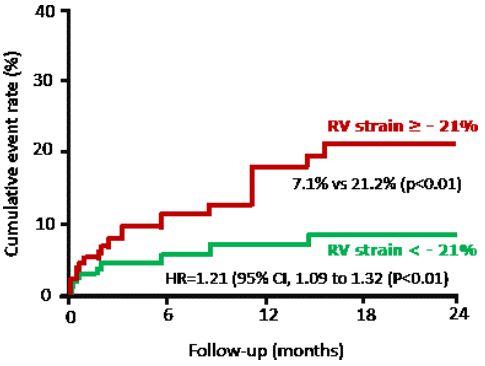
P1738

Right ventricular-2 dimensional strain as a prognostic factor in patients with dilated cardiomyopathy

IH Jung[1]; JH Park[1]; KS Kim[1]
[1]*Inje University, Seoul, Korea Republic of*

Funding Acknowledgements: Hanmi Pharm.Co.,Ltd.

Background: Several studies reported that systolic function of right ventricle (RV) influence the prognosis of patients with heart failure (HF). The aim of this study is to investigate the role of RV-2D strain as a prognostic factor for adverse events in patients with dilated cardiomyopathy (DCMP).



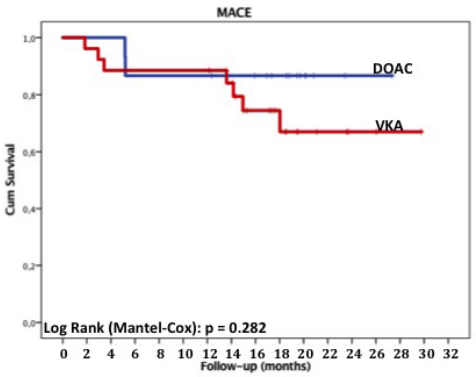
Cumulative incidence of adverse event

Methods: We reviewed medical records and analyzed echocardiographic data of 89 patients who had been newly diagnosed and registered the list of dilated cardiomyopathy at our institute from January 2015 to March 2016. Enrolled patients had been performed echocardiography annually according to our study protocol and the occurrence of adverse events including death, hospitalization, atrial fibrillation and fatal arrhythmia were noticed.
Results: The mean age of study population was 53 ± 17 years including 68 male patients (76.4%) and they have LVEF of 26 ± 10%. There was none of death during the follow-up period (mean 19 ± 7 months). Eleven patients (12.3%) presented with hospitalization for worsening HF. Atrial fibrillation newly occurred in 4 patients (4.5%) but fatal arrhythmia was none. Tricuspid annular plane systolic excursion (TAPSE), fractional area change of RV (FAC) and RV strain were related to adverse prognosis by Cox univariate analysis. However, mulivariate analysis showed that FAC and RV strain were independent predictors. FAC and RV strain demonstrated HRs of 0.92 (95% CI, 0.89 to 0.96; p < 0.01) and 1.21 (95% CI, 1.09 to 1.32; p < 0.01). Patients divided in RV strain < - 21% (n = 56) and -21% (n = 33) demonstrated a 2-year event rate at of 7.1% and 21.2% (p < 0.01).
Conclusion: This study demonstrated that RV strain would be a strong prognostic factor with other representing values of RV function including TAPSE and FAC in patients with DCMP.

P1739
The clinical impact of intraventricular thrombi

A Nunes-Ferreira[1]; R Santos[1]; JR Agostinho[1]; T Rodrigues[1]; N Cunha[1]; J Rigueira[1]; I Santos Goncalves[1]; I Aguiar-Ricardo[1]; T Guimaraes[1]; R Placido[1]; C David[1]; FJ Pinto[1]; AG Almeida[1]
[1]*Cardiology Department, Santa Maria Hospital, CHLN, CCUL, Lisbon University, Lisbon, Portugal*

Introduction: The occurrence of intracardiac thrombi is a condition of increasing clinical significance due to its frequency, potential embolic complications and scarce clinical evidence regarding optimal therapy. The impact on cardiovascular prognosis also remains uncertain.
Objective: Evaluate the impact of the presence of left intraventricular thrombus (LVT) on cardiovascular prognosis.
Methods: Retrospective unicentric study with the inclusion of all patients with echocardiographic diagnosis of LVT during 2016. Clinical, echocardiographic, therapeutic and follow-up data were collected. Predictors of major cardiovascular events (MACE) - acute myocardial infarction (AMI), stroke/transient ischemic attack (TIA), peripheral embolism and death were determined through multivariate Cox regression and Kaplan-Meier survival analysis.



Anticoagulation regimen in LVT

Results: We identified 48 patients (85% men, age 63 ± 13 years) with the diagnosis of LVT; 77% with ischemic heart disease. The mean left ventricular ejection fraction (LVEF) was 32.5 ± 9.2%; LV telediastolic volume 94 ± 41.4 mL; presence of apical aneurysm in 58% and segmental alterations in another location in 27%. 85% of patients had apical thrombus and 15% had another LV location. In 29% the thrombus was diagnosed during an episode of AMI. Mortality during follow-up was 14.6% (7.1 + 5.5 months). There was an association of MACE with age > 65 years (p = 0.01), presence of apical aneurysm (p = 0.02), creatinine > 1.9 (p = 0.004) and previous stroke / TIA (p = 0.024). In the multivariate analysis, age > 65 (p = 0.011, HR = 11.97 CI 95% 1.77-80.16) was the only independent predictor of MACE. On the other hand, the absence of previous stroke / TIA was a protective factor of MACE (p = 0.006, HR 0.16 95% CI 0.015-0.487). Regarding the anticoagulation strategy, direct oral anticoagulant (DOAC) therapy was not associated with an increased incidence of MACE (p = NS), with no difference between this strategy and vitamin K antagonists (VKA, p = NS).
Conclusion: In this study, in which the majority of the sample was anticoagulated, the independent predictors of the occurrence of MACE identified were age > 65 years and history of stroke / TIA. Although there is no evidence to support the safety of anticoagulation strategy with DOAC in the context of LVT, this strategy was not associated with a higher incidence of MACE when compared to vitamin K antagonists. Large randomized clinical trials are necessary to confirm these results.

P1740
Appearance of L wave Predicts the change of Left Ventricular and the Poor Outcome

K Kumiko Masai[1]; A Goda[1]; M Sugahara[1]; A Daimon[1]; M Asakura[1]; T Masuyama[1]
[1]*Hyogo College of Medicine, cardiovascular, Nishinomiya, Japan*

Background: L wave is easily recorded as mid-diastolic mitral forward flow with conventional Doppler echocardiography. L wave is occasionally detected in heart failure (HF) patients but its mechanism to produce L wave and the prognostic value is still unknown.
The aim of this study is to clarify the related factors of L wave in patients of HF with preserved ejection fraction (HFPEF) and reduced ejection fraction (HFREF) and the prognostic impacts of L wave in HF patients.
Methods and **Results:** One hundred fifty one HF patients were enrolled (HFREF: 82, HFPEF: 69). Both in HFPEF and HEREF, transmitral E velocity (E), E to mitral annulus velocity ratio and Left atrial volume index were higher with L wave than in those without L wave. Relative wall thickness (RWT) was lower in HFREF with L wave than those without L wave (0.26 ± 0.07 vs 0.30 ± 08). Meanwhile, in HFPEF patients, RWT was higher in patients with L wave than those without L wave (0.42 ± 0.07 vs 0.39 ± 0.07). Kaplan-Meier survival curve revealed that the patients with L wave demonstrated significant poorer prognosis compared those without L wave in HF patients (P < 0.05).
Conclusion: L wave is associated with LV diastolic dysfunction and LV geometry. Also L wave has potentially predicting value for the prognosis in patients of HF.

Echocardiographic characteristics

	ALL	HFpEF	HFrEF			
	L wave (+) (n = 48)	L wave (-) (n = 103)	L wave (+) (n = 25)	L wave (-) (n = 44)	L wave (+) (n = 23)	L wave (-) (n = 59)
SBP (mmHg)	128 ± 25	121 ± 24	132 ± 22	122 ± 24	120 ± 26	120 ± 24
HR(bpm)	65 ± 17	75 ± 18*	63 ± 13	75 ± 18*	66 ± 10	75 ± 17*
E (cm/s)	100 ± 28	74 ± 31*	106 ± 27	75 ± 24*	93 ± 27	74 ± 36*
e'(cm/s)	4.8 ± 1.8	4.9 ± 2.0	5.7 ± 1.8	5.7 ± 2.4	3.8 ± 1.2	4.3 ± 1.3
E/e'	23 ± 10	17 ± 9*	21 ± 11	16 ± 9*	25 ± 9	18 ± 9*
E/A	1.7 ± 0.8	1.2 ± 0.7*	1.5 ± 0.5	1.0 ± 0.7*	2.0 ± 1.0	1.2 ± 0.8*
LAVI (ml/m2)	58 ± 24	42 ± 18*	56 ± 24	38 ± 15*	60 ± 24	45 ± 19*
LVDd (mm)	55 ± 10	53 ± 10	49 ± 5	45 ± 7*	61 ± 9	59 ± 8
LVDs (mm)	40 ± 14	40 ± 13	30 ± 6	28 ± 6	51 ± 12	48 ± 10
LVMI (g/m2)	116 ±36	110 ± 40	119 ± 36	91 ± 32*	125 ±32	124 ± 38
RWT	0.31 ± 0.08	0.34 ± 0.09	0.43 ± 0.07	0.39 ± 0.07*	0.26 ± 0.07	0.30 ± 0.07

P1741
Association of global longitudinal strain and cmr t* to define iron overload in major b thalassemia

DR Pourzand[1]; DR Vakilian Aghouee[1]; DR Layegh[1]; TAY Manzari[1]; FAR Norouzi[1]
[1]*Mashad University of Medical Sciences, Cardiology Department, Mashad, Iran (Islamic Republic of)*

On behalf of: mashhad university of medical sciences
Funding Acknowledgements: atherosclerosis research center,mashad university of medical sciences

Background: beta-thalassemia major is a genetic disease that makes the patient dependent to blood transfusion so iron overload is common in these patients. Defining a reliable and feasible modality to assess iron overload in initial steps

can lower the chance of cardiomyopathy.In this study we tried to to find a reliable echocardiography index and cut of point to assess iron overload.
Methods:A cross sectional study was conducted from June 2016 to May 2017. Demographic features physical findings and Para clinic tests including CBC test and serum ferritin were gathered. All the patients underwent standard T2* CMR and Tissue Doppler Imaging (TDI) echocardiography. We used inter-evaluator agreement method to omit the biases .Patients were categorized in three classifications: Those with T2*>20ms as negative iron overload, 20ms>T2*>10ms as moderate and T2* < 10ms as sever iron overload. Echocardiography findings were compared in groups. Result:44 patients enrolled , 23 (52.35%) were male and 21 (47.7%) were female. Patients with hypertension, Rheumatic heart disease and cardiac disorders were excluded. Only one patient was diabetic. All the patients received chelator drugs. There was a significant difference in left ventricular global longitudinal strain average in positive or negative iron overload groups.(LV GLS average, p = 0.012).The cutoff point of -17.5 in LV GLS had a specificity of 100% and sensitivity of 43.8% in defining iron overload. Also in case of detecting severity between moderate and sever iron overload, LV GLS average (p < 0.001), left ventricular end diastolic volume index (LVEDI, p = 0.016), left ventricular end systolic index (LVESI, p = 0.016), and S velocity of tricuspid valve (p = 0.32) showed significant difference between the two groups.
Conclusion: LV GLS average may be used as a specific and somehow sensitive echocardiography parameter for detection of iron overload.
Keywords: left ventricular global longitudinal strain, major thalassemia, CMR T*, Iron overload

Table 1

Specificity	Sensitivity	Cut point
32%	68.8%	-20.5
40.5%	62.5%	-19.5
100%	43.8%	-17.5
100%	25%	-16.5
100%	6.2%	-15

specificity, sensitivity, and cut point of GLS echocardiography

P1742

2D phase contrast flow in the ascending aorta at 7 tesla: preliminary results

A Kosmala[1]; MR Stefanescu[2]; D Lohr[2]; M Terekhov[2]; LM Schreiber[2]
[1]University Hospital Würzburg, Comprehensive Heart Failure Center, Chair of Cellular and Molecular Imaging; Department of Radiology, Würzburg, Germany; *[2]University Hospital Würzburg, Comprehensive Heart Failure Center, Chair of Cellular and Molecular Imaging, Würzburg, Germany*

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Introduction: Due to its high potential there is growing demand for the application of ultra-high field (B0 = 7T) scanners in cardiovascular magnetic resonance (CMR) imaging, although technical challenges increase significantly with the static magnetic field strength. For evaluation and follow-up of patients with cardiovascular disease, ventricular morphology and function are important clinical parameters, which can be assessed non-invasively and comprehensively using CMR. First studies have shown a high level of agreement for ventricular volumetric parameters measured at 7T and routine clinical field strengths. Another fast way of obtaining basic hemodynamic parameters is 2D phase contrast CMR, which can be used to measure blood flow in the ascending aorta. In the absence of valve disease, the aortic forward flow should resemble the left ventricular stroke volume. However, to date flow parameters in the ascending aorta based on 2D phase contrast measurements at 7T have not yet been validated.

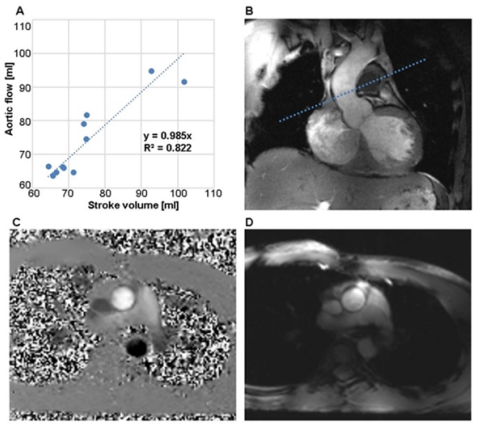


Figure 1 (A) Positive correlation between aortic forward flow determined by phase contrast imaging and stroke volume derived from CINE images. (B) Exemplary plane used for acquisition of phase contrast measurements at 7T (dotted blue line). (C) and (D) Phase contrast velocity and magnitude images at 7T, respectively.

Purpose: To assess the agreement between parameters of cardiac function derived from 2D phase contrast measurements in the ascending aorta and left ventricular short axis gradient-echo (GRE) CINE pulse sequences at 7T in healthy subjects.
Methods: 11 healthy volunteers (6 female, 5 male) were scanned using a 1TX/16RX thorax coil. Mean subject age was 27.3 years (range 22-39), and body weight 67.6 kg (range 52-92 kg). For triggering both the integrated ECG (n = 6) and an external acoustic triggering (n = 5) system were used. Sequence parameters for the short axis GRE CINE stack were TE = 3.57 ms, TR = 30.6-88.3 ms, voxel size 0.6x0.6x6.0 mm, segments 6-11, phases 20-35, slices 14-17. The parameters for the phase contrast sequence were TE = 98.9 ms, TR = 3.2 ms, voxel size 1.5x1.5x6.0 mm, segments 7-9, phases 20-25, VENC = 150 m/s. Volumetric and flow analyses were performed on an integrated scanner-side software. Agreement between stroke volume und aortic forward flow was analysed using the Pearson correlation coefficient and a two-sided t-test.
Results: Mean left ventricular stroke volume determined by CINE sequences was 74.9 ml (standard deviation (SD) 11.3 ml) and mean forward flow in the ascending aorta based on phase contrast imaging was 73.9 ml (SD 10.8 ml), showing no significant difference (p = 0.52) and a strong positive correlation (r = 0.91) (Figure 1).
Conclusion: We found a high level of agreement between stroke volume based on short axis GRE CINE sequences and aortic forward flow derived from 2D phase contrast imaging at 7T. This suggests that phase contrast CMR at 7T can correctly quantify ascending aortic flow and thus may play an important role in potential future clinical assessment of valve disease and cardiac function at 7T. However, a larger patient sample, in particular of patients with cardiac disease is essential for improving clinical acceptance. Moreover, validation against flow parameters acquired at routine clinical field strengths is necessary.

P1743

Relationship between myocardial viability and development of chronic heart failure in patients after ST elevation myocardial infarction

M Mirmaksudov[1]; S Kenjaev[2]; A Alyavi[1]; SH Turg'unboyev[1]; ML Kenjayev[3]; R Saydaliyev[1]
[1]Tashkent Medical Academy, 2nd department of hospital and facultative therapy, Tashkent, Uzbekistan; *[2]Republican Research Center of Emergency Medicine, Tashkent, Uzbekistan*; *[3]Bukhara branch of Republican Research Center of Emergency Medicine, Bukhara, Uzbekistan*

Background: Myocardial infarction (MI) is remaining the most common cause of heart failure (HF) worldwide. The presence of a viable myocardium in the damage area after adequate reperfusion prevents development of severe LV dysfunction and chronic heart failure(CHF).
Purpose: to study the relationship between identifying the myocardial viability of the left ventricle and the development of heart failure in patients after ST segment elevation myocardial infarction(STEMI).
Methods. 134 patients with STEMI of anterior wall were examined. The average age is 61 ± 5,3 year. Successful PCI was performed in all patients within maximum 12 hours. All patients initially underwent transthoracic echocardiography. In all patients, average LVEF was 45 ± 4,2%. All patients underwent low dose dobutamine stress echocardiography for verifying the myocardial viability (in 2-3th days). Depending on the results of low dose dobutamine stress echocardiography, the patients were divided into 2 groups. The 1st group comprised 78 patients (58,2%) with viable myocardium, the 2nd group of 56 patients (41,8%) without viable myocardium. A follow-up examination of the patients was carried out after 3 months.
Results: In our study, low dose dobutamine stress echocardiography didn't cause any complication in acute period of disease. The average value of LVEF in the first group with the introduction of low dose of dobutamine significantly increased to 52 ± 4,3%, while in the second group it practically did not change. After 3 months, as suggested by the results of low dose dobutamine stress echocardiography in the first group, LVEF was improved to 51+3,9% and in the second group LVEF decreased to 42 ± 2,3%. Among the patients of the first group, in the third month, Class I HF (NYHA) was observed in 67 patients (85,9%) and Class II HF in 11 patients (14,1%). Among patients of the second group, Class I HF developed in 19 patients (33,9%), Class II HF in 21 patients (37,5%), Class III HF in 10 patients (17,8%). In 2 patients (3,6%) developed Class IV HF. In the 2nd group, 1 (1,8%) fatal outcome was identified.
Conclusions: Thus, the presence of myocardial viability after MI, determines the improvement of global contractile function of the left ventricle after 3 months. The

absence of myocardial viability in patients after STEMI is an important predictor of the development of severe HF classes and death in our followed-up patients.

P1744

Cardiac sympathetic activity and global contractile function in patients with dilated cardiomyopathy

VV Viktor Saushkin[1]; AI Mishkina[1]; KW Zavadovsky[1]; VV Shipulin[1]; AV Mochula[1]; DI Lebedev[2]; YUB Lishmanov[1]; SV Popov[2]
[1]Cardiology Research Institute, Tomsk NRMC, Nuclear Medicine Department, Tomsk, Russian Federation; *[2]Cardiology Research Institute, Tomsk NRMC, Department of surgical treatment of cardiac rhythm disorders and pacing, Tomsk, Russian Federation*

Funding Acknowledgements: Grant of the President of the Russia Federation

Background: Cardiac sympathetic activity dysfunction has a huge impact on the development of dilated cardiomyopathy. Radionuclide assessment of cardiac sympathetic activity and ventricular dyssynchrony may help to develop new predictors of dilated cardiomyopathy treatment efficacy.
Purpose: Aim of this study was to evaluate the relationship between cardiac sympathetic activity and global contractile function in patients with dilated cardiomyopathy before cardiac resynchronization therapy.
Methods: The study comprised 32 patients (mean age of 66 ± 11 years) with chronic heart failure (NYHA III) due to dilated cardiomyopathy. All patients underwent 123I-MIBG imaging and gated blood-pool SPECT (GBPS). Systolic and diastolic functions (EDV, ESV, and EF) as well as mechanical intraventricular dyssynchrony both for the left (LV) and the right ventricles (RV) were analyzed. Late Heart to mediastinum ratio (H/M) as well as 123I-MIBG washout rate (WR) were calculated. All examinations were performed using GE Discovery NM/CT 570C with cadmium-zinc-telluride detectors.
Results: According to GBPS data in all patients the LV and RV dilatation and contractility impairment were revealed. The main parameters of cardiac volumes were the following: LV_EDV 291 ml (237-388 ml); LV_EF 24% (20-32%); LV peak ejection rate (PER) 0,89 EDV/s (0,75-1,39 EDV/s); RV_EDV 176 ml (132-217 ml); RV_EF 39% (19-54%); RV_PER 1,81 EDV/s (0,75-1,38 EDV/s). Moreover, severe mechanical dyssynchrony of both ventricles was detected: LV intraventricular dyssynchrony - 119 ms (91-161 ms); RV intraventricular dyssynchrony - 102 ms (77-161ms); interventricular dyssynchrony - 66 ms (37-92 ms). According to 123I-MIBG imaging median values of late H/M was 1,6 (1,43-2,13), median value of 123I-MIBG WR was 24% (18-29%).
The correlation between the cardiac sympathetic activity and contractile indexes of both ventricles was found out: H/M and LV_EDV (r=-0,54; p = 0,05), H/M and LV_ESV (r=-0,49; p = 0,05), H/M and RV_EDV (r = 0,39; p = 0,05), H/M and LV intraventricular dyssynchrony (r = 0,39; p = 0,05). The 123I-MIBG washout rate correlated with: LV_EDV (r = 0,47; p = 0,05), LV_ESV (r = 0,41; p = 0,05), RV_EF (r = 0,40; p = 0,05), RV PER (r=-0,42; p = 0,05).
Conclusion: In patients with dilated cardiomyopathy the relationship between cardiac sympathetic activity and contractile function was found out. These data may be used in the follow-up study after CRT device implantation in order to develop new predictors of CRT outcomes.

P1745

The first and last echocardiographic examination in patients with chronic heart failure; experience from a single outpatient clinic

V Arva[1]; I Krajnc[2]; FH Naji[2]
[1]Faculty of Medicine, University of Maribor, Maribor, Slovenia; *[2]University Medical Centre Maribor, Department of Cardiology and Angiology, Maribor, Slovenia*

Background: In patients with chronic heart failure echocardiographic examinations are routine procedures used to confirm the diagnosis of heart failure (HF) and to evaluate heart function. Left ventricular ejection fraction (EF) is one of the most basic echocardiographic parameters measured in patients with HF and clinicians rely on it heavily. The course of HF may be very heterogeneous. It is often nonlinear, with many fluctuations. It is probable that different pathophysiological processes play a different role in HF subgroups.
Purpose: Aim of this study was to examine the possible connection between basic echocardiographic measurements and the duration of HF in patients with chronic HF, managed in an outpatient clinic. We used data from the first echocardiographic examination at the beginning of HF, and their last examination before their death.
Methods: This is a retrospective study from a single outpatient clinic for chronic HF. Inclusion criteria were clinically confirmed diagnosis of HF, and a known cause of death. Due to a small number of patients with HFpEF only HFrEF and HFmrEF patients were included. Patients were treated according to the current standard guidelines. Ultrasound measurements included LVEDD, RVEDD, LA, mitral and tricuspid regurgitation grade, diastolic dysfunction, tricuspid gradient, EF, and a composite parameter of LVEDD and EF. We also analysed the differences between the first and the last measurement and the association between different measurements and the duration of heart failure.
Results: The study included 97 patients with HF. The average age was 67.5 ± 12.1 years and 81 (83.5%) patients were male. The average duration of heart failure was 7.1 ± 4.5 years. Ischemic aetiology was found in 52 patients (53.6%). Cardiovascular cause of death was found in 72 patients (74.2%). On the initial ultrasound, the mean LVEDD was 60.5 ± 9.2 mm, LA 45.4 ± 8.0 mm, and EF 29.7 ± 10.5 %. On their last examination mean LVEDD was 60.5 ± 10.6 mm, LA 48.7 ± 9.4 mm and EF 26.8 ± 12.3 %. The composite parameter (LVEDD x EF) in the initial measurement was 17.5 ± 6.1 mm, and 15.4 ± 5.7 on the last.
There was a correlation between the duration of HF and the initial EF (0.26 p = 0.017) and while the correlation was not significant with LVEDD, we observed a significant correlation for the composite parameter LVEDD x EF (0.35 p = 0.001). In the group of patients that died from cardiovascular causes, the correlation was accentuated (EF: 0.39 p = 0.002; composite parameter: 0.41 p = 0.001). There was no significant association between the measurements from the last examination and the duration of HF.
Conclusion: Our study shows that the initial, but not the last echocardiographic measurements can provide important prognostic factors for the duration of HF. EF, while important, can be overemphasised, and even the simple composite parameter of LVEDD and EF showed a better fit, suggesting that a more complex picture must be taken into account.

P1746

The prognostic significance of the 12-lead ECG in peripartum cardiomyopathy

J Hoevelmann[1]; CA Viljoen[2]; J Baard[1]; K Manning[3]; J Bauersachs[4]; K Sliwa[1]
[1]University of Cape Town, Hatter Institute for Cardiovascular Research in Africa, Cape Town, South Africa; *[2]University of Cape Town, Division of Cardiology, Cape Town, South Africa*; *[3]University of Cape Town, Department of Medicine, Cape Town, South Africa*; *[4]Hannover Medical School, Department of Cardiology and Angiology, Hannover, Germany*

Background: Peripartum cardiomyopathy (PPCM) is defined as heart failure secondary to left ventricular (LV) systolic dysfunction, which develops in previously healthy women towards the end of pregnancy or up to five months following delivery. PPCM contributes significantly to maternal morbidity and mortality, with only 23 to 54% of patients having full LV recovery at 6 months. The degree of systolic dysfunction and ventricular dilatation on echocardiography have previously been reported as predictors of poor outcome in PPCM. However, it remains elusive whether any features on the electrocardiogram (ECG) have a prognostic value in this condition.
Purpose: We aimed to assess the predictive utility of the ECG in the long-term outcome of PPCM.
Methods: 12-lead ECGs of women with PPCM were analysed at index presentation, and at 6 and 12 months follow-up. Poor outcome was determined by the combined endpoint of death, rehospitalisation, NYHA class III/IV or left ventricular ejection fraction (LVEF) < 35% at follow up.
Results: This cohort of 59 patients with PPCM (median age 28.68, IQR 25.69-31.71) presented with a median LVEF of 33% (IQR 25-40), which improved to 46% at 6 months (P < 0.001) and 54% at 1 year (P = 0.001). 30.77% and 37.93% of patients had a poor outcome at 6 and 12 months respectively. The median heart rate was 87bpm (IQR 71-102) at baseline. Initial sinus tachycardia (<100bpm) was associated with poor outcome at 6 months (OR 7, 95% CI 1.55-31.52, P = 0.011) and 1 year (OR 9.33, 95% CI 1.65-52.68, P = 0.011). The median QRS width was 82ms (IQR 78-88). Only 3 patients presented with left bundle branch block. Fragmented QRS and pathological Q waves did not predict poor outcome. Poor R wave progression (R/S ratio < 1 in V4), which declined from 46.2% at baseline to 26.9% after 1 year (P = 0.019), had no prognostic value. While 17 patients met Sokolow-Lyon criteria for left ventricular hypertrophy (LVH) on ECG, echocardiography showed LVH in only 1 patient (PPV 0, NPV 97%). T wave inversion was often encountered at baseline (69%), but tended to resolve with time (56% at 6 months, P = 0.527; 44% at 12 months, P = 0.02). T wave inversion in any lead was associated with LVEF < 35% at presentation (OR 5.45, 95% CI 1.64-18.09, P = 0.006), but did not predict poor long-term outcome. The baseline median QTc interval (454ms, IQR 427-471) reduced significantly within 1 year (426ms, IQR 411-454, P = 0.001). An initial prolonged QTc interval (<460ms) predicted poor outcome at 6 months (OR 10, 95% CI 1.8-55.63, P = 0.009). On multivariate logistic regression analysis, prolonged QTc and sinus tachycardia at baseline were independent predictors of poor outcome at 6 months (OR 14.58, 95% CI 1.41-150.74, P = 0.025) and 1 year (OR 24.38, 95% CI 1.44-410.43, P = 0.028) respectively.
Conclusions: Sinus tachycardia and prolonged QTc at baseline are predictors of poor long-term outcome in PPCM. T wave inversion is associated with an initial LVEF < 35%, but does not predict long-term outcome.

P1747

Plasma clusterin but not neprilysin levels are associated with ischemic acute myocardial injury

D Traxler-Weidenauer[1]; M Gyongyosi[1]; J Winkler[1]; K Zlabinger[1]; A Gugerell[1]; M Riesenhuber[1]; C Mueller[1]; D Lukovic[1]; N Pavo[1]
[1]*Medical University of Vienna, Division of Cardiology, Vienna, Austria*

Background: Currently a variety of biomarkers, e.g. plasma neprilysin (NEP), clusterin (CLU), neutrophil gelatinase-associated lipocalin (NGAL), endothelin-1 (ET1) and osteopontin, are under thorough investigation as cardiac biomarkers for prognosis and diagnosis in the setting of ischemic myocardial infarction (MI) and cardiac remodeling as a consequence of MI.
Purpose: The aim of this study was to assess suitability of the above-mentioned biomarkers in a porcine model of acute MI and correlate them with cardiac magnetic resonance imaging (cMRI) parameters.
Methods: A total of 24 pigs underwent MI induced by 90min percutaneous balloon occlusion of the mid left anterior descending coronary artery (LAD). cMRI was performed at day 3 and after 6 weeks to assess infarction size, left ventricular end-systolic volume (LVESV), left ventricular end-diastolic volume (LVEDV) and left ventricular ejection fraction (LVEF). NEP and CLU concentrations as well as other cardiac biomarkers (NT-proBNP, NGAL, ET1, osteopontin, troponin I) were measured by ELISA and miRNA21 and miRNA29 through rtPCR during the acute and subacute phase of MI. Troponin I and cMRI were used to validate our porcine MI model. Furthermore NT-proBNP was assessed as a heart failure marker. The course of biomarkers and correlations with cMRI parameters were investigated.
Results: The area at risk was 16.4% of LV at day 3 after acute MI and was accompanied by a depressed LV function (LVEF = 36.1%). LVEF remained depressed (39.5%) with signs of adverse remodeling reflected by increased LVESV (93.9ml) and LVEDV (153.5ml) during the 6-week follow-up period. Further NT-proBNP levels were significantly increased after 3 weeks (pre vs. 3 weeks: 112.3 vs. 189.9 pg/ml, $p = 0.03$). Plasma levels of NGAL (pre vs. 3 weeks: 122.7 vs. 224.1 pg/ml, $p < 0.05$), miRNA21 (pre vs. 3 weeks: 1.0 vs. 7.6 fold increase, $p < 0.0001$) and miRNA29 (pre vs. 3 weeks: 0.6 vs. 14.3 fold increase, $p < 0.0001$) were significantly elevated at 3 weeks post MI. CLU levels were significantly decreased (post vs. 3 weeks: 8276 vs. 5250 pg/ml, $p < 0.001$). However, a correlation with troponin I levels was not observed. Changes in plasma NEP concentrations could not be observed ($p = 0.59$).
No correlations of cMRI parameters with CLU were identified, however, NEP levels post MI correlated with LVEDV ($r = 0.424$, $p = 0.049$) and LVESV ($r = 0.470$, $p = 0.027$) at day 3.
Conclusions: As opposed to recent data on NEP in chronic heart failure, plasma NEP levels were not associated with acute ischemic injury in a porcine model of reperfused myocardial infarction. However, CLU, NGAL, miR21 and miR29 were significantly associated with acute myocardial injury.

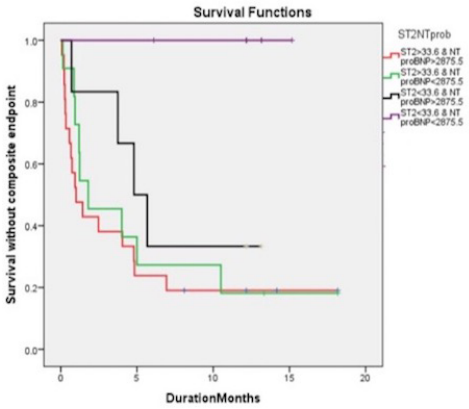
P1748

Comparing sST2 with the classical biomarkers (Troponin T and NTproBNP) in the prognostication of patients with heart failure with reduced ejection fraction

M N Dilip[1]; A G Koshy[1]; K S Viswanathan[1]; P N Gupta[1]; K Sivaprasad[2]; V V Radhakrishnan[1]; M Iype[1]
[1]*Government Medical College, Cardiology, Trivandrum, India*; [2]*Government T D Medical College, Cardiology, Alappuzha, India*

Funding Acknowledgements: Kerala Heart Foundation

Introduction: Suppressor of Tumorgenicity 2 (ST2) is a member of the IL-1 receptor family. Its soluble form (sST2) has been implicated as a marker of poor outcome in patients with heart failure.
Purpose: The aim of the study was to find out the prognostic value of serum levels of sST2 biomarker and compare it with NT-proBNP and Troponin T in patients presenting with Heart failure with reduced ejection fraction (HFrEF) for predicting composite endpoint of cardiac death and need for re-hospitalisation for worsening HF.
Methods: We prospectively recruited 51 patients admitted with HFrEF and followed them up for 1 year. Patient with recent(<2months) ACS or revascularisation, severe valvular heart disease, end-stage renal disease, cardiogenic shock or heart failure due to acute myocarditis, anemia, thyrotoxicosis or hypocalcemia were excluded.
Clinical evaluation, echocardiography along with serial measurements of biomarkers were done at admission, discharge, 1 month, 6 months and at the end of 1 year. Patients were categorised in to Group A - who did not meet endpoint and group B who met the composite endpoint.



Biomarkers and Survival analysis

Results: Ischemic heart disease (48%) followed by dilated cardiomyopathy (43.8%) were the most common cause for heart failure in the study cohort. Baseline characteristics were fairly similar in both the goups (mean age 57 years) except for total leucocyte counts (group B = 14437 vs group A = 8331/mm3, $p = 0.043$) and LV volumes, both end diastolic (group B = 165.9ml vs group A = 134.2ml, $p = 0.012$) and end systolic volumes (group B = 124.5ml vs group A = 99.6ml, $p = 0.031$). Receiver Operating Characteristic (ROC) analysis of % change in sST2 was strongly reflective of cardiac decompensation with area under the curve (AUC) of 0.746 which was better than NTproBNP (AUC 0.737; $p = 0.006$) and ST2 on admission alone (AUC 0.696, $p = 0.024$). Cut off values of sST2 = 33.6ng/ml (sensitivity = 70%, specificity = 66.7%, $p = 0.0001$), NT-proBNP = 2875.5 pg/ml (sensitivity = 86.7%, specificity = 66.7%, $p = 0.013$) was associated with worse outcomes while Troponin T was not found to be significant in predicting prognosis($p = 0.253$). A percentage reduction in sST2 levels of less than 24.76% from baseline value was associated with unfavourable future course (sensitivity = 90%, specificity = 66.7%, $p = 0.013$). Age >60 years, atrial fibrillation, baseline sST2 >33.6ng/ml and reduction in sST2 levels of <24.76% were found to be independent predictors of outcome on multivariate analysis. Patients with both sST2 and NTproBNP levels exceeding 33.6ng/ml and 2875.5 pg/ml respectively had an event free survival of less than 20% at the end of 1 year.
Conclusion: We concluded that serial measurement of sST2 is a useful tool to predict future course of the disease. sST2 = 33.6ng/ml is an independent predictor and has a 3.25 fold higher risk of cardiac death or heart failure re-hospitalisation. Combining sST2 and NT-proBNP has an incremental value in prognostication in patient presenting with HFrEF.

Chronic Heart Failure - Treatment

P1749

Tertiary heart failure care in the netherlands: what is the added value

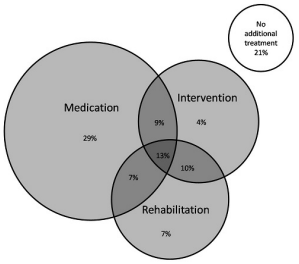
MPM Marijke Vester[1]; LF Tops[1]; ML Antoni[1]; J Braun[2]; RJM Klautz[2]; HF Verwey[1]; R Wolterbeek[3]; MJ Schalij[1]; SLMA Beeres[1]
[1]*Leiden University Medical Center, Cardiology, Leiden, Netherlands*; [2]*Leiden University Medical Center, Cardiothoracic Surgery, Leiden, Netherlands*; [3]*Leiden University Medical Center, Department of Statistics, Leiden, Netherlands*

Background/introduction: Ideally, heart failure care is provided in a multi-professional manner with a seamless transition across primary, secondary and tertiary care. For this to succeed, it is essential that the added value of each part in the chain of the heart failure care is clear.
Aim :The aim of the current study was to evaluate the added value of a dedicated heart failure management program in a tertiary referral hospital.
Methods : Heart failure patients with a reduced left ventricular ejection fraction (LVEF) referred by a cardiologist between 2011 and 2015 to our tertiary heart failure outpatient clinic to assess their additional heart failure treatment options were included. Treatment options were identified systematically and the effect on clinical outcome and hospital admissions were evaluated.

Clinical outcome							
	Baseline	6 months	12 months	P - value*			
NYHA functional class	2.4	(95% CI 2.3 - 2.5)	1.9	(95% CI 1.9-2.0)	1.9	(95% CI 1.8-2.0)	P <0.001
LVEF (%)	29	(95% CI 29 - 30)	33	(95% CI 32 - 36)	34	(95% CI 33 - 35)	P <0.001
NT-pro BNP (ng/L)**	7.6	(95% CI 7.4 - 7.7)	7.1	(95% CI 6.9 - 7.2)	7.0	(95% CI 6.9 - 7.2)	P <0.001
Heart rate (/min)	75	(95% CI 74 - 77)	72	(95% CI 71 - 73)	70	(95% CI 68 - 72)	P <0.001
Systolic blood pressure (mmHg)	115	(95% CI 113 - 116)	113	(95% CI 111 - 115)	114	(95% CI 112 - 116)	P = 0.540
Diastolic blood pressure (mmHg)	70	(95% CI 69 - 71)	70	(95% CI 68 - 71)	70	(95% CI 68 - 71)	P = 0.970
	-6 months - baseline	Baseline - 6 months	6 months - 12 months				
Admission (%)	33		25		11	P <0.001	

* P value compared with baseline** Estimated using log transform.Clinical outcome at baseline and 6- and 12 months follow up. Continuous data are presented as mean (SD). Categorical data are presented as numbers (%). NYHA, New York Heart Association; N-terminal pro B type natriuretic peptide.

Results: 454 patients (62 ± 12 year, 69% male) were included. Additional treatment options were identified in 79% of patients comprising optimisation of medication in 58%, invasive treatment in 41% and cardiac rehabilitation in 40%. At 1 year, NYHA class improved from 2.4 (95% CI 2.3-2.5) to 1.9 (95% CI 1.8-2.0;P <0.01) and LVEF increased from 29% (95% CI 29-30%) to 34% (CI 33-35%;P <0.01). Moreover, the percentage of patients admitted for decompensated heart failure declined from 33% before referral to 25% (P <0.01) in the first 6 months and 11% (P <0.01) in the 6-12 months after referral.
Conclusion : A dedicated heart failure management program in a tertiary referral hospital is of added value since additional treatment options can be identified in the majority of patients yielding improved clinical outcome and a reduction in hospital admissions for decompensated heart failure.



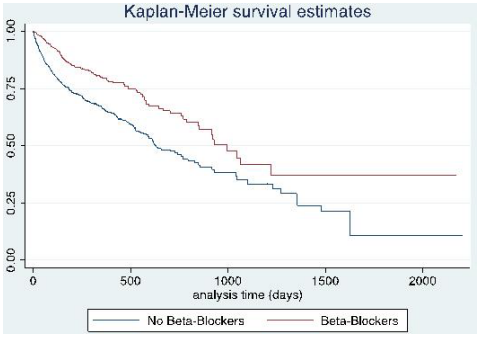
The additional treatment options

P1750
The protective effect of beta-blockers in 3,278 advanced heart failure patients treated with continuous inotropes

O Havakuk[1]; M Wilson[2]; T Artig-Brown[3]; S Savel[3]; N Meux[3]; LP Grazette[4]
[1]Tel Aviv Sourasky Medical Center, Tel Aviv, Israel; *[2]University of Southern California, Preventive Medicine, Los Angeles, United States of America*; *[3]Option Care, Chicago, United States of America*; *[4]University of Southern California, Cardiology, Los Angeles, United States of America*

Funding Acknowledgements: None

Background: Continuous inotropic therapy is considered deleterious in the management of advanced heart failure (HF) patients. Nevertheless, data supporting this deleterious effect were drawn from studies in which the utilization of ß-blockers therapy was scarce.
In the present study we sought to examine the potential protective effect of additive ß-blockers therapy in a large cohort of advanced HF patients treated with continuous inotropic therapy.



Beta-blockers effect on survival

Methods and Results: Data were prospectively drawn from a US nationwide home infusion company. The cohort included 3,278 advanced HF patients treated with inotropes between May 2009 and June 2016. Mean age was 60.8 ± 16.1 years and 74% were male. Median time on inotrope therapy was 121 days (IQR 35-207), 2,289 patients were treated with milrinone, 935 with dobutamine and 54 with dopamine. ß-blockers therapy was applied in 799 (24.2%) patients and reduced mortality rates considerably (HR1.8, CI 95%:1.6-2.0, p <.001). Additionally, the use of ß-blockers therapy eliminated survival advantages in milrinone-treated compared with dobutamine-treated patients (HR 1.12, CI 95% 0.92-1.27, p = 0.19 and HR 1.65, CI 95%1.4-1.95, p = 0.001 with and without ß-blockers therapy respectively) and was shown to further improve survival rates with patients' advancing age (HR 0.76, CI 95%: 0.51-1.13, p = 0.178; HR 0.49, CI 95%: 0.31-0.79, p = 0.003; HR 0.46, CI 95%: 0.31-0.68, p <0.001; HR 0.42, CI 95%: 0.3-0.59, p <0.001 for age groups <53, 54-63, 64-73 and 73> years respectively).
Conclusion: Our results suggest that additive ß-blocker therapy can significantly improve survival rates in advanced HF patients treated with continuous inotropic therapy.

P1751
The benefits of ivabradine in the management of angina pectoris and heart failure.

Z Zainab Raissuni[1]
[1]Ibn Sina University Hospital, Cardiology B, Rabat, Morocco

On behalf of: ESSENTIEL Study group

Introduction: Several studies have shown the benefit of Ivabradine, in the management of both angina and heart failure.
Purpose: The study ESSENTIEL 2 aims to observe in the real clinical practice conditions in Morocco, over a 4-month follow up period, the effects of an exclusive HR reduction with Ivabradine in stable coronary angina and chronic heart failure patients. Methodology: Non-interventional, observational study conducted on an open cohort in Morocco, in patients with stable angina or chronic heart failure. Heart rate, Ejection Fraction, functional classification of NYHA for heart failure patients as well as SEATTLE self-assessment quality of life questionnaire for angina patients, were documented at baseline and after 1 and 4 months. The results were analyzed using descriptive statistical methods, by the SPSS version 20.
Results: 420 patients were included in 39 cardiology centers over the country. The global population mean age was 65,61 ± 11,02 years and 67,1% of them were men. 92,8% were receiving beta-blockers, 49,4% of which were carvedilol and 24,5%

Bisoprolol. The HF group represent 54,8% (n = 230) of the global population. Its mean HR was 90,73 ± 15,45bpm, with a LVEF of 39,35 ± 11,47. The NYHA classification at baseline was 16,6% NYHA II, 63,3% NYHA III and 20,1% NYHA IV. After 1 and 4 months of prescribing Ivabradine the HR was reduced to 71,65 ± 12,21 bpm and 64,21 ± 9,59 bpm, respectively. A 8,21% improvement of the LVEF was observed after 1 month, and reached 13,7% (p < 0,0001) after 4 months . It was accompanied by a shift in NYHA classification towards better functional class: 35,2% in NYHA I, 50% NYHA II, 14,3% NYHA III and only 0,5% remained NYHA IV after 4 month follow up.The angina group represents 45,2% (n = 190), the mean HR was 85,41 ± 13,99bpm with a LVEF 52,32 ± 11,91. After 1 and 4 months of prescribing Ivabradine the HR was reduced to 67,99 ± 9,80bpm and 62,14 ± 8,15 bpm, respectively. The evolution of the five SAQ domains are resumed in the table. The rate of adverse events was 3,1%, the main adverse events reported with Ivabradine are those related to its mechanism of action namely bradycardia.Conclusion: over 4 months of treatment, using Ivabradine is associated with a significant reduction in HR, an improvement in LVEF and symptoms of heart failure and stable angina; these benefits were accompanied with an improved QoL and good tolerability.

	Baseline (V0)			4-months follow up (V2)		
	Poor	Good	Excellent	Poor	Good	Excellent
Physical limitation	137(77,8%)	30(17%)	9 (5,1%)	46(29,3%)	75(47,7%)	36(22,9%)
Anginal stabilization	98(52,4%)	38(20,3%)	51(27,2%)	2(1,2%)	12(7,3%)	150(91,4%)
Anginal frequency	73 (41,4%)	20(11,3%)	83(47,1%)	1(0,6%)	9(5,7%)	148(93,6%)
Treatment satisfaction	138(76,6%)	27(15%)	15(8,3%)	8(4,8%)	87(53%)	69(42%)
Disease perception	157(84,8%)	12(6,4%)	16(8,6%)	33(20,1%)	68(41,4%)	63(38,4%)

table1

P1752

Anti diabetic therapy in patients with heart failure and type 2 diabetes mellitus in general population.

N Nabil Kraiem[1]; I Fomin[1]; NG Vinogradova[1]; DS Polyakov[1]; M Zhirkova[1]; M Farzaliev[2]; A Azariashvili[2]; N Anyutochkina[2]; E Farafonova[2]
[1]Nizhny Novgorod State Medical Academy, Department of internal medicine, Nizhny Novgorod, Russian Federation; *[2]Nizhny Novgorod State Medical Academy, Nizhny Novgorod, Russian Federation*

Introduction: The prevalence of type 2 diabetes mellitus (T2DM) in heart failure (HF) patients ranges from 24% to 40%, coexistence of HF and T2DM needs an appropriate management.
Purpose: To analyze the use of anti diabetic drugs in real clinical practice among patients after acute heart failure decompensation.
Methods: 700 patients with HF decompensation were studied, all patients were 18 years old or older. At the moment of hospitalization 35.7% patients had T2DM, of them 9.7% patients were diagnosed of T2DM for the first time (group1; G1), 26% were diabetic before decompensation (group2; G2).
Results: Before hospitalization, Hb1ac was not checked in G1, in G2 only 8,2% patients had checked their Hb1ac the last year, mean Hb1ac was 7.0 ± 0.9%. Patients in G1 were never treated with anti diabetics whereas 59.9% patients in G2 were treated. DM treatment was present as mono-therapy (48.6%), bi-therapy (45%) and tri-therapy (6.4%). Anti diabetics were Metformin (41.2%), sulfonylurea (32.7%), DPP4 inhibitors (1.2%), SGLT2 inhibitors (6.1%) and different types of insulin (19%). Conclusion: In real clinical practice, one of ten decompensated HF patients is diagnosed with T2DM for the first time. DM treatment control was only in 8.2% patients. The majority of diabetic patients needs more than one anti diabetic drug for glucose control. Most popular anti diabetics are Metformin, sulfonylureas and insulin with a low compliance to treatment.

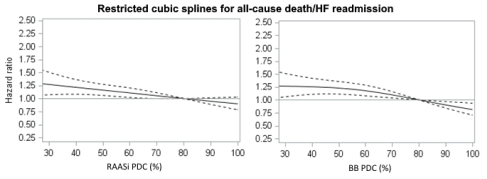
P1753

The association between adherence to evidence-based medicines and outcomes in seniors with heart failure: a landmark analysis

XW Qin[1]; J Hung[2]; M Knuiman[1]; T Briffa[1]; THK Teng[3]; FM Sanfilippo[1]
[1]The University of Western Australia, School of Population and Global Health, Perth, Australia; *[2]The University of Western Australia, Medical School, Sir Charles Gairdner Hospital Unit, Perth, Australia*; *[3]National Heart Centre Singapore, Singapore, Singapore*

On behalf of: Cardiovascular Research Group
Funding Acknowledgements: National Health and Medical Research Council (NHMRC) of Australia

Background: Sub-optimal adherence to evidence-based medicines (EBM), renin-angiotensin aldosterone system inhibitors (RAASis) and beta-blockers (BBs), in patients with heart failure (HF) is associated with adverse outcomes.
Purpose: To determine the association between adherence to EBM and subsequent HF rehospitalisations and/or death in a landmark analysis of patients who survived to 1-year after the index HF hospitalisation.
Methods: Patients aged 65-84 years and alive at 1 year post hospitalisation with non-valvular HF between 2003 and 2008 were identified from linked morbidity and mortality data in Western Australia. National pharmaceutical dispensing records for RAASis and BBs were identified within 1 year post-HF discharge. Medication adherence was measured by proportion of days covered (PDC). Outcomes during 12-months follow-up from the 1-year landmark were: (i) all-cause death, and (ii) all-cause death/HF readmission. Adjusted restricted cubic splines (RCS) were used to determine the adherence-response cutoff (see Figures). Cox regression models were used to calculate adjusted hazard ratios (HR).
Results: At the 1-year landmark, there were 4234 patients with heart failure: mean age 76 +/- 5.5 years, 56% male. Among these, 3668 (87%) and 2822 (67%) were dispensed a RAASi and BB, respectively, in the preceding year. Good adherence (PDC = 80%) was seen in 74% and 52% of patients dispensed a RAASi and BB respectively. Sub-optimal adherence (PDC < 80%) to RAASi was associated with an increased risk of all-cause death (adjusted HR 1.38, 95% CI 1.14-1.67) and all-cause death/HF readmission (HR 1.24, 95% CI 1.07-1.44). The corresponding HRs for BB were 1.30, 95% CI 1.05-1.62 and 1.31, 95% CI 1.12-1.54, respectively. The Figures (HR = solid lines; 95% CIs = dotted lines) confirm that a PDC adherence threshold < 80% for either RAASi or BB had significantly higher risk for both non-fatal and fatal events, although lower thresholds may exist for HF readmissions.
Conclusion: In seniors with HF, adherence to RAASi and BB are sub-optimal, and PDC below 80% was associated with higher risks of subsequent HF readmissions and/or death. Adherence-response curves for EBM will help to determine thresholds for adherence that clinicians should target to improve major HF outcomes.



P1754

Sacubitril/valsartan improves functional class and objective parameters in heart failure patients with reduced ejection fraction and its discontinuation is associated with a poor prognosis.

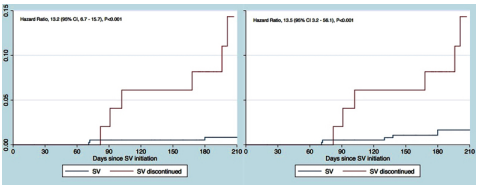
L Vicent Alaminos[1]; A Esteban-Fernandez[2]; M Gomez-Bueno[3]; J De Juan[4]; P Diez-Villanueva[5]; A Manuel Iniesta[6]; A Ayesta[1]; H Gonzalez Saldivar[1]; A Rojas[5]; R Bover Freire[2]; D Iglesias[7]; M Garcia Aguado[8]; J Perea Egido[9]; M Martinez-Selles[1]
[1]University Hospital Gregorio Maranon, Cardiology, Madrid, Spain; *[2]Hospital Clinic San Carlos, Madrid, Spain*; *[3]University Hospital Puerta de Hierro Majadahonda, Madrid, Spain*; *[4]University Hospital 12 de Octubre, Madrid, Spain*; *[5]University Hospital De La Princesa, Madrid, Spain*; *[6]University Hospital La Paz, Madrid, Spain*; *[7]University Hospital Infanta Sofia, Madrid, Spain*; *[8]Hospital de Mostoles, Madrid, Spain*; *[9]Hospital de Getafe, Madrid, Spain*

Background: Sacubitril/valsartan (SV) is a new milestone therapy in heart failure with reduced ejection fraction.
Purpose: Our aim was to ascertain the efficacy and safety of this drug in a real-world setting.
Methods. Prospective registry in 10 hospitals including all outpatients who started SV in everyday clinical practice.
Results: From October 2016 to March 2017, 427 patients started treatment with SV. During a mean follow-up of 7.0 ± 0.1 months, 49 (11.5%) discontinued SV and 12 (2.8%) died. SV discontinuation was associated with cardiovascular (hazard ratio [HR] 13.22, 95% confidence interval [CI]: 6.71 - 15.73, P <0.001) and all-cause mortality (HR 13.51, 95% CI 3.22 - 56.13, p <0.001). Figure shows Kaplan-Meier curves according to sacubitril/valsartan (SV) treatment. [Death from cardiovascular causes (A), and all-cause death (B)]. Symptomatic hypotension was documented in 71 patients (16.6%). Baseline parameters improved at the end of follow-up in patients that continued with SV, including median N-terminal pro–B-type natriuretic peptide (Nt Pro-BNP) levels 1879.0 (Interquartile Range [IQR] 904-3816) ng/L to 1326.0 (IQR: 618-2673) ng/L, rate of functional class >II 29.8% to 5.6%, and left ventricular ejection fraction (LVEF) 28.7 ± 6.8% to 32.3 ± 9.3%; all p values = 0.001. This improvement was not significant in patients with SV discontinuation: median Nt Pro-BNP 3052.5 (IQR 1844.1-6178.5) ng/L to 2237.5 (IQR 1267.5-5393.0) ng/L, rate of functional class >II 42.9% vs. 32.7%, and LVEF 27.8 ± 7.0% vs. 30.0 ± 11.2%; all p values = 0.21.
Conclusions: SV withdrawal in a real-world cohort of heart failure with reduced ejection fraction is independently associated with all-cause mortality. Patients that continued with SV at the end of follow-up showed an improvement in functional class and objective parameters.

Clinical events and follow-up

Variable	SV n = 378	SV discontinued n = 49	p
All cause death	6 (1.6)	6 (12.2)	<0.001
Cardiovascular death	3 (0.8)	6 (12.2)	<0.01
Hospital admissions	43 (11.4)	25 (51.0)	<0.001
Visits to the emergency department	54 (19.4)	24 (49.0)	<0.001
Reason for admission/visit to the emergency department: - Heart failure - Ventricular arrhythmias - Others	44 (11.6) 5 (1.3) 23 (6.1)	17 (34.7) 4 (8.2) 6 (8.2)	<0.001 0.012 0.372
SV related adverse clinical events	84 (22.2)	27 (56.3)	<0.001
Type of adverse effect: - Symptomatic hypotension - Renal failure - Hyperkaliemia - Ventricular arrythmias - Angioedema - Cough - Epistaxis	62 (16.4) 22 (5.8) 19 (5.0) 0 0 1 (0.2) 0	9 (18.4) 7 (14.3) 2 (4.1) 4 (8.2) 2 (4.1) 0 1 (0.2)	0.84 0.13 0.461 0.04 0.05 - -

Clinical events in patients who continued SV and in those who required drug discontinuation.



Kaplan-Meier survival curves

P1755

Design and rationale of the EMPagliflozin outcome trial in patients with chronic heart failure (EMPEROR-Reduced)

F Faiez Zannad[1]; G Filippatos[2]; J Butler[3]; A Salsali[4]; K Kimura[5]; J Schnee[4]; C Zeller[6]; S Pocock[7]; J George[8]; M Brueckmann[8]; SD Anker[9]; M Packer[10]
[1]Hospital Brabois of Nancy, Vandoeuvre les Nancy, France; *[2]University of Athens, Athens, Greece*; *[3]New York University School of Medicine, New York, United States of America*; *[4]Boehringer Ingelheim Pharmaceuticals, Ridgefield, United States of America*; *[5]Boehringer Ingelheim Canada Ltd, Burlington, Canada*; *[6]Boehringer Ingelheim Pharma GmbH & Co, Biberach, Germany*; *[7]School of Hygiene and Tropical Disease, London, United Kingdom*; *[8]Boehringer Ingelheim Pharma GmbH & Co, Ingelheim, Germany*; *[9]Charité - Universitätsmedizin Berlin, Berlin, Germany*; *[10]Baylor University Medical Center, Dallas, United States of America*

Funding Acknowledgements: The trial is sponsored by Boehringer Ingelheim

Background and aims: Despite available therapies for heart failure with reduced ejection fraction (HFrEF), rates of hospitalization and mortality remain high. With an aging population and high prevalence of diabetes and obesity, there is an unmet medical need for additional treatments on top of guideline-directed medical therapy for HFrEF. In the EMPA-REG OUTCOME trial in patients with type 2 diabetes mellitus (T2DM) and established cardiovascular disease, the sodium-glucose co-transporter-2 (SGLT-2) empagliflozin reduced the risk of cardiovascular (CV) mortality by 38% and the risk of HF hospitalizations by 35%. Several mechanisms have been put forward to explain these benefits, which may go beyond the blood glucose lowering effect of empagliflozin. This raises the possibility of using empagliflozin as treatment for patients with established HF regardless of the presence or absence of T2DM.

Methods: The phase III randomized, double-blind EMPEROR-Reduced trial will explore the efficacy and safety of once daily empagliflozin 10 mg compared with placebo, in patients with chronic HFrEF on top of guideline-directed medical therapy. The trial includes patients with left ventricular ejection fraction (EF) = 40% and elevated NT-proBNP levels (NT-proBNP cut-offs for patients without/with atrial fibrillation are: NT-proBNP = 2500 / 5000 pg/ml with EF 36-40%, = 1000 / 2000 pg/ml with EF 31-35%, = 600 / 1200 pg/ml with EF = 30%). Alternatively, patients with EF = 40% qualify, if they had a hospitalization for HF within 12 months and present with NT-proBNP levels of = 600 pg/ml (without AF) or = 1200 pg/ml (with AF). The composite primary endpoint for this trial is the time to first adjudicated CV death or HHF. Approximately 2850 patients are planned to be randomized. The number of patients in this event-driven trial may be increased based on a blinded assessment of the primary event rate. The incidence of adjudicated HHF (first and recurrent) and the renal outcome of eGFR slope of change from baseline are key secondary endpoints.
Perspectives: The EMPEROR-Reduced study evaluates empagliflozin in patients with chronic heart failure with reduced ejection fraction. Together with the EMPEROR-Preserved study, which is evaluating empagliflozin in patients with preserved ejection fraction (EF > 40%), these trials are expected to deliver conclusive insights regarding the value of empagliflozin treatment for patients with heart failure.

P1756

Sacubitril/valsartan and circulating catecholamine levels during a 6 month follow-up in stable heart failure patients

G Chalikias[1]; P Kikas[1]; A Thomaidis[1]; P Rigopoulos[1]; A Pistola[1]; A Zissimopoulos[1]; D N Dimitrios N Tziakas[1]
[1]Democritus University of Thrace, Alexandroupolis, Greece

Funding Acknowledgements: None to report

Background Recently, the PARADIGM-HF (Prospective comparison of ARNI with ACEI to Determine Impact on Global Mortality and morbidity in Heart Failure) trial demonstrated the superiority of sacubitril/valsartan over enalapril on the composite of death from cardiovascular causes or hospitalization for heart failure (HF).
Purpose The present study assessed the effect of sacubitril/valsartan on circulating catecholamine levels in patients with HF in an observational cohort study.
Methods We included 54 consecutive HF patients attending our HF outpatients clinic who were eligible for sacubitril/valsartan according to the PARADIGM-HF inclusion and exclusion criteria. Norepinephrine and epinephrine were measured with immunoradiometric assays at baseline and at 3 and 6 month time follow-up.
Results Compared with baseline levels, there was no change at 3 months in epinephrine (P = 0.177) or norepinephrine (P = 0.815) concentrations. At 6 months, norepinephrine remained unchanged (P = 0.359). However, at 6 months, we observed a significant increase in epinephrine levels compared with baseline [66 pg/mL (37-93) vs. 38 pg/mL (18-74), P < 0.001] (Table).
Conclusions: This study is the first to report on the effect of the new drug sacubitril/valsartan on circulating catecholamine levels in HF patients. Our data show a significant increase in epinephrine levels during a 6 month follow-up in stable HF patients.

Measured change in catecholamine levels

Laboratory Data

	Baseline (n = 48)	3 months (n = 46)	6 months (n = 34)
NT-proBNP, pg/mL	388 (196 - 944)	361 (140-727)	149 (61 - 373)
Epinephrine, pg/mL	38 (18-74)	31 (23-81)	66 (37 - 93)
Norepinephrine, pg/mL	563 (419-762)	522 (324-833)	364 (300 -829)
Creatinine, mg/dL	1.2±0.2	1.2±0.2	1.1±0.2
eGFR, mL/min/m^2	68.1±14.7	67.8±17.7	71.9±17.3

Values are expressed as mean (standard deviation) or median (interquartitile range)eGFR; estimated glomerular filtration rate, NT-proBNP; N-terminal pro-brain natriuretic peptide

P1757

Population wide introduction of novel heart failure treatments - experience with sacubitril-valsartan in a community based heart failure population in northern Sweden

H Norberg[1]; E Bergdahl[2]; K Hellstrom Angerud[3]; K Krister Lindmark[2]
[1]Umea University, Pharmacology and Clinical Neuroscience, Umea, Sweden; *[2]Umea University, Public Health and Clinical Medicine, Umea, Sweden*; *[3]Umea University, Nursing, Umea, Sweden*

Funding Acknowledgements: The Heart Foundation of Northern Sweden

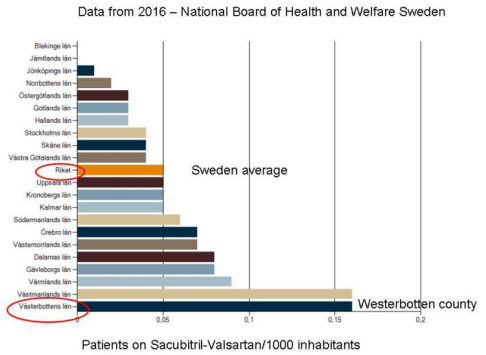
Population wide introduction of novel heart failure treatments
–Experience with Sacubitril-Valsartan in a community based heart failure population in northern Sweden

Background: Heart failure is a chronic disease where many patients do not have regular contact with heart failure cardiologists but are instead taken care of by primary care physicians or general cardiologists. When novel heart failure treatments arrive the introduction phase often takes several years before all eligible patients have been considered. With the computerization of medical records and emergence of quality registries we wanted to investigate the feasibility of using local registries for mass screening of patients eligible for Sacubitril-Valsartan and introducing treatment on all appropriate patients.

Methods: All patients with a main or side diagnosis of heart failure that had had at least one contact with the dept of cardiology or internal medicine at Umeå University Hospital between 2010-2016 were identified in the hospital records. The PARADIGM-HF criteria were applied and all patients who would have been eligible for the study were identified and were summoned to an out patient visit. If the latest echocardiography was older than 18 months a new echo was performed.

Results: Out of 2029 patients with heart failure, 622 had ejection fraction (EF) = 40%, 250 of these tolerated at least half dose ACE-inhibitor/ARB and fulfilled other formal criteria for inclusion in the PARADIGM-HF study. After discussion with the local pharmaceutical committee, for budget reasons we decided to summon all patients who were on maximum dose ACE-inhibitor/ARB and had EF = 35%, a total of 95 patients. After manually checking medical records on these patients and excluding patients with other terminal illness, whose condition had changed, a total of 76 patients were summoned to the out patient clinic.

Conclusion: Using a local registry for mass screening was feasible and helped identify patients in need for treatment. Even with a strict interpretation of the study criteria, Westerbotten county had the fastest introduction of Sacubitril-Valsartan in Sweden. Using this method patients receive the benefit of novel treatments considerably faster than the conventional way of identifying patients when they present themselves in the clinic. It is also likely that this approach helps with the cost effectiveness of new treatments guaranteeing that strict criteria is used in the selection process. It remains to be seen if larger scale registries are useful for this purpose.



Patients on Sacubitril-Valsartan

P1758

Relative efficacy of spironolactone, eplerenone, and canrenone in patients with chronic systolic heart failure - a systematic review and network meta-analysis of randomized controlled trials

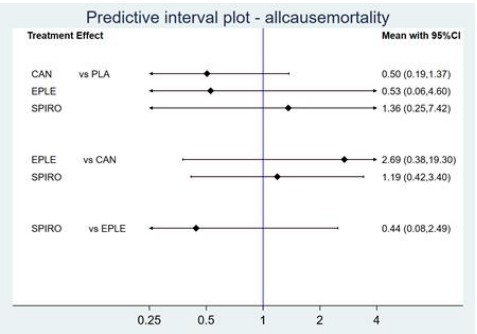
L Lutz Frankenstein[1]; T Taeger[1]; H Froehlich[1]; JGF Cleland[2]; M Grundtvig[3]; T Hole[4]; H Katus[1]; S Agewall[5]; A Clark[6]; D Atar[5]
[1]The Medical Faculty of Heidelberg, Heidelberg, Germany; *[2]Robertson Centre for Biostatistics & Clinical Trials, Glasgow, United Kingdom*; *[3]Innlandet Hospital, Lillehammer, Norway*; *[4]Norwegian University of Science and Technology, Trondheim, Norway*; *[5]University of Oslo, Oslo, Norway*; *[6]Castle Hill Hospital, Hull, United Kingdom*

Objectives: To assess the comparative benefit and risk profile of treatment with spironolactone, canrenone, or eplerenone with regards to all-cause mortality (primary endpoint), cardiovascular mortality, or heart failure related hospitalisation (secondary endpoints) and the safety endpoints hyperkalaemia, acute renal failure, and gynaecomastia.

Design: Systematic review and network meta-analysis following PRISMA-P and PRISMA-NMA guidelines.

Data sources: search in seven individual databases, six individual clinical trial registries, and three individual grey literature databases, no time-restrictions for start date, up to January 2017, cross-checking of reference lists of retrieved publications.

Eligibility criteria for selecting studies: Randomized controlled trials with an active treatment of either spironolactone, eplerenone, or canrenone/potassium-canreonate in adults (age >18 years) with symptomatic heart failure (NYHA II - IV) due to systolic dysfunction (left ventricular ejection fraction < 40%) reporting any of the above endpoints were included - the availability of full reports being the only restriction.



adjusted predictive interval plot

Results: Pairwise meta-analysis confirmed efficacy for all MRAs for the primary endpoint. Uncorrected network meta-analysis favoured spironolactone over eplerenone (OR: 0.74 [0.60-0.93]) but not canrenone (OR: 1.21 [0.44-3.35]). Beta-blocker adjustment did not confirm superiority of spironolactone (OR: 0.44 [0.08-2.49]). Sensitivity analysis excluding either trials with < 30 patients per arm or < 12 months of follow-up confirmed the base case. Cumulative probability ranking plots of benefit vs. safety favoured spironolactone for acute renal failure and hyperkalaemia but eplerenone for gynaecomastia. Results for the secondary endpoints essentially mirrored these findings.

Conclusion: In head-to-head comparisons, spironolactone, eplerenone, and canrenone show comparable efficacy with respect to all-cause mortality, cardiovascular mortality, heart failure related hospitalisations, acute kidney failure, hyperkalaemia, and gynaecomastia.

P1759

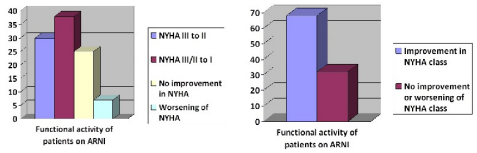
Impact of ARNI (Angiotensin Receptor Neprilysin Inhibitor) on functional status of patients with heart failure and reduced ejection fraction (HFrEF).

M A Muhammad Adil Soofi[1]; F Alsamadi[1]
[1]King Fahad Medical City, Prince Salman Heart Center, Riyadh, Saudi Arabia

Introduction: Pharmacological measures have improved the survival and functional class among patients with heart failure. ARNI is the newest medication approved for patients with HFrEF and associated with significant improvement in survival and hospital readmissions. Functional activity can be assessed by NYHA class.

Method: Retrospective analysis of the patients switched from ACEI/ARB to ARNI at out patient clinic of our hospital. Patients were regularly seen at the clinic after the initiation of ARNI. Symptoms, clinical examination and demographic and hemodynamic data were recorded at each visit along with modification and

adjustment of medications. Their NYHA class were assessed before the initiation and recorded at each visit.
Result: 82 patients were switched from ACEI/ARB to ARNI in last 1 year. 62% of patients were in NYHA class II and 38% of patients in NYHA III/IV. ARNI was stopped in 10 patients (7 patients due to kidney injury, hypotension and non-compliance and 3 patients expired with 15-20 days of initiation).
Baseline characteristics were studied in 72 patients. Renal dysfunction was present at baseline in 35% of patients. Beta blockers were prescribed in 100% of patients (optimum dosage: 40%, 50% - < 100% of optimum dosage: 44%, < 50% of optimum dosage: 15%). MRA was prescribed in 54% of patients.
Follow up completed for 60 patients. ARNI was titrated to optimum dosage in 58% of patients. No mortality recorded in the long term follow up. Drop in systolic BP were recorded in 58% of patients (maximum drop was of 42 mmHg and average was 19 mmHg). No worsening of renal function was noted in 42% of patients. NYHA class improved in 68% of patients (NYHA III to II: 30%, NYHA II/III to I: 38%).
Conclusion: ARNI was tolerated in 88% of patients when switched from ACEI/ARB and was associated with significant improvement in NYHA class in 68% of patients.



Functional activity of patients on ARNI

P1760

Differences in patient characteristics and cardiovascular events between low dose and medium-high dose of Sacubitril-Valsartan

JSM Seller Moya[1]; CNP Nunez Piles[2]; HMC Morillas Climent[1]; AVD Vicedo Lopez[1]; EMJ Galcera Jornet[1]; EAT Alania Torres[1]; LRA Larumbe Rodriguez[1]; AVM Valle Munoz[1]
[1]Hospital Marina Salud, Cardiology, Denia, Spain; *[2]University Hospital Doctor Peset, Cardiology, Valencia, Spain*

Sacubitril-Valsartan (SV) is the most recent drug approved for the treatment of heart failure (HF) with depressed ejection fraction. Results in clinical trials are remarkable. Introduction of SV into daily practice should aim to achieve maximum tolerated dose. However, real world data are limited, mainly due to a short postcommercialization period.
Purpose: The primary objective of our study is to describe, in real word practice, basal patient (p) characteristics together with imaging and laboratory markers related to the used SV dose. We also analyze cardiovascular events during follow-up.
Methods: We performed a retrospective evaluation of SV prescriptions from the first drug prescription until 10th January 2018. P were excluded if no data were available, drug indication was inadequate or if the drug was stopped before 2 months of follow-up
We divided p into 2 groups: low dose (24/26 mg, LD) and medium-high dose (49/51 and 97/102 mg, MHD) of SV. We collected data regarding baseline characteristics, imaging parameters, laboratory markers and major adverse cardiovascular events.
Results: From the 19th of October 2016 to the 10th of January 2018, 114 p were included. Eighteen patients were excluded from final analysis (3 had no data available, 2 had a inadequate indication for prescription, 13 stopped the drug prematurely without a reason). Ninety-six p remained. 72,3% of them were men, 31.7% were diabetic, 83,4% hypertensive and 52% receive lipid lowering drugs. Mean age was 69,9 years. Baseline treatment was optimal: 95% of patients were treated with angiotensin-converting enzyme inhibitors, 90% with beta-blockers and 75% with mineralcorticoid receptor antagonists.
The percentage of low, medium and high dose at the end of the study was 58,33, 37,50 and 4,16% respectively. 60% of the p reported NYHA functional class II symptoms, 33% NYHA III and 7% NYHA I (no significant differences were found between groups). Ischaemic heart disease was the main etiology of heart failure (51,8%)
Mean LVEF was 30,37%, with no differences between groups (29,89 vs 30,95, p = 0,559). Lower pretratment levels of NTproBNP were significantly associated with MHD (3405,63 vs 1609,78 p = 0,014). Ca125 presented a non-significant trend towards higher values in LD (39,11 vs 21,11, p = 0,076). Medium and median dose of furosemide were 60 and 65.54 mg per day (54,91 vs 49,55, p = 0,623).
During a medium follow-up of 203 +/- 101 days, 8 p (8,4%) were admitted to the hospital due to HF and 4 p died (all cardiovascular deaths). We did not find any significant differences, maybe due to the low event rate.
Conclusion: 58% of p remained with LD of SV during follow-up. This dose was associated with higher initial values of NTproBNP and a non-significant trend towards higher levels of Ca125. No differences were identified in NHYA class, LVEF and dose of furosemide.

P1761

Safety of ambulatory intermittent cycles of levosimendan in patients with advanced heart failure listed for heart transplant

I Ponz De Antonio[1]; J De Juan Baguda[1]; A Rodriguez Chaverri[1]; L Moran Fernandez[1]; C Ortiz Bautista[1]; MD Garcia Cosio[1]; R Gutierrez Garcia[1]; C Munera Jimenez[1]; N Tejada Hernandez[1]; R Salguero Bodes[1]; F Arribas Ynsaurriaga[1]; JF Delgado Jimenez[1]
[1]University Hospital 12 de Octubre, Cardiology, Madrid, Spain

Introduction: Intermittent use of inotropes for the long-term treatment of advanced HF (AdHF) remains controversial.
Methods: Observational, prospective study of patients with AdHF awaiting heart transplant (HTx), who received ambulatory intermittent cycles of levosimendan (ICL) between January 2016 and November 2017. All patients received a previous cycle in hospital for 24 hours. Levosimendan was administered every 2 weeks, initiated at 0.1 μg/kg/min and increased to 0.2 μg/kg/min for 6 hours. Implantable cardioverter defibrillators (ICD) were periodically interrogated.

Baseline characteristics	% (n = 11)
Age (years)	53.0 (IQR 41-63)
Male	63.6% (7)
Arterial hypertension	36.4% (4)
Dyslipidaemia	27.3% (3)
Diabetes mellitus	18.2% (2)
Aetiology - Ischaemic disease - Hypertrophic cardiomyopathy - Dilated cardiomyopathy	- 45.5% (5) - 9.1% (1) - 45.5% (5)
LVEF (%)	28 (IQR 19-30)
ICD	100% (11)
CRT	27.3% (3)
INTERMACS Stage 3	100% (11)
Creatinine (mg/dl)	1.5 (IQR 1.3-1.9)
Creatinine clearance (ml/min/1.73m^2)	45.9 (IQR 36.9-59.7)
NTproBNP (pg/dl)	4858.0 (IQR 3047.0-5801.0)
Treatment - ACEI - ARB - Betablockers - MRAs - Ivabradine - Hidralazine + Nitrates	- 54.5% (6) - 9.1% (1) - 90.9% (10) - 100% (11) - 36.4% (4) - 18.2% (2)

IQR: 25% to 75% interquartile range

Results: 11 patients (baseline characteristics in table) received 12.0 ICL (3-49), median follow up was 6.0 months (1.5-12). One patient (9.1%) suffered a symptomatic hypotension during treatment infusion, which forced a reduction of the infusion velocity, remaining afterwards asymptomatic. No patient suffered ventricular tachycardia during infusions, and no significant arrhythmia was detected means ICD interrogations.
In 2 patients (18.2%) ventricular assist devices were implanted as bridge to transplant, 1 (9.1%) experienced clinical improvement and 8 (72.7%) underwent HTx, 25% of them (2) in urgent circumstances. One patient (9.1%) continues with ICL.
Conclusions: : Levosimendan administration was safe in all patients, without significant arrhythmia during treatment infusions nor between cycles. ICL may contribute in reducing the emergency transplantation rate.

P1762

In HFrEF patients, reduced doses of sacubitril / valsartan do not result in increased mortality or heart failure hospitalizations compared to target dose. A retrospective cohort study

R De Vecchis[1]; C Ariano[2]; G Di Biase[3]; M Noutsias[4]
[1]Preventive Cardiology and Rehabilitation Unit, DSB 29 " S. Gennaro dei Poveri Hospital", Napoli, Italy; *[2]Division of Geriatrics, " Casa Sollievo della Sofferenza" Hospital, S.Giovanni Rotondo, Italy*; *[3]Division of Geriatrics, Clinic "S. Maria del Pozzo", Somma Vesuviana, Italy*; *[4]Division of Cardiology, Angiology and Intensive Medical Care, University Hospital Halle, Martin-Luther-University Halle, Halle, Germany*

Introduction: In HFrEF patients, the dosage of sacubitril/−valsartan is modulated according to a gradual increase scheme adjusting to arterial blood pressure tolerance. Nevertheless, if candidate patients exhibit tolerability problems, a provisional reduction of the dose of sacubitril−valsartan or even its interruption are suggested.

Methods: This study provides estimates of respective proportions of HFrEF patients receiving minimum or intermediate dose of sacubitril /valsartan. In addition, a comparison was made to detect possible differences regarding all–cause mortality and heart failure hospitalizations in patients treated with the recommended optimal dose compared to those receiving submaximal maintenance doses of sacubitril/valsartan.
Results: N = 68 HFrEF patients were treated with sacubitril –valsartan in addition to beta–blocker and mineralocorticoid receptor antagonists. Among them, 20 patients (29.4%), were identified as having clinical features that were contra–indicating the administration of sacubitril– valsartan at target doses. The cause eliciting or propitiating the interruption or missing achievement of maximal drug dosage was annotated: symptomatic hypotension (11 cases / 16%), worsening renal function (3 cases), systolic blood pressure = 95 mmHg (3cases), palpebral angioedema (1 case), paradoxical worsening heart failure(1 case), hyperkalemia(1 case). The subsequent decision was to maintain an intermediate dose in 11 patients and to reduce the dose at the minimum allowed level, i.e., 24 mg/26 mg twice daily in 9 patients. After a median follow–up of 5.25 months, no differences were found concerning the risk of all–cause death in the comparison between patients treated with different dosages of sacubitril valsartan. Likewise, patients subjected to submaximal doses of sacubitril–valsartan had similar risk of heart failure hospitalization when compared to patients treated with full dosages of the drug (odds ratio: 1.7083 ; 95% CI: 0.4887- 5. 9718 ; p = 0.5011).
Conclusions: During a median follow–up of 5.25 months. in HFrEF patients who had been proven to be intolerant to the maximum dose of sacubitril/ valsartan, the use of reduced doses of the drug did not result in increased mortality or hospitalization for heart failure compared to patients who tolerated the target dose of sacubitril/valsartan.

P1763

Oral diuretics in very intensive treatment, an early intervention in outpatients with heart failure. DIVINE STUDY

EJJ Eduardo Julian Jose Chuquiure[1]; C Silva-Ruz[1]; K Jacobo-Garcia[1]; G Gabriela Mendez[2]; M Chuquiure-Gil[1]; R Hernandez-Isidro[1]; E Morales-Hinojosa[1]; O Fiscal-Lopez[1]
[1]Instituto Nacional de Cardiologia "Ignacio chavez", Mexico City, Mexico; *[2]Universidad del estado de México, Medicina, ciudad neza, Mexico*

Background: In patients with heart failure (HF), majority of hospital admissions at emergency room are caused by hydric retention, with increase in: Mortality and hospital costs. The purpose of the present investigation is to apply high doses of oral diuretics in patients with HF clinical deterioration.
Material and Method: In the present pilot study, consecutive patients, older than 18 years, of both genders were included. The diagnosis of reduced Heart Failure (HfrEF) according to: Clinical pattern, laboratories and Cardiac imaging (ESC criteria). Treatment was assigned in two groups: Bumetamide and the other group received Indapamide. Each groups received maximum tolerated dose for fourteen days with Clinical evaluations every 48 hrs. (Face-to-face and/or telephone). Serum labs (Sodium, Potassium, NT-PRO-BNP and Creatinine) were evaluated. Daily in-home register were made. Final points were: Mortality, Urinary failure, Clinical Impairment, Hospital admissions, Oedema. (MUCHO). They were followed for 30 days.
Results: We evaluated 14 HfrEF patients with LVEF mean 23.4 ± 9.43%, age: 48.8 ± 12.13 years, 53% with ischemic etiology, Mean Risk Scores: MAGGIC (20.13 ± 4.47) and EMPHASIS (3.74 ± 1.13), only three were female. Nine Patients were assigned in the Bumetamide Group and five in the Indapamide Group.
At Basal: Main signs were worsening dyspnea at rest and Hydric retention.
Intensive pharmacological Stage (1-14 day): Oral average doses were: Bumetamide 7 mg/day and Indapamine 5 mg/day. During the follow-up, dose titration was assessed clinically, every 48 hrs. Orthopnea was the first symptom to be controlled (86%, 24-48 hrs.), followed by Elevated jugular venous pressure, Oedema and Hepatomegaly (in the first 48-72 hrs. in 84%, 79%, 53%, respectively). In the first 48 hours, there was no greater difference in abdominal perimeter and weight. After 72 hours, the reduction began. At 7-10 days there was a mean reduction of 5.7 ± 0.9Kg, and Abdominal perimeter of 2.3 ± 0.2cm. Without modification in creatinine levels. Two patient had cramps, corrected with an oral potassium supplement. Decreases in blood pressure levels were observed, without significant hypotension. In this period, Hospital readmission and Mortality were not observed.
At the 30-day follow-up: No mortality was reported, only two patients attended at emergency room (diarrhea and flu).
Conclusions: Diuretic maximum tolerated doses were safe in both groups. In the present study there was no 30 days mortality.

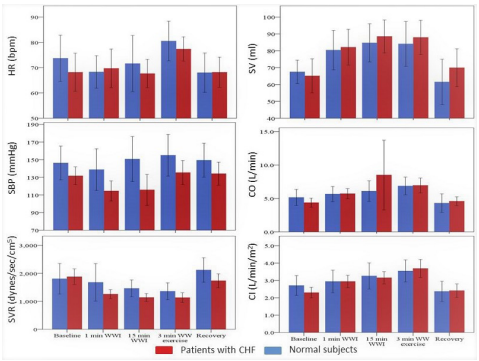
P1764

Warm water immersion in patients with chronic heart failure: A pilot study

P Parin Shah[1]; P Pellicori[1]; A Kallvikbacka-Bennett[1]; D Pan[1]; A Clark[1]
[1]Castle Hill Hospital, Academic Cardiology, Hull, United Kingdom

Funding Acknowledgements: Hull & East Riding Cardiac Trust Fund (Registered with the Charity Commission No. 252918)

Background: Little is known about the acute effects of warm water immersion (WWI) in patients with chronic heart failure (CHF).
Methods: Seventeen patients with clinically euvolaemic CHF (mean age 67 years, 88% male, mean left ventricular ejection fraction 33%) and 10 normal subjects were immersed up to the neck in a pool (33-35°C). Cardiac haemodynamics were measured non-invasively, and echocardiography was performed at baseline, during WWI, 3 minutes after kicking in the supine position and after emerging.
Results: In patients with CHF, compared to baseline, WWI immediately increased stroke volume (SV, mean ± standard deviation; from 65 ± 21 to 82 ± 22 ml, P = 0.01), cardiac output (from 4.4 ± 1.4 to 5.7 ± 1.6 L/min, P < 0.001) and cardiac index (from 2.3 ± 0.6 to 2.9 ± 0.70 L/min/m^2, P < 0.001) with decreased systemic vascular resistance (from 1881 ± 582 to 1258 ± 332 dynes/sec/cm5, P < 0.001) and systolic blood pressure (132 ± 21 to 115 ± 23 mmHg, P < 0.001). The haemodynamic changes persisted for 15 minutes of WWI. In normal subjects, compared to baseline, WWI increased SV (from 68 ± 11 to 80 ± 18 ml, P = 0.03). In patients with CHF, compared to baseline, WWI caused an increase in left atrial volume (from 57 ± 44 to 72 ± 46 ml, p < 0.05) and tricuspid annular plane systolic excursion (from 1.9 (0.6) to 2.1 (0.5) cm, p < 0.05), without any changes in left ventricular size or function or amino terminal pro B-type natriuretic peptide.
Conclusions: In patients with CHF, WWI causes an acute increase in cardiac output and a fall in systemic vascular resistance. The changes were well-tolerated.



haemodynamic changes during immersion

P1765

Identifying accelerometers to measure physical activity in patients with heart failure

L Klompstra[1]; M Kyriakou[2]; T Jaarsma[1]; A Stromberg[3]; M Piepoli[4]; E Lambrinou[2]
[1]Linkoping University, Department of Social and Welfare studies, Linkoping, Sweden; *[2]Cyprus University of Technology, Department of Nursing, Cyprus, Greece*; *[3]Linkoping University, Department of Medical and Health Science, Linkoping, Sweden*; *[4]Guglielmo da Saliceto Hospital, Heart Failure Unit, Piacenza, Italy*

Introduction: Physical activity limitation is a major problem in patients with heart failure (HF) and needs to be accurately measured if therapies aiming to improve this are to be properly evaluated. A range of devices is available for this purpose but most of them have been validated in young, healthy subjects. Their applicability to the HF populations, where movements tend to be slower, is not well established. The number of activity monitors available to measure physical activity is growing, but it remains a challenge to assess physical activity in patients with HF.
Purpose: The aim of this research was to identify activity monitors used to measure physical activity in patients with HF and give an overview of the characteristics of these devices with focus on costs, size, placement, data storage time, outcomes, validity and reliability.
Method: An extensive search of online electronic databases (PubMed, Scopus, CINAHL, Web of Science) was conducted in October 2017. Search words were: ("accelerometer" OR accelerometry OR "motion sensor" OR "activity monitor") AND ("heart failure"). Two reviewers independently reviewed the results and third reviewer adjudicated.

Results: Overall, 27 publication were identified as relevant studies, 6 uniaxial activity monitors, 4 triaxial and 1 multisensor were identified. Most activity monitors placement was on the hip, ankle or wrist (n = 5), two on the thigh, one on the waist and one on the upper arm. Data storage was between no data storage at all and 378 days. Most of the activity monitors measured steps (n = 8) and/or activity counts (n = 6), and some also calculated activity (intensity) level (n = 2) and/or the mean vector magnitude unit (n = 2). Results show that most of the activity monitors (n = 8) were field validated in healthy adults with the total energy expenditure calculated from the activity monitor compared to the total energy expenditure measured with doubly labelled water (r = 0.18 - 0.83). Two activity monitors were also field validated in people with chronic disease (r = 0.33-0.83). Additionally 8 activity monitors were validated in healthy adults with laboratory validation where the total energy expenditure with indirect calometry was compared to the activity monitor outcomes (r = 0.46-0.93). Two activity monitors were also laboratory validated in people with chronic disease (r = 0.72-0.93). Additional data will be presented on costs and reliability of the activity monitors.
Conclusion: The results of this study gives an overview of the devices which measures physical activity in patients with HF in order to help researchers and clinicians in identifying the appropriate accelerometer to measure physical activity in their HF population.

P1766
Assesment of symptom limited stair climbing test efficacy in patients with chronic heart failure

B Busra Alkan[1]; S Ozalevli[2]; N Gullu[3]
[1]KTO Karatay University, Physical Therapy and Rehabilitation, Konya, Turkey; *[2]Dokuz Eylul University, Physical Therapy and Rehabilitation, Izmir, Turkey*; *[3]Konya Kizilay Hospital, Cardiology, Konya, Turkey*

Introduction: To assess the efficacy of symptom-limited stair climbing test (SLSCT), in determining exercise capacities of patients with chronic heart failure (CHF) by comparing cardiopulmonary exercise test (CPET) and 6-minute walk test (6 MWT) and to interpret the results according to clinical characteristics of patients.
Methods: The study included 31 patients aged 50-75 years with stage II-III according to the NYHA (Newyork Heart Association) classification, diagnosed with CHF, with a left ventricular ejection fraction (LVEF) of 45% or less. Demographic and clinical characteristics of the patients were questioned. Exercise capacity was assessed by SLSCT, 6 MWT, CPET. Patients dyspnea and effort perception were assessed by Modified Borg Scale (MBS), pulmonary functions by spirometric measurements, health-related quality of life (HRQOL) by Chronic Heart Failure Questionnaire (CHFQ).
Results: It was determined that the test with the highest VO2 max value among the tests was SLSCT. A significant difference was noted between the other tests ($p < 0.05$). In heart rate changes before and after the tests, SLSCT was found to increase heart rate more than 6MWT and less than CPET. A significant correlation was found between the predicted VO2max values of CPET and SLSCT (r = 0.52, p = 0.003). It was also found that SLSCT was more related to clinical characteristics of patients.
Conclusion: SLSCT is effective in evaluating exercise capacity and easy to use in CHF patients. Compared with the 6MWT, it gives better results in determining the clinical characteristics and hemodynamic responses of the patients. It is an alternative to assessing exercise capacity in the absence of CPET.

P1767
Functional evaluation of resynchronization therapy by means of non invasive cardiac output measurement during cardiopulmonary exercise test

C Carlo Vignati[1]; A Scoccia[1]; G Cattadori[2]; E Salvioni[1]; S Farina[1]; P Agostoni[1]
[1]Cardiology Center Monzino IRCCS, Heart Failure Unit, Milan, Italy; *[2]IRCCS Multimedica of Milan, Milan, Italy*

Background: More than one third of patients with heart failure (HF) shows an LBBB. This is associated to a mechanical dyssynchrony, which cause a suboptimal left ventricular filling and consequently a decrease in cardiac performance. These patients show more severe symptoms, worse prognosis, and an increase risk of death. Cardiac resynchronization therapy (CRT), stimulating properly the right and left ventricles, restores the coordination of contraction. Multiple studies have shown the benefits of CRT, in patients with enlarged QRS complex and optimized medical therapy. However, the wider diffusion of CRT, has shown that ˜30% of candidates don't benefit from the treatment. Little is known about prediction of the non responders.
Aim of the study: to assess the effects of CRT, through the evaluation of oxygen consumption (VO2) and the measurement of cardiac output (CO) by means of inert gas rebreathing technique.
Results: We have enrolled 81 patients who had a standard indication for an CRT (NYHA class = II, LBBB brunch block, optimized medical therapy, LVEF = 35%) and peak VO2 = 16 ml/kg/min. In the overall population we observed an improvement of NYHA class (from 2.6 ± 0.5 to 1.9 ± 0.4), an increase of LVEF (from 29.3 ± 7.4 to 34.1 ± 9.5), a reduction of telediastolic (EDV from 212.6 ± 71.9 to 188 ± 71.1 ml) and telesystolic volume (from 151.1 ± 62.9 to 127.7 ± 60.4) and a improvement of mitral regurgitation. Also peak VO2 improved (from 1094 ± 345 to 1199 ± 376 ml/min). This was related to an increase of CO (from 6.15 ± 1.86 L/min to 7.05 ± 2.2 L/min), whereas the arteriovenous oxygen difference (Ca-vO2) was unchanged. We have then compared the CRT-responder (reduction of EDV >10% or increase of LVEF>10%) and CRT-non responder from a clinical, functional and echocardiographic point of view.
Using the reduction of EDV as criterion the two groups differ at baseline for heart rate, and rest VO2, while using the increase of LVEF CRT responder patients have a lower LVEF than non responders.
During CPET we assessed differences in peak VO2 (from 1153.5 ± 339.5 to 1280.6 ± 369.8 in CRT-responder vs from 1050.4 ± 289.3 to 1147 ± 335.2 in CRT-non responder), O2 pulse (from 10.8 ± 2.9 to 12.5 ± 2.9 in CRT-responder vs from 10.3 ± 2.6 to 11.1 ± 3.34 in CRT-non responder) and CO (from 6.4 ± 2.1 to 7.7 ± 2.3 in CRT-responder vs from 5.8 ± 1.3 to 6.4 ± 1.8 in CRT-non responder) but no differences in baseline functional characteristics.
Conclusion: We can assess the benefits of CRT through the increase of peak VO2. Through the simultaneous measurement of CO, we could assess that the increase of peak VO2 was related to an increase of CO, whereas the (Ca-vO2) difference was unchanged. In both groups we observed an increase in CO, but in CRT-responder this was related exclusively to the increase of stroke volume whereas (Ca-vO2) difference and heart rate were unchanged.
After CRT implantation we have assessed an improvement of LVEF, but in CRT Non Responder we have not observed a reverse remodeling.

P1768
Role of fibrosis detected by cardiac magnetic resonance in predicting the response to cardiac resynchronization therapy in ischemic heart failure.

P Manca[1]; S Cossa[2]; GF Tola[1]; A Scalone[1]; B Schintu[1]; A Setzu[1]; S Mameli[1]; N Sanna[1]; A Giardina[1]; L Minerba[3]; G Matta[2]; M Porcu[1]
[1]G. Brotzu Hospital, cardiology, Cagliari, Italy; *[2]G. Brotzu Hospital, radiology, Cagliari, Italy*; *[3]University of Cagliari, Public health, Cagliari, Italy*

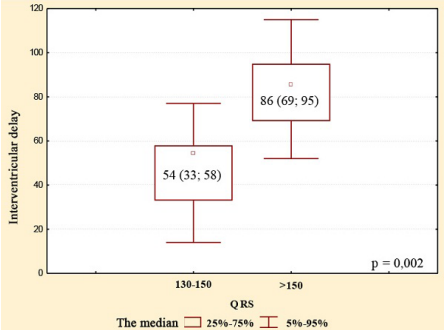
Background. Cardiac resynchronization therapy (CRT) can reduce mortality and morbidity in selected patients with ischemic heart failure (IHF). However, the indication to this treatment is still based mainly on electric parameters and the role of myocardial scar is not completely defined.
Purpose: To evaluate the significance of the extension and localization of left ventricle fibrosis, assessed by cardiac magnetic resonance (CMR), in the response to CRT in patients with IHF. Methods. We retrospectively enrolled 36 symptomatic IHF patients (30 M, 6 F, mean age 68 ± 8 years), who had a complete cardiovascular evaluation, including clinical examination, blood parameters, ECG, echocardiography and cardiac magnetic resonance (CMR). The diagnosis was supported by a definite clinical history of coronary artery disease and at least one stenosis = 50% in one epicardial artery at coronary angiography. At baseline, the ejection fraction (EF) was $27 \pm 5\%$, NYHA class $2,7 \pm 0,6$ and QRS 150 ± 17 msec. Thirty patients (83%) were in sinus rhythm and 6 (17%) in atrial fibrillation. All patients were treated with optimal medical therapy for at least 3 months before the implant (ßb 86%, ACEI/ATIIA 88%, furosemide 100%, AA 50%). The effectiveness of CRT was defined according to the following criteria: 1) Responders: improvement = 1 NYHA functional class and/or improvement = 15% in the EF; 2) Non-Responders: no improvement or even worsening of NYHA class and improvement < 15% in the EF.
Results: At a mean follow up of 36 ± 12 months, 20 patients (55%) were considered responders, while 16 (45%) did not show any benefit. Responders had a baseline higher NYHA class (3,1 vs 2,2, p= < 0,0001). No other factors, including baseline QRS length and its shortening after CRT, showed a prognostic value. Four patients did not show a significant myocardial scar and all of them were responders. The percentage of left ventricle fibrosis (23.2% vs 14.5%), the number of transmural fibrotic segments (4.8 vs 2.6) and the number of lateral fibrotic segments (1.6 vs 0.8) were higher in non-responders. However, these differences were not statistically relevant, probably for the limited sample size. Conclusions. These data support the hypothesis that in IHF the extension and the localization of myocardial fibrosis documented by CMR can influence the response to CRT. Larger studies are needed to confirm it.

P1769

Effect of cardiac resynchronization therapy on parameters of myocardial dissynchrony in patients with chronic heart failure and atrial fibrillation

T Tatyana Troyanova-Shchutskaia[1]; A Kurlianskaya[1]; D Goncharik[1]; A Chasnoyt[1]; T Denisevich[1]; O Shatova[1]
[1]*Republican Scientific and Practical Centre of Cardiology, Minsk, Belarus*

Background: Myocardial dissynchrony is one of the most important causes of chronic heart failure (CHF). The matters of the effect of cardiac resynchronization therapy (CRT) on myocardial dissynchrony has not been studied in patients with permanent atrial fibrillation (AF).
Purpose: to study the effect of CRT on myocardial dissynchrony in patients with chronic heart failure complicated by PAF.
Methods. The study included 50 patients with CHF III NYHA, PAF, ejection fraction < 35%, QRS >130ms. Patients were divided into 2 groups (1 - QRS 130-150ms, 2 - QRS >150ms) and underwent CRT with ablation of atrioventricular node. Echocardiography with determination of myocardial dissynchrony was performed at baseline and in 12 months after CRT.
Results: At baseline presystolic aortic delay was higher in group 2 (p = 0.001). Association of presystolic aortic delay and QRS-duration was confirmed by a significant correlation (rs = 0.51 at p < 0.001). In group 1 interventricular dyssynchrony was also significantly higher than in group 2 (p = 0.002) (Picture). The correlation coefficient indicated a moderate correlation of interventricular delay and QRS-duration (rs = 0.38 at p = 0.018).
Analyzing presystolic aortic delay the difference in the frequency of effects of CRT was statistically significant only in group I (p = 0.010). In 12 months after CRT the presystolic aortic delay disappeared in 23% of patients, remained in 57% and appeared in 8%. No presystolic aortic delay was observed before or after CRT in 12% of patients. In 12 months after CRT presystolic aortic delay decreased significantly from 161 (140, 168) ms to 147 (133, 155) ms (p = 0.014) despite a rather large percentage of the absence of positive dynamics (57%). In group 2 there was no statistically significant positive effect of CRT on the incidence of presystolic aortic, but it decreased from 211 (183; 223)ms to 172 (155; 179)ms (? = 0,028). In both groups interventricular delays decreased significantly (p < 0,001). Parameters of intraventricular dyssynchrony decreased insignificantly. Perhaps these changes are caused by different coefficients of variability.
Conclusions: The positive dynamics of parameters of interventricular and intraventricular dyssynchrony was revealed in 12 months after CRT. The severity of mechanical dissynchrony depends on the width of the QRS complex. Presystolic aortic delay, interventricular delay and all segments maximum delay were higher in patients with QRS > 150 ms.



P1770

The prognostic value of age in patients with continuous flow left ventricular assist devices and association with ICD/CRT-D treatment

N Jakus[1]; M Cikes[1]; JJ Brugts[2]; K Holcman[3]; E Gaizauskas[4]; A Gigase[5]; LM Jacquet[6]; E Barge-Caballero[7]; S Adamopoulos[8]; D D'amario[9]; I Planinc[1]; LH Lund[10]; A Flammer[11]; F Ruschitzka[11]; D Milicic[1]
[1]*University of Zagreb School of Medicine, Department of Cardiovascular diseases, Zagreb, Croatia*; [2]*Erasmus Medical Center, Rotterdam, Netherlands*; [3]*John Paul II Hospital, Krakow, Poland*; [4]*Vilnius University Hospital, Vilnius, Lithuania*; [5]*University Hospital Antwerp, Antwerp, Belgium*; [6]*Cliniques Saint-Luc UCL, Division of Cardiology, Brussels, Belgium*; [7]*Hospital Universitario de A Coruña, A Coruña, Spain*; [8]*Onassis Cardiac Surgery Center, Athens, Greece*; [9]*Catholic University of the Sacred Heart, Rome, Italy*; [10]*Karolinska Institute, Department of Medicine, Stockholm, Sweden*; [11]*University Hospital Zurich, Clinic for Cardiology, Zurich, Switzerland*

On behalf of: The PCHF VAD-ICD/CRT Registry

Introduction: There is an increasing interest in exploring the association between implantable defibrillators (ICD and CRT-D) and outcomes in ventricular assist device (VAD) carriers. Through a VAD registry formed by 10 European heart failure centres, we aimed to investigate the baseline differences among VAD carriers subgrouped by age quartiles, the prognostic role of age and its association with ICD/CRT-D treatment.
Methods: At current, the registry includes data on 246 patients with continuous flow LVADs (median age 56 (IQR 48-63), 83% male), 63% of which are also ICD or CRT-D carriers. For this subanalysis, patients were subgrouped in quartiles according to age (Table 1). Median follow-up time was 1.3 years (IQR 0.4-2.0) from index date, defined as time of LVAD or ICD/CRT-D implant, whichever came later.
Results: The baseline patient characteristics are presented in Table 1. The crude event rates for the primary outcome (all-cause mortality) increased with age (event rates per 100 person-years: Q1: 9.8 [5.1-18.8], Q2: 11.3 [6.3-20.5], Q3: 27.1 [17.5-42.0], Q4: 36.2 [24.8-52.8]). In unadjusted analysis, the hazard ratio for all-cause death was significantly higher in Q3 and Q4 compared to Q1 (HR [95% CI] for Q2, Q3 and Q4 was 1.15 [0.48-2.79], p = 0.8, 2.48 [1.13-5.45], p = 0.024 and 3.31 [1.55-7.06], p = 0.002, respectively), remaining significant after adjusting for HF aetiology, INTERMACS class and prior cardiac surgery. ICD use was associated with reduced mortality, and age strata at LVAD implantation did not modify the association between ICD/CRT-D therapy and reduced mortality (interaction p = NS for all age quartiles).
Conclusion: Although increasing age at LVAD implantation is associated with a higher risk of all-cause death, it does not appear to modify the treatment effect of ICD/CRT-D therapy in cf-LVAD carriers.

Table 1.

	Q1 (16-48 y) (N = 62)	Q2 (48-56 y) (N = 61)	Q3 (56-63 y) (N = 62)	Q4 (63-75 y) (N = 61)	P value
Male gender, n (%)	47 (75.8%)	52 (85.2%)	52 (83.9%)	52 (85.2%)	0.45
Dilated cardiomyopathy, n (%)	39 (62.9%)	28 (45.9%)	14 (22.6%)	20 (32.8%)	<0.001
Ischemic cardiomyopathy, n (%)	15 (24.2%)	28 (45.2%)	43 (69.4%)	32 (52.5%)	
Other cause of HF, n (%)	8 (12.9%)	5 (8.1%)	5 (8.1%)	9 (14.8%)	
INTERMACS class 1, n (%)	18 (29.0%)	9 (14.5%)	8 (13.1%)	2 (3.4%)	0.006
INTERMACS class 2, n (%)	14 (22.6%)	16 (25.8%)	15 (24.6%)	13 (22.0%)	
INTERMACS class 3, n (%)	21 (33.9%)	21 (34.4%)	18 (29.5%)	19 (32.2%)	
INTERMACS class 4-7, n (%)	9 (14.5%)	15 (24.2%)	20 (32.8%)	25 (42.4%)	
ICD and CRT-D therapy during VAD support, n (%)	30 (48%)	38 (62%)	44 (71%)	43 (72%)	0.022

Baseline characteristics of the studied LVAD population according to age quartiles.

P1771

Haemodynamic parameter analysis during impella-protected pci in high risk patients with reduced ejection fraction

D Domenico D'amario[1]; F Burzotta[1]; G Russo[1]; F Ribichini[2]; A Piccoli[2]; L Paraggio[1]; L Previ[1]; C Aurigemma[1]; C Trani[1]; F Crea[1]
[1]*Catholic University of the Sacred Heart, Institute of Cardiology, Rome, Italy*; [2]*University of Verona, Verona, Italy*

Background: The use of cardiac assistance devices represents a promising strategy to facilitate percutaneous coronary intervention (PCI) in high risk patients. The haemodynamic response to Impella-protected PCI (pIMP) in real-world patients has not been systematically investigated.
Purpose: To assess the haemodynamic response to pIMP in patients with heart failure with reduced ejection fraction undergoing high risk PCI.
Methods: We extracted and analyzed the device console data continuously recorded during assistance in consecutive patients who underwent elective pIMP-protected PCI in two high volume centers. Patients with established cardiogenic shock before intervention were excluded. Coronary artery disease burden was graded using the British-Cardiovascular-Intervention-Society jeopardy-score (BCIS-JS) score. pIMP motor speed and pressure signals (systolic blood pressure, SBP, and mean blood pressure, MBP) recorded during pIMP

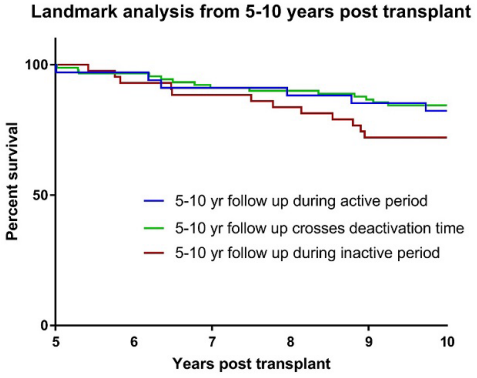
assistance were analyzed to evaluate the occurrence of device malfunctions and arterial pressure drops. Primary haemodynamic pre-determined end-points were "major systolic blood pressure (SBP) drop" (SBP decrease = 20 mmHg reaching = 90 mmHg values) and "major mean blood pressure (MBP) drop" (MBP decrease reaching = 60 mmHg).
Results: The study population comprised 37 patients who underwent pIMP-protected PCI. All patients enrolled in the study had severe left ventricular dysfunction (EF 31 ± 10%) and 86% had a New-York-Heart-Association class III or IV. Pre-PCI BCIS-JS was 11 ± 2 and more than a half underwent left main PCI. Mean assistance duration was 254 ± 549 minutes and no device malfunction occurred. SBP and MBP significantly decreased during PCI , but all patients had SBP values >78 mmHg. Major SBP and MBP drops occurred in 10.8% of patients in both cases. BCIS-JS was the only significant predictor of both SBP (p = 0.001) and MBP drop (p = 0.001). No correlations were found between lactate levels and haemodynamic pre-determined end-points.
Conclusions: PCI is becoming the treatment of choice for complex, fragile patients that are considered to be not amenable to surgical revascularization at reasonable risk. Unfortunately, there is an ever-enlarging gap between the supply and the demand for such complex procedure, a gap which is made more severe by the expanding indications and less conservative criteria widely used for candidacy.
In patients with reduced ejection fraction, undergoing pIMP-protected PCI, a significant pressure decrease occurs during PCI but pressure is systematically maintained at levels warranting vital organ perfusion. Pressure drops during PCI may occur in patients with higher jeopardized myocardium. Therefore, as patients' selection is a crucial moment, a major effort has to be performed in order to have every single candidate undergoing a comprehensive evaluation, during Heart Team discussion and before pIMP planning.

P1772

Does deactivation of a site's surgical cardiac transplant program affect the long-term survival of its recipients?

WA Parker[1]; HJ Ramshaw[1]; EK D'arcy[1]; J Pickering[1]; RR Burger[2]; K Adatia[2]; O Ogunleye[2]; KW Ow[2]; SJ Armour[2]; AA Girach[2]; PC Braidley[1]; A Al-Mohammad[1]
[1]Northern General Hospital, The Heart & Lung Transplant Unit, Sheffield, United Kingdom; *[2]University of Sheffield, The Medical School, Sheffield, United Kingdom*

Background: When a cardiac transplant centre permanently ceases its surgical programme, it may continue ongoing follow-up of its recipients. The effects of this transition on the long-term survival of the recipients have not been well studied. It remains unclear whether follow-up should continue at such a site or be transferred to a surgically active centre.
Purpose: We explored factors, including site deactivation, affecting mortality before and after our centre's surgical programme was deactivated.
Methods: Baseline and mortality data were collected on the 215 patients who underwent orthotopic cardiac transplantation over a 13 year period at a single centre that voluntarily ceased its programme in September 2002 but continued a dedicated service for follow-up of the surviving recipients, now all at least 15 years post-transplant. Kaplan-Meier curves were constructed and relationships assessed using log-rank testing and a 17-factor Cox proportional hazards model. To compare long-term mortality during similar periods of follow-up before and after site deactivation, patients were divided into those undergoing 5-10 year follow up before, through and after deactivation and a landmark analysis performed to compare mortality outcomes during these periods. Statistical analyses were performed using IBM SPSS v23.



p=0.21 between groups (Cox regression)

Summary figures

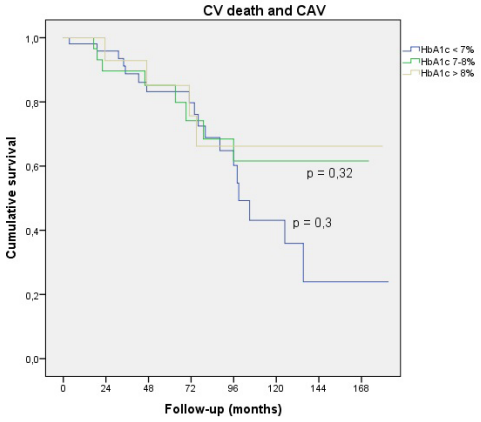
Results: Overall 1, 5, 10 and 15-year survival rates were 88%, 77%, 62% and 37% respectively. Non-ischaemic indication for transplant (hazard ratio [HR] 0.63 [95% CI 0.40-0.99], p = 0.046) and lower pre-transplant pulmonary vascular resistance (exp[B] = 0.71 [95% CI 0.57-0.89], p = 0.004) were identified as significant independent predictors of lower long-term mortality in this cohort. Survival curves did not significantly differ between chronological quartiles (chi square 3.24, p = 0.36) and a landmark analysis performed from 5-10 years post-transplant showed no significant difference in survival curves between the 3 analysis groups (log-rank chi square 1.54, p = 0.21). There was no relationship between date of transplant and risk-adjusted 15-year survival (p = 0.89 by Cox regression).
Conclusion: Based on these data, cessation of cardiac transplant activity at a centre does not appear to significantly affect long-term outcomes of its recipients and follow-up can safely continue there, with advantages of continuity and geographical convenience.

P1773

Is glycated hemoglobin a prognosis factor in Heart Transplant Recipients with diabetes?

A Antonio Grande-Trillo[1]; JM Sobrino-Marquez[1]; D Rangel-Sousa[1]; E Lage-Galle[1]
[1]University Hospital of Virgen del Rocio, Seville, Spain

Introduction: Diabetes mellitus (DM) is associated with poor survival after heart transplant (HT). However, the significance of glycemic control in diabetic HT recipients have not been studied yet. Our aim is to establish if poor glycemic control evaluated by glycated hemoglobin (HbA1c) is related with a poor prognosis.
Methods: We analyzed prospectively all HT recipients in our center from 2002. Those with pre-existing DM before HT and those who developed DM after HT attending on DM diagnostic criteria from American Diabetes Association were included as diabetic patients. In-hospital mortality cases were excluded. We evaluated survival free of cardiovascular (CV) death and cardiac allograph vasculopathy (CAV) in diabetic and non-diabetic patients. Finally, we assessed influence of glycemic control using average HbA1c in their follow-up after HT.
Results: 209 patients were included in the analysis (figure 1). Univariate analyses reveals an increase of combined endpoint (CV death and CAV) in DM patients (pre-existing and new onset) with an OR of 2,5 (p = 0,04; IC 95% 1,29 - 5,02). However, diabetic patients subgroups attending on HbA1c did not show differences in combined endpoint (figure 1).
Conclusions: DM is associated with poor prognosis after HT as happen in another series, including both pre-existing and new onset DM. However, specifically in DM patients, mean HbA1c is not related with a worse outcome. It may means that HbA1c is not a good marker for HT patients or we don't know nowadays optimal target HbA1 for HbA1c recipients.



P1774

Predisposing factors for development of acute right ventricular failure after heart transplantation

J Ljubas Macek[1]; D Fabijanovic[1]; B Skoric[2]; M Cikes[2]; J Samardzic[2]; D Lovric[1]; H Jurin[1]; H Gasparovic[3]; N Jakus[1]; I Planinc[1]; M Pasalic[1]; D Milicic[2]
[1]University Hospital Centre Zagreb, Department of cardiovascular diseases, Zagreb, Croatia; *[2]University of Zagreb School of Medicine, and University Hospital Centre Zagreb, Dpt. of cardiovascular diseases, Zagreb, Croatia*; *[3]University Hospital Centre Zagreb, Dept of Cardiac surgery, Zagreb, Croatia*

Introduction: Isolated acute right ventricular failure (ARVF) is one of the most common haemodynamic complications after heart transplantation (HTx), often requiring

mechanical circulatory support (MCS) as the only possible treatment option. Irreversibly elevated pulmonary vascular resistance (PVR) despite vasodilators (= 4 Wood units) is a major risk factor for ARVF and presents contraindication for HTx, but other contributing factors could also be recognized.
Purpose: The aim of our study was to detect other less known predisposing conditions for the development of ARVF, including patient (PT) comorbidites and peritransplant injury as well as early postHTx PT clinical characteristics. Clinical intention was to better prepare the PT before the transplant procedure and more precisely stratify PT's risk factors for postHTx ARVF.
Methods: 145 HTx PTs, mean age 51 ± 12 years, were included in the study. ARVF was treated medicamentously or in combination with MCS. We analyzed potential predisposing conditions for ARVF, such as preHTx comorbidities: chronic obstructive pulmonary disease, diabetes mellitus type II, chronic renal failure (CRF) and INTERMACS score. Donor age, ischemic time and cardiopulmonary bypass time (CPB) were also considered. Early postHTx clinical parameters such as acute renal failure with the use of perioperative hemodialysis (pHD), average heart rate (HR) during 1st month, high-sensitivity troponine T (hsTnT) and NT-proBNP levels and liver enzymes (alanin-aminotransferase - ALT and gamma-glutamyl transferase - GGT) were also collected.
Results: 16% of PTs developed ARVF (N = 23), among who 60% were treated with short-term MCS. PTs with ARVF have significantly increased mortality (p = 0,005). From preHTx comorbidites, only CRF significantly predisposes to ARVF (p = 0,009, creatinine clearance: ARVF vs normal RV, 50 vs 62 ml/min). INTERMACS score has no impact (p = 0,112) as well as donor age (p = 0,215), ischemic time (p = 0,225) and CPB (p = 0.272). Lower HR is a significant predisposing condition (p = 0,028, ARVF vs normal RV: 80 vs 90 /min) and preHTx use of amiodarone could be the cause of lower HR early postHTx (p = 0,026). Development of ARVF is marked with significantly higher levels of early hsTnT (2nd postHTx day: ARVF vs normal RV: 1520 vs 800 ng/L, during the 1st week 1230 vs 533 ng/L), ALT (p = 0,003), GGT (p = 0,005) and expectedly NT-proBNP (10207 vs 2211 pg/ml).
Conclusion: ARVF developed in 16% of PTs and MCS was required in majority cases. CRF predisposes to development of ARVF potentially through more pronounced volume overload and further on, perioperative deterioration with use of pHD is a significant contributor. Peritransplant graft ischemic-reperfusion injury does not seem to be relevant, as well as donor age. PTs with lower HR early posttransplant are at higher risk to develop ARVF and those PTs were often more pretreated with amiodarone. ARVF significantly elevates early hsTnT, NT-proBNP and liver enzymes.

P1775

Assessing and comparing the need for palliative care in different advanced HF cohorts

F Strangl[1]; J Ehlert[2]; A Ullrich[2]; S Vehling[2]; S Blankenberg[1]; C Bokemeyer[2]; K Oechsle[2]; M Rybczynski[1]
[1]University Heart Center Hamburg, Klinik für Allgemeine und Interventionelle Kardiologie, Hamburg, Germany; *[2]University Medical Center Hamburg Eppendorf, II. Medizinische Klinik, Hamburg, Germany*

Objective: The psycho-social burden of cardiovasvular disease is vast and frequently under-estimated. Within a multi-modal and interdisciplinary treatment approach to advanced chronic heart-failure (CHF), palliative treatment has gained rising attention. While psychological treatment has been well implemented in the treatment of VAD and HTX patients, the role of palliative care (PC) in advanced CHF patients is unclear.
Methods: In a cross-sectional single-center pilot study, we evaluated 243 CHF patients regarding a need for palliative care. Both inpatients from the heart-failure unit (HFU, n = 148) and outpatients from the heart transplantation (HTX, n = 69), ventricular assisted device (VAD, n = 21) and CHF department (CHF, n = 5) were included.
The feasibility of the tools used had been demonstrated earlier (Oechsle et al. 2017). The "Minimal Documentation System For Palliative Medicine" (MIDOS) and "Distress-Thermometer" (DT) were used for self-assessment of symptom burden and distress, and a modified version of the "Five-Item-Palliative-Care-Screening-Tool" (Glare et al. 2011) served as screening-tool by treating cardiologists.
Results: Patient-reported outcomes showed a significantly higher symptom burden (as assessed by MIDOS and DT) among hospitalized HFU patients than HTX outpatients. Two thirds (66%) of patients scored above the cut-off (DT = 5) for "clinically relevant" distress, and HFU patients were more likely to do so when compared to HTX outpatients (74% vs. 57%, p = 0.018). "Fatigue" (45%), "weakness" (42%), "dyspnea" (38%), "lack of appetite" (19%), and "pain" (17%) were the most frequent symptoms with moderate or severe intensity.
While the highest mean symptom-score was encountered among VAD outpatients, MIDOS and DT score did not differ significantly between the VAD and HTX outpatient group (p = 0.21).
The Glare-Screening revealed a need for PC support (Score = 5) in more than two thirds (68%) of all patients. The need was significantly higher among HFU than HTX patients (84% vs. 32% above cut-off, each p < 0.001), mirroring the increased symptom burden among hospitalized patients.
Among outpatients, the Glare-Score was significantly higher in the VAD than the HTX group (p < 0.001), as was the concluded need for PC support (67% vs. 32%, p = 0.006).
Discussion: Data suggest a distinctive need for PC within a multi-modal treatment approach for advanced CHF. Hospitalized patients with a significant symptom burden and, in outpatient care, especially VAD patients may benefit from integrating interdisciplinary PC into standard CHF care.
Psychological treatment may already be well implemented among HTX and VAD patients - However, enhancing therapy with additional PC approaches and expanding it to other advanced CHF patients seems advisable.

P1776

Usefulness of hypertonic saline solution plus intravenous furosemide as treatment for acute heart failure in patients with refractory congestion

C Aguilera Agudo[1]; J Baena Herrera[1]; M Torres Sanabria[1]; A Restrepo Cordoba[1]; P Garcia Pavia[1]; I Zegri Reiriz[1]; M Marta Cobo Marcos[1]
[1]University Hospital Puerta de Hierro Majadahonda, Department of Cardiology, Madrid, Spain

Background: Refractory congestion in heart failure (HF) is related with a poor prognosis. Treatment with saline hypertonic solution (HSS) in combination with intravenous furosemide has shown promising results.
Aim: Analyze the safety and effectiveness of HSS together with furosemide in patients with HF and persistent congestion.

Results

	24 h before HSS (mean and standard deviation)	24 h after HSS (mean and standard deviation)	Difference	p
Diuresis (ml)	1375 (733)	2146 (971)	+ 771	0,000
Weight (kg)	80,2 (21)	79,3 (20)	-0,95	0,000
Systolic arterial pressure (mmHg)	112 (16)	107 (18)	-5	0,02
Cr (mg/dl)	1,7 (0,9)	1,7 (0,9)	0	0,75
Na (mEq/L)	137,2 (4,6)	137,6 (4,1)	0,37	0,258
K (mEq/L)	4,2 (0,4)	4,1 (0,6)	-0,1	0,144
NTproBNP (pg/ml)	15222 (18482)	9675 (8079)	-5546	0,056

Cr: creatinine, Na: sodium, K: potassium, NTproBNP: N-terminal pro b-type natriuretic peptide

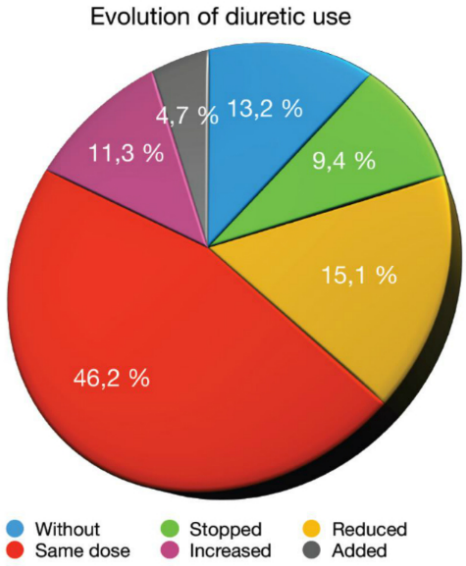
Methods: Retrospective analysis of patients admitted in our hospital during 2016 and 2017 in which we used this strategy. The infusion consisted on 100 mL of 2,9% NaCl saline solution with 125 mg of furosemide, once a day, for 30 minutes. We compared diuresis, weight, serum sodium, potassium, creatinine and systolic blood pressure 24 hours before and after the infusion. We evaluated intra-hospital mortality and readmissions for decompensated HF within the first 30 days.
Results: 341 patients were admitted for HF. 51 (15%) had persistent congestion and received HSS + intravenous furosemide (median: 2, rank 1-13). The mean age was 73 years old , 67% were men, and there were a high prevalence of comorbilities (80% AHT, 45% DM, 65% chronic kidney disease) and advanced cardiopathy (50% with LVEF < 35%, mean NTProBNP 15222 pg/mL). 24 hours after the treatment the diuresis had a mean increase of 771 mL and the weight had a mean decrease of 1 kg, with a slight decrease of systolic blood pressure (- 5mmHg). There were no differences in serum sodium, potassium and creatinine levels. 80% of the patients had a favourable response in terms of diuresis or weight. At discharge, the weight had a mean decrease of 6 kg and the NTproBNP decreased in 36%. Intra-hospital mortality was 19%, with a 10% of early hospital readmissions. None of the deaths were related to the treatment.
Conclusions: In our experience, intravenous furosemide together with HSS is an effective, cheap, easy and safe strategy and should be considered in the patientes with HF and persistent congestion.

P1777

Clinical impact of Sacubitril/valsartan in patients with heart failure with reduced ejection fraction and management of loop diuretic during follow up

M Fernandez-De-Sanmamed-Giron[1]; M Galvan Ruiz[1]; M Blanco-Nuez[1]; M Singh[1]; M Groba-Marco[1]; R Montiel Quintero[1]; E Perez-Nogales[2]; JM Medina Gil[2]; E Caballero Dorta[1]; H Mendoza Lemes[1]; M Lopez Perez[1]; A Antonio Garcia Quintana[1]
[1]University Hospital De Gran Canaria "Dr. Negrin", Las Palmas de Gran Canaria, Spain; [2]University Hospital Insular of Gran Canaria, Las Palmas De Gran Canaria, Spain

Background: Diuretic therapy in heart failure with reduced ejection fraction (HFrEF) is recommended to reduce signs and symptoms of congestion. Sacubitril/valsartan, an angiotensin receptor-neprilysin inhibitor (ARNI), is a novel treatment of HFrEF that has shown to reduce symptoms and improve survival. No real world data is available to study the association between clinical response to ARNI and loop diuretic management over time.



Diuretic use after ANRI treatment

Purpose: The aim of our study is to assess the clinical impact of ARNI treatment in patients with HFrEF and evaluate diuretic treatment patterns in these patients.
Methods: Overall, 106 patients with HFrEF started on ANRI during September 2016 to December 2017 in two university hospitals were analysed in an ambispective, multicentre study. Baseline characteristics, clinical response using the NYHA class and assessment of the dosage of loop diuretics during the follow up was carried out.
Results: The cohort included 68.9% men and 31.1% women, with a mean age of 63.5 ± 11.6 years. Regarding comorbidities, 74.5% had hypertension, 51.9% dyslipidaemias, 49.1% diabetics and 30.2% had AF. 37.7% had a LBBB, 20.8% had a CRT and 28.3 had an ICD. 44.3% were on NYHA class III, 49.1% NYHA class II, and 6.6% had no detailed NYHA class. At the baseline, treatment included: 63.2% ACEIs, 33% ARBs, 94.3% betablockers, 82% had antialdosterone drugs and 24.5% had ivabradine.
Of the total cohort, 82% of the patients were treated with oral diuretic (94% furosemide or 6% torasemide) before the start of INRA. In a mean follow up of 219 (51-304) days, 13,2% was maintained without loop diuretic, in 9,4% was discontinued, in 15,1% reduced, 46,2% continued with the same dose, 11,3% needed to be increased and 4,7% (n 5) loop diuretics were newly introduced. In those patients who required an increase in diuretic treatment, 25% presented hospitalization after INRA initiation and 2 patients worsened their functional class.
A further analysis of the loop diuretic patters of those patients during follow-up in NYHA class I was performed (n = 16, 15%), concluding that 37.5% had no diuretic at the end of the follow-up, 6% decreased the diuretic dosage, 25% increased dosage, and in 31.5% the same dose was continued despite clinical improvement and no symptoms of heart failure. Interestingly, the average dosage in these patients was of 35 mg/day. No worsening of the renal function, no increase of NT-proBNP or secondary effects were related to maintained diuretics on these patients.
Conclusion: INRA treatment usually allows to stop or decrease diuretic dose. Nevertheless, in our serie no significant dosage reduction of loop diuretics was observed despite improvement in the symptomatology of patients with HFrEF under treatment with INRA. Efforts should be made to adjust diuretic dosage according to individual needs over time, achieving the lowest needed dose (including discontinuation) to maintain euvolemia and therefore avoid possible adverse effects.

P1778

Elevated pulmonary vascular resistance is superior to mean transpulmonary gradient in predicting right heart failure after heart transplantation: a 12-year single center analysis

CMF Christopher Strong[1]; A Tralhao[1]; C Aguiar[1]; MJ Rebocho[1]; T Nolasco[2]; M Marques[2]; A Ventosa[1]; M Mendes[1]; M Abecasis[2]; JP Neves[2]
[1]Hospital de Santa Cruz, Cardiology, Lisbon, Portugal; [2]Hospital de Santa Cruz, Lisbon, Portugal

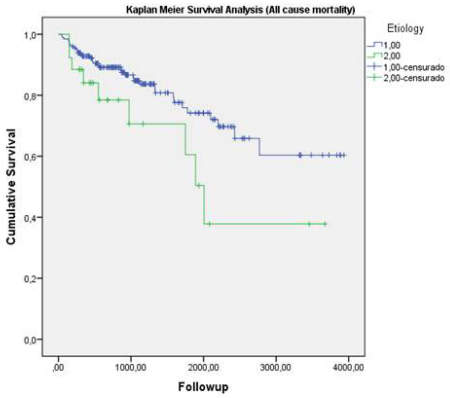
Background: Right heart failure (RHF) after heart transplantation (HTx) may adversely affect prognosis. Risk prediction is mostly based on invasive hemodynamic data but there is no consensus about the single best parameter to aid in risk stratification.
Purpose: We sought to compare the ability of usual right heart catheterization (RHC) derived parameters in predicting RHF after HTx.
Methods: Single-center retrospective study of all adult patients undergoing orthotopic bicaval HTx between January 2006 and November 2017 in a single-center. Pulmonary artery (PA) pressures (mean [mPAP], diastolic [dPAP]), transpulmonary gradients (mean [mTPG], diastolic [dTPG]) and pulmonary vascular resistance (PVR) were obtained from each patient's last RHC before HTx. RHF after HTx was defined as right ventricular dilatation (right ventricle/left ventricle basal diameter > 1) and dysfunction (tricuspid annular systolic plane excursion < 12 mm) on transthoracic echocardiography plus signs of end-organ dysfunction (creatinin increase > 0.5 mg/dL from baseline or spontaneous prothrombin time > 14 s), without a plausible alternative cause. Univariate and multivariate analysis were performed to find independent predictors of RHF and receiver operating curve (ROC) analysis was used to assess discriminative power.
Results: Fifty-eight heart transplant patients were identified and analyzed (mean age 51 ± 11 years, 58 % male). The most frequent etiologies were ischemic heart disease (n = 21) and dilated idiopathic cardiomyopathy (n = 16). Pre-operative PVR was 3.3 ± 2.1 Wood units, mean PAP was 38 ± 10 mmHg, dPAP was 27 ± 7 mmHg and mTPG and dTPG were 10 ± 5.3 and 3.5 ± 2.7 mmHg, respectively. 14% of patients (n = 8) were on inotropic support and 10% (n = 6) required pre-HTx mechanical circulatory support (MCS). After HTx, RHF incidence was 5.2 % (n = 3) and one patient required temporary right ventricular MCS. In univariate analysis, elevated PVR, mTPG, mPAP and dPAP were associated with increased incidence of RHF. After multivariate logistic regression modelling, only PVR remained significantly associated with post-HTx RHF (OR 1.6 [CI 95%, 1.1-2.6], p = 0.03). ROC curve analysis using PVR as the discriminator yielded a C-statistic of 0.8 [CI 95%, 0.7-1.0, p = 0.03) for RHF occurrence after HTx. In a mean follow-up of 4.2 years, overall mortality was not different between those with RHF and those without (p = 1.0).
Conclusions: In our population, RHF after HTx was an uncommon finding. Elevated PVR seems to be superior to other RHC derived parameters in predicting RHF following HTx.

P1779

Effectiveness of cardiac resynchronization therapy in heart failure patients with valvular heart disease: comparison with patients with dilated cardiomyopathy

V Vera Marinho[1]; J Milner[1]; P Alves[1]; C Domingues[1]; F Ferreira[1]; N Antonio[1]; L Elvas[1]; F Goncalves[1]; M Pego[1]
[1]University Hospitals of Coimbra, Cardiology, Coimbra, Portugal

Introduction: Heart failure (HF) may occur in the presence of a wide range of underlying heart diseases, including valvular heart disease (VHD). In the majority of randomized clinical trials that validated the clinical use of cardiac resynchronization therapy (CRT), the presence of a clinically significant valvular heart disease were exclusion criteria. The aim of this study was to analyze the effectiveness of CRT in patients with VHD in comparison with dilated cardiomyopathy patients.
Methods: Retrospective single-centre study that included all patients submitted to CRT therapy between January 2006 and December 2015. For the aims of current analysis, the following groups were considered: 1) patients with valvular heart disease (evidence of clinically significant primary valvular disease or previous valve replacement or repair; 2) patients with dilated cardiomyopathy (presence of a typical pattern of this heart disease, without ischaemic or organic VHD). The response to CRT was evaluated comparing the baseline with 6 month follow-up echo data. In long term follow-up we evaluated all-cause mortality, transplantation rate and admissions for HF.



	Chi square	df	Sig.
Log Rank (Mantel-Cox)	4,337	1	,037

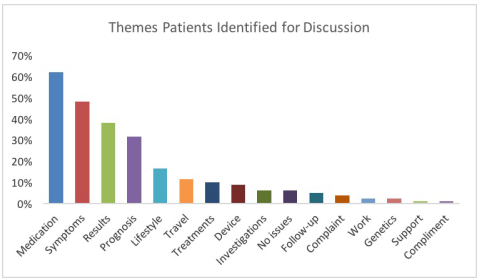
Results: A total of 431 patients submitted to resynchronization therapy in our centre were included. Of these, 199 patients (46%) had dilated cardiomyopathy and 26(6.0%) had valvular heart disease. Age did not differ between groups [65 (+11) vs 69 (+9) years, p = 0.253)]. There were no differences between the distribution of Diabetes Mellitus (29% vs 24%, p = 0.574), hypertension (51% vs 42%, p = 0.531), dyslipidemia (62% vs 75%, p = 0.331) and chronic kidney disease (29%vs53%, p = 0.07). The distribution of LBBB (82% vs 89%, p = 0.402), and basal LV end diastolic volume [219(104) vs 210(110), p = 0.867] was similar between groups. At 6 months echo, there was a trend to a more positive response to CRT in group of patients with dilated cardiomyopathy (55% vs 49%, p = 0.06). Interestingly, group 1 patients were more frequently super responders (29 vs 6.3%, p = 0.04). The mean follow up was 42(+33) months. Mortality (18% vs 35%, p = 0.04) was significantly lower in dilated cardiomyopathy. Both groups did not differ in transplantation rate (6.1 vs 3.8, p = 0.538) and admissions for acute HF (29% vs 35%,p = 0.33). The survival curves for all-cause mortality obtained by Kaplan–Meier analysis are shown in Figure 1 and revealed a worse prognosis of patients with VHD (Log-rank test, p = 0,037). In multivariate logistic regression analysis, the presence of Diabetes Mellitus [4.0 (1.1-16), p = 0.04] and the VHD etiology [6.1(1.1-33), p = 0.03] significantly increased the risk, while responsiveness to CRT proved to have a significant protective role in the whole patient population [0.13(0.03-0.4), p = 0.02].
Conclusions: No randomized controlled trial has specifically evaluated the effects of CRT in patients affected by a VHD, but on the basis of 'real world' clinical practice, CRT appears more effective in dilated cardiomyopathy than VHD.

P1780

"The patient will see you now". Use of a clinic proforma to help clinicians identify the heart failure patients' agenda

MG Williams[1]; R Baker[1]; B Pearson[1]; H Lightfoot[1]; H Donaldson[1]; AK Nightingale[1]; Y Ismail[1]
[1]Bristol Heart Institute, Department of Cardiology, Bristol, United Kingdom

Background: Heart failure patients have significant comorbidities and present complex decision-making issues in clinic. As a result, issues that are important to patients and their carers can easily be overlooked. Often this can mean that clinicians do not give sufficient time to identify the issues of most importance to a patient. Shared decision-making helps to improve patient quality of life and outcomes.
Purpose: We wanted to identify if a proforma given to patients and their carers to complete prior to their clinic appointment would help identify the patients' agenda for the appointment.
Methods: We designed a proforma for patients to complete while they were waiting to be called in for their clinic appointment. We asked them to record any topics or specific questions they would like to discuss in the clinic. We collected this data from our doctor or nurse led outpatient specialist heart failure clinics between August and December 2017. Individual responses were then thematically analysed and divided into 16 broad categories. Patients were asked after the clinic to rate how useful they found the form on a scale of 1 to 5.
Results: We received completed forms from 79 patients with a total of 202 questions or themes to be discussed. The main topics to discuss were medication (62%), symptoms (48%) and test results (38%). In addition to these subjects, almost one third of patients wanted to discuss the future and a significant proportion asked about lifestyle and travel. Other themes are shown in figure 1.
Patients found the survey useful with an average rating of 3.9 out of 5. All clinicians found the proforma helpful.
Conclusions: The use of a proforma to identify topics that patients wanted to discuss in their heart failure clinic appointment was helpful to clinicians and valued by patients. This may give further opportunities to increase shared decision-making and provide opportunities to discuss complex issues such as planning for the future and prognosis. These results would also suggest a beneficial role for cardiac pharmacists and palliative care specialists within our heart failure clinic to help meet patient and carers' needs.



P1781

Incidence and factors related to vasoplegia in the early postoperatory period of orthotopic heart transplantation

R Raquel Lopez Vilella[1]; I Sanchez Lazaro[1]; MJ Paniagua Martin[2]; G Barge Caballero[2]; E Marques-Sule[3]; E Barge Caballero[2]; M Crespo Leiro[2]; L Almenar Bonet[1]
[1]Hospital Universitario y Politécnico La Fe, Heart Failure and Transplant Unit. Cardiology Department, Valencia, Spain; [2]University Hospital Complex A Coruña, Cardiology Department, A Coruña, Spain; [3]University of Valencia, Physiotherapy Department. , Valencia, Spain

Background and objective: The vasoplegia syndrome is a serious complication that may occur after any surgery with extracorporeal circulation. It is defined as hypotension, acidosis and vasodilation with normal or increased cardiac output. Our purpose was to describe the incidence of vasoplegia after heart transplantation (HT), the factors related to the presence of vasoplegia, and its repercussion on mortality in the early postoperatory period of heart transplantation
Methods: All HT performed between June 2010 and December 2016 were consecutively recruited in two Spanish centres. Combined transplants, pediatric transplants and retransplants were excluded. Definition of vasoplegia: mean arterial pressure < 50 mmHg, serum bicarbonate < 19 mE / L and lactic acid > 2.
Results: 100 patients, 78% males, average age 52 ± 15 years. 39% of HT (37) were urgent, 98% of them (38) with circulatory / ventricular assistance. 16 patients presented post-transplant vasoplegia (16.8%). The development of post-transplant vasoplegia was related to: elevation of GOT before HT (30% vs 11%, p 0.022), previous mechanical ventilation (33% vs 13%, p 0.041), perioperative bleeding (31% vs 6%, p 0.02) and number of previous sternotomies (p 0.01). In the multivariate analysis, only perioperative bleeding was independently associated to the presence of post-transplant vasoplegia. The presence of vasoplegia was associated to an increase of mortality at one month (50% vs 11%, p < 0.01) and at 6 months after HT (31% vs 6%, p 0.003).
Conclusions: The incidence of vasoplegia after heart transplantation may reach high values 16.8% . The presence of vasoplegia is independently related to perioperative bleeding, whilst it is associated to an increase in early mortality and mortality at 6 months after HT.

P1782

Effects of a home-based nurse monitoring program on treatment compliance, quality of life, and hospitalizations of patients with chronic heart failure

V Bistola[1]; M Thodi[1]; E Lambrinou[2]; G Bakosis[1]; S Katsanos[1]; K Toli[1]; J Parissis[1]; G Filippatos[1]
[1]Attikon University Hospital, Athens, Greece; [2]Cyprus University of Technology, Nicosia, Cyprus

Background: Home-based nurse monitoring programs have been shown to reduce unplanned readmissions of patients hospitalized due to decompensated heart failure.

Purpose: To investigate whether a home-based nurse-provided monitoring program, combined with standard multidisciplinary outpatient heart failure clinic care improves treatment compliance, quality of life and reduces risk of unplanned HF-related hospitalization in patients with chronic heart failure (CHF).
Methods: Eighty patients with CHF were randomized by a 1:1 ratio to either standard heart failure clinic care alone (Group ?, n = 40) or to standard care combined with a home-based nurse-provided monitoring program (Group B, n = 40). Home-based monitoring was delivered through regular home visits or telephone contacts by a heart failure nurse. Monitoring included recording of vital signs, HF symptoms and assessment of treatment compliance by Morisky scale and quality of life by Kansas City Cardiomyopathy Questionnaire (KCCQ). Data collected were communicated to the heart failure physician who made drug changes or advised further specific monitoring according to standard protocols. We compared changes in treatment compliance and quality of life between Groups A and B as well as the effect of home monitoring program on rates of HF hospitalizations during a 6-month follow up.
Results: At baseline, Groups A and B did not differ with respect to gender (male: 67.5% vs 77.5%, respectively, p = 0.317), HF etiology (ischemic: 40% vs 55%, p = 0.467), NYHA class (I/II: 65% vs 60%, p = 0.255), LVEF (35 ± 10% vs 33 ± 10%, p = 0.299), treatment compliance (High compliance: 37.5% vs 20%, p = 0.192), and the overall summary (OS) (59.9 ± 24.4 vs 55.1 ± 23.2, p = 0.366) and clinical summary (CS) KCCQ score (68.7 ± 24.6 vs 60.9 ± 26, p = 0.174). At follow up, Group B patients showed better treatment compliance compared to Group A (High compliance: Group B 82.5% vs Group A 32.5%, p < 0.001), and improved both OS and CS KCCQ score, as compared to Group A patients whose KCCQ scores deteriorated (d(KCCQ-Overall): Group B, 17.3 ± 17.7 vs Group ?, -7.9 ± 17.7, p < 0.0001; d(KCCQ-Clinical): 20.8 ± 23.6 vs Group A, -8.5 ± 19.7, p < 0.0001). During a median follow up of 178 days (min 27-max 250 days), 8 patients in Group A compared to 3 in Group B were hospitalized due to HF. Age-adjusted Cox regression analysis showed that randomization to Group B was associated with lower risk of HF hospitalization (HR, 95%CI: 0.217, 0.054-0.865, p = 0.03).
Conclusions: Enrolment of CHF patients to a home-base nurse-provided monitoring program combined with standard multidisciplinary heart failure clinic care may improve treatment compliance, quality of life and reduces risk of unplanned HF hospitalizations.

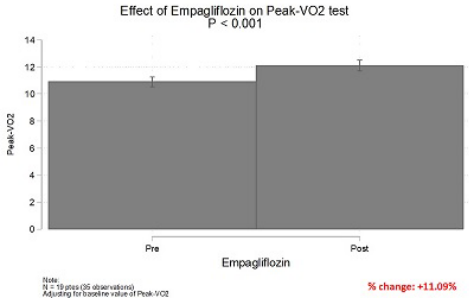
P1783

Early effects of empagliflozin on exercise tolerance in patients with heart failure: a pilot study

A Anna Mollar Fernandez[1]; P Palau[2]; E Dominguez[2]; E Nunez[1]; JM Ramon[1]; G Minana[1]; E Santas[1]; L Facila[1]; JL Gorriz[3]; J Sanchis[1]; A Bayes-Genis[4]; J Nunez[4]
[1]University Hospital Clinic of Valencia, Cardiology, Valencia, Spain; *[2]Hospital General de Castellón, Cardiology, Castellon, Spain*; *[3]University Hospital Clinic of Valencia, Nefrology, Valencia, Spain*; *[4]University Hospital Trias i Pujol, Cardiology, Barcelona, Spain*

Funding Acknowledgements: CIBER CV 16/11/00420, 16/11/00403; FEDER and PIE15/00013

Background: Sodium-glucose transporter 2 (SLGT2) inhibition recently emerged as a promising therapy for reducing the risk of heart failure (HF) in patients with type 2 diabetes. However, there is a lack of data endorsing its role in symptomatic HF patients. We sought to evaluate the short-term effects of empagliflozin on maximal exercise capacity in these patients.
Methods and Results: Nineteen type 2 diabetes patients with symptomatic HF were prospectively included and underwent a cardiopulmonary exercise testing before and 30 days after initiation of empagliflozin therapy. A mixed-effects model for repeated-measures was used. Median (IQR) age was 72 years (60-79) and 42.1% were on New York Heart Association class III. Baseline mean (SD) peak oxygen consumption (peak VO2) was 10.9 ± 4.0 ml/min/kg. Peak VO2 increased significantly at 30-day (?=+1.21 (0.66-1.76); p <0.001). A significant improvement in ventilatory efficiency during exercise, distance walked in 6-minute, quality of life, and a reduction in plasma levels of antigen carbohydrate 125 were also found. Estimated glomerular filtration rate and natriuretic peptides did not significantly change.
Conclusions: In this pilot study, empagliflozin was associated with 1-month improvement in exercise capacity in type 2 diabetic patients with symptomatic HF. This beneficial effect was also found for other surrogates of severity.



Effect of Emplaglifozin on Peak-VO2 test

P1784

Possibilities of differentiated immunosuppressive therapy in patients after orthotopic heart transplantation

A Kurlianskaya[1]; YU Ostrovkiy[1]; T Troyanova-Shchutskaia[1]; O Shatova[1]; T Denisevich[1]; T Dubovik[1]
[1]Republican Scientific and Practical Centre of Cardiology, Minsk, Belarus

Backgroud: Coronary artery disease of the transplanted heart is one of the serious problems reducing patients' life expectancy, despite the successful clinical experience of orthotopic heart transplantation.
Purpose: to evaluate the effectiveness of various schemes of immunosuppressive therapy in patients after orthotopic heart transplantation
Methods. After the initial intravascular ultrasound (IVUS) all patients were randomized according to different immunosuppressive therapy: tacrolimus+mycophenolate mofetil (group 1, n = 60) and tacrolimus+everolimus (group 2, n = 17). The next IVUS was performed in 24 months after surgery.

Tge degree of affection of coronary arteries	tacrolimus + mycopheno-late mofetil (n = 60)	p	tacrolimus + everolimus (n = 17)	p		
Intravascular ultrasound 1	Intravascular ultrasound 2	Intravascilar ultrasound 1	Intravascular ultrasound 2			
Moderate	0.40 (0.37; 0.43)	0.60 (0.53; 0.65)	0.031	0.43 (0,40; 0.58)	0.39 (0.36: 0.43)	0.851
Severe subclinical	0.68 (0.59; 0.82)	0.60 (0.50; 0.79)	0.835	0.76 (0.56; 0.90)	0.66 (0.61; 0.74)	0.046

Results: Some differences between analizing groups were noted from the primary to the second IVUS. The body mass index significantly increased from 26.0 (26.0, 30.0) to 28.0 (25.0, 31.5) in group 1 (p = 0.002) vs. no significant changes in group 2 (p = 0.500). Statistically significant differences were revealed between groups before recurrent IVUS by the following echocardiographic indices: myocardial contractility, estimated by the index of local contractility (ILC) and global peak strain. The ILC was 1.10 (0.96, 1.49) in group 1 and 1.00 (1.00, 1.13) group 2, p < 0.001. The average global peak strain was lower in group 1 (-16.95 (-16.10, -18.70) vs. -18.60 (-13.10, -22.30), p = 0.012. In both groups a significant increase in VO2 and VO2AT was revealed. However in the group 2 the growth of these indicators was greater. The VO2 index increased by 84.00% (p = 0.018), the VO2AT index by 48.70% (p = 0.002). In group 1 these indicators increased by 12.4% (p = 0.001) and by 16.7% (p < 0.001), respectively.
The regression of intima thickness was observed in patients of the group 2 and with severe subclinical coronary arthery lesions. Intimal thickness changed from 0.76 mm to 0.66 mm (p = 0.046) in 24 ± 3 months after the start of treatment. In group 1 there was no statistically significant decrease in intimal thickness (table).
Conclusion. The regression of intimal thickness was observed in patients with severe subclinical coronary artery lesions, diagnosed 24 ± 3 months after heart transplantation. Everolimus needs to be included into the scheme of immunosuppressive therapy.

P1785

Meldonium and gamma-butyrobetaine combination improves cognitive function and flow-mediated vasodilatory response in chronic systolic heart failure: the results of open-label pilot study.

L Voronkov[1]; A Anastasiia Solonovych[1]; A Liashenko[1]; A Dudnik[1]
[1]*NSC Institute of Cardiology M.D. Strazhesko, Heart Failure Department, Kiev, Ukraine*

Background: Cognitive impairment and endothelial dysfunction are observed in majority of chronic heart failure (CHF) patients (pts). There is evidence that new formulation - meldonium (M) and gamma-butyrobetaine (GGB) combination - improves cognitive function (CF) in patients with neurological disorders. M partially blocks fatty acid transport to mitochondria through inhibition of carnitine synthesis that results in elevation of gamma-butyrobetaine GBB tissue content. It was shown that through its muscarinic receptor agonism, GBB ethyl- and methyl ethers stimulate endothelial nitric oxide synthesis and, therefore, cause improvement of endothelium-mediated vasodilator response.
Purpose: to evaluate the dynamics of CF, quality of life and flow-mediated vasodilatory response (FMVR) in pts with systolic CHF under M+GGB administration.
Methods: 22 cognitively impaired pts with stable CHF, NYHA II-IV and left ventricular ejection fraction (LVEF) < 40% were examined. Informed consent was mandatory. CF was evaluated by standard MMSE and Shulte tests, anxiety/depression score - by HADS scale. Quality of live was evaluated by The Minnesota Living with Heart Failure Questionnaire (MLHFQ). FMVR of the brachial artery was detected ultrasonically by the standard cuff test. M 360 mg + GBB 120 mg combination was prescribed t.i.d. (every 8 hours) for four weeks. Statistic methods descriptive statistics, Wilcoxon signed-rank test.
Results: after 4-week M + GBB administration pts demonstrated significant improvement of MMSE score (p = 0.001), Schulte score (p = 0.002) and MLHFQ score (p = 0.029). M + GBB combination also demonstrated pronounced improvement of FMVR (p = 0.0001). However, there were no significant changes of anxiety and depression levels by HADS score (p = 0.16 and p= 0.09, respectively).
Conclusion: our pilot study demonstrates that 4-week M + GBB administration improves CF and quality of life in pts with CHF associated with significant FMVR improvement.

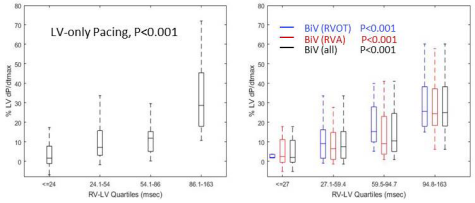
P1786

The Effect of Interventricular Delay on Acute Hemodynamic Response with Cardiac Resynchronization Therapy

A Auricchio[1]; K Siejko[2]; Y Nancy Yu[2]
[1]*Cardiocentro Ticino, Lugano, Switzerland*; [2]*Boston Scientific Corporation, St. Paul, United States of America*

Funding Acknowledgements: Boston Scientific

Background: Despite the benefits of CRT, the non-responder rate still remains challenging. Measurement of electrical interventricular delay (i.e. RV-LV delay) has been shown as a strong determinant of clinical outcomes. Thus, pacing at site of longest RV-LV delay shall increase LV contractility. Moreover it is unknown whether LV pacing alone or biventricular pacing determines the same increase in LV contractility.
Methods: This study included 88 patients (65% male, mean age 60 ± 9 years, LV ejection fraction (LVEF): 23% ± 7%, QRS duration 156 ± 21 ms, 87% LBBB) undergoing CRT implants. At implant, invasive left ventricular (LV) dP/dtmax was measured by a micromanometer catheter during biventricular (BiV) or LV-only pacing at different LV sites while the right atrium was in sense mode. During BiV pacing, different RV sites (i.e. RV apex (RVA) and RV outflow tract (RVOT)) were also tested in combination with different LV sites. For each pacing configuration, 4 different AV delays were tested in randomized order. The intrinsic RV-LV duration was defined as the time interval from the peak of the RV electrogram (EGM) to the peak of the LV EGM. The maximum LV dP/dtmax responses were calculated for BiV and LV-only mode per LV pacing site in each patient.
Results: The RV-LV delay for this cohort ranged from -68 to 163 ms. The improvement in the LV dP/dtmax response increased progressively as RV-LV increased for both LV-only and BiV pacing, as well as for BiV pacing with RV pacing at RVA and RVOT (see figure).
Conclusions: Longer RV-LV delay was associated with larger acute hemodynamic response during both LV-only and BiV pacing regardless of the RV lead location. The RV-LV delay can be easily measured at implant and by CRT devices and may provide a simple means of selecting/optimizing LV stimulation site and possibly maximizing CRT response.



P1787

Evaluation of the optimal energy, protein, fat and carbohydrate needs in obese patients with chronic heart failure.

T Tatiana Zaletova[1]; A Bogdanov[1]; T Feofanova[1]; S Derbeneva[1]; I Shevchenko[2]
[1]*Research Institute of Nutrition of Russian Academy of Medical Sciences, Moscow, Russian Federation*; [2]*Gazprom Transgas Diagnostic and Rehabilitation Center, Internal Medicine, Moscow, Russian Federation*

Introduction: Obesity in chronic heart failure (CHF) patients is a new clinically significant factor. Previously, suboptimal food intake or even a strict caloric restriction used to be widespread in treating obesity, which significantly deteriorated comorbidities. The need for energy, necessary to prevent malnutrition of obese patients with heart failure is not still completely determined. Objective. To evaluate resting energy expenditure in obese patients with chronic heart failure. Methods. A total of 392 obese people were examined. According to the results of echocardiography and 6 minute walk test (SMWT), 152 people were included in the group with confirmed CHF. Assessment of basal metabolic rate was performed in all patients using indirect calorimetry with a stationary metabolograph.
Results: We demonstrated lower basal metabolic rate in patients with CHF compared to patients without CHF: in grade 1 obesity: 1687 ± 148 kcal/day vs. 1715.5 ± 63 kcal/day, p> 0.05, in grade 2 obesity: 1635 ± 164 kcal/day vs 1843 ± 52 kcal/day, p>0.05, in grade 3 obesity 2072 ± 51 kcal/day vs 2334 ± 110 kcal/day, p < 0.05, respectively. Also patients with CHF had a significantly (p < 0.01) lower carbohydrate oxidation rate compared with patients without CHF. The study showed that protein oxidation rate increased in CHF patients with progressive obesity; while in patients without CHF this tendency was not observed. Thus, depending on the presence or absence of CHF, in grade 1 obesity patients protein oxidation rate was 79 ± 11 g/day and 55 ± 3.2 g/dayin grade 2 - 88 ± 6 g/day and 69.4 ± 3.94 g/day, with grade 3 - 92 ± 4 g/day for and 73.75 ± 3.98 g/day, respectively. Conclusions. Thus, obesity along with CHF compared with obesity without it is accompanied by significant changes in the nutritional metabolic status of patients, in particular a lower basal metabolic rate, lower carbohydrate oxidation rate and a higher protein oxidation rate, which can be caused by such pathogenetic processes as decreased energy consumption in the mitochondrial system, by insulin resistance and muscular tissue catabolism. The revealed data confirm the need to optimize diets for this category of patients.

Distribution of subjects by group

Value	Obesity Grade 1 with CHF (n = 18)	Obesity Grade 2 without CHF (n = 78)	Obesity Grade 3 with CHF (n = 23)	without CHF (n=81)	with CHF (n = 111)	without CHF (n=81)

Chronic Heart Failure - Clinical

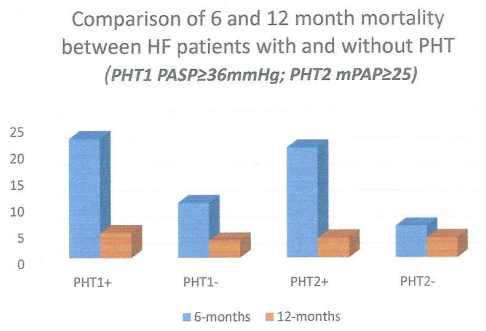
P1788

Influence of pulmonary hypertension on the 6 and 12 months outcome in acutely decompensated heart failure patients.

A Amam Chinyere Mbakwem[1]; O Kushimo[2]; JNA Ajuluchukwu[1]
[1]*University of Lagos, Lagos, Nigeria*; [2]*Lagos University Teaching Hospital, Lagos, Nigeria*

Background: Pulmonary hypertension (PHT) is highly prevalent amongst heart failure (HF) patients and now recognized as an independent predictor of poor prognosis. There is paucity of data on the frequency and correlates of PHT in HF in our environment, effect on management and its impact on outcomes. We therefore evaluated the 6 and 12 months influence of PHT on HF outcomes in our environment.

Purpose: To Evaluate effect of PHT on the 6 and 12 months outcomes in acutely decompensated HF patients seen at a West African academic hospital.
Methods This was a prospective study of 219 HF patients in NYHA II-IV with acute decompensation, consecutively recruited from the emergency room and the cardiology out-patient clinic. HF patients with other co-morbidities that can cause PHT were excluded. Data on demographic parameters, clinical features and echo parameters were collected with a CRF. Correlation between elevated PASP / mPAP and selected clinical parameters were further interrogated. Patients were followed up for 6 and 12 months post discharge for death or rehospitalisation.
Results The frequency of PHT was determined by two criteria. PHT using a PASP cut off of = 36mmHg was present in 85 (38.8%) of subjects and 136(61.6%) of subjects using the mPAP criteria of = 25mmHG. HF subjects with PHT were more likely to be male, p = 0.001, with a lower BMI, p < 0.001, lower systolic blood pressure, p < 0.001 and a worse NYHA functional class, p < 0.001 compared with subjects without PHT. The PHT subjects also had significantly higher LV filling pressures, p = 0.001), severe mitral regurgitation (higher mitral regurtitant volume, p = 0.001), poorer LV systolic function, and worse RV structure and function compared with those without PH.
Echocardiographic variables that correlated significantly with PASP include parameters of LV filling pressures (p < 0.001 for all), mitral regurgitant volume (r = 0.269, p < 0.001) LV and ejection fraction (r = -0.239, p > 0.001). Similar correlations were obtained with mPAP. On multivariate analyses, the left atrial volume index and E/e' ratio were independently associated with PASP, while the LV ejection fraction, E/e' ratio and the left atrial volume index were independently associated with mPAP.
At 6-months, 33(15%) of the patients had died; higher in the PHT group, 19(22.4%) vs 14(10.4%), p 0.02 using PASP and 28(20.7%) vs 5(6.0%), p = 0.003 using mPAP. There were 7(3.8%) more deaths at 12-months but there was no difference between the patients with or without PHT using both criteria. About 5 people were rehospitalised over the 12 month period, 3(1.4%) within 6 months and 2(0.9%) by the end of 12 months with no differences seen between the PHT groups
Conclusion: PH is common amongst HF in our environment with a variable frequency depending on the assessment method employed. It is associated with a worse 6-month mortality but no effect on 12-month mortality.



6 and 12 month mortality of HF with PHT.

P1789

Prognostic impact of serum metabolomic profiling of patients with heart failure with reduced ejection fraction

R Pistulli[1]; S Neugebauer[2]; T Kretzschmar[1]; D Kretzschmar[1]; B Heidecker[3]; M Franz[1]; M Kiehntopf[2]; P C Schulze[1]
[1]University Hospital of Jena, Internal Medicine I, Dept. of Cardiology, Jena, Germany; *[2]University Hospital of Jena, Institute for Clinical Chemistry and Laboratory Medicine, Jena, Germany*; *[3]University Heart Center, Cardiology, Zurich, Switzerland*

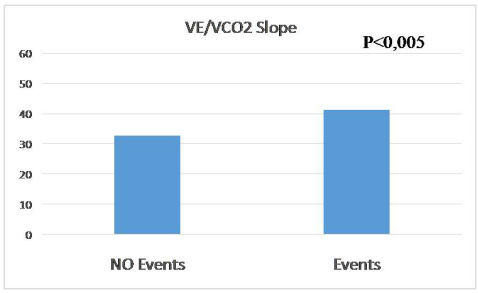
Aims: Recent studies on metabolomics of patients with heart failure with reduced or preserved ejection fraction have shown several alterations of metabolites. Systematic screening allows the characterization of new pathways for the discovery of prognostic markers or therapeutic targets in heart failure. We used this novel technique in order to characterize metabolic changes in heart failure patients, as well as asses their prognostic potential.
Methods: 181 serum metabolites of 40 chronic severe heart failure patients (n = 20 ICM, n = 20 DCM, mean EF 28.3%, 65% NYHA III/IV), as well as 10 control individuals were quantified by liquid chromatography tandem mass spectrometry. Significantly altered metabolites (using a predefined Bonferroni corrected level of significance) were then correlated to an extensive patient database of clinical parameters at the time of the measurement, as well as after a 12 months follow-up period. Altered metabolites were analyzed for their specificity of the severity of HF, as well as their correlation to dEF (calculated EF difference during the follow-up period).
Results: In HF patients compared to controls, we found a significant decrease of phosphatidylcholines and sphingolipids, as well as an increase of acylcarnitines, the aminoacids aspartate, methionine and phenylalanine. The specificity of long-chain acylcarnitines for the severity of HF was similar to BNP (ROC for NYHA III/IV, AUC 0.796 and 0.761 respectively), while both were better than EF (AUC 0.343). Such was also observed for phosphatidylcholines (AUC: 0.8, vs. BNP 0.86 vs EF 0.73). Correlation statistics between altered metabolites and follow-up parameters revealed a significant inverse correlation between acylcarnitines and dEF (r -0.681, p < 0.01).
Conclusions: We observed significant alterations of serum metabolites in severe HF patients. Phosphatidylcholines and acylcarnitines were strongly related to heart failure severity, while acylcarnitines also correlated with disease progression in terms of LV function. This novel technique could possibly identify prognostic markers of HF and lead to a better understanding of metabolic abnormalities of HF.

P1790

Left ventricular ejection fraction is unable to prognostic stratification in patients with chronic heart failure. the role of cardiopulmonary exercise test and right ventricular evaluation

A Antonio Pagliaro[1]; R Molle[2]; E Iardino[3]; M Cameli[1]; S Bernazzali[4]; M Iacoviello[5]
[1]University Hospital AOUS, Department of Heart,Thorax and Vessels, Cardiology Division, Siena, Italy; *[2]Misericordia Hospital, Cardiology, Grosseto, Italy*; *[3]University of Siena, Cardiology, Siena, Italy*; *[4]Polyclinic Santa Maria alle Scotte, Cardiothoracic Surgery, Siena, Italy*; *[5]Policlinic University Hospital, Cardiothoracic, Bari, Italy*

Background: It is well know how hard is the prognostic stratification in patients with chronic
heart failure reduced ejection fraction (CHFrEF). At the same time it is well know how is important this information to optimize resources. Many different parameters, including left ventricular ejection fraction (LVEF), right ventricular (RV) function, cardiopulmonary exercise test (CPET) data, are available in literature for this goal. LVEF is current used to assemble patients in consistent groups, to justify many therapeutic decisions and it is also the most noted and cited heart failure indicator but it is an inadequate parameter to achieve a correct prognostic stratification.
Aim: we analyzed CPET and echocardiographic data collected in our center during outpatients visits for heart transplantation screening to understand which parameters had correlation to hard cardiac events (heart failure hospitalization, cardiac death, heart transplantation -HTx, left ventricular assist device -LVAD- implantation).



VE/VCO2 Slope and events

Methods and Results: 410 patients with CHFrEF underwent incremental CPET and echocardiographic evaluation from January 2012 to October 2016; of these patients we analyzed data from 170 (mean ± SD age: 55,09 ± 9,94; 88% male; non-ischemic: 63%; LVEF: 30,44 ± 7,61 %; end-diastolic diameter EDD: 66,53 ± 9,36 mm; end-systolic diameter ESD: 53,71 ± 11,5 mm; RV EDD 35,26 ± 6,95 mm; tricuspid annular plane systolic excursion TAPSE 18,55 ± 3,98; peak oxigen uptake VO2: 17,08 ± 4,6 mL/Kg/min; % predicted Peak Oxigen uptake %pVO2: 61,07 ± 13,95; minute ventilation VE/carbon dioxide production VCO2 relationship VE/VCO2 Slope: 34,81 ± 8,7) and collected prognostic information of 133 (follow up from January 2012 to October 2017, total events 60, of these 37 hospitalizations, 4 deaths, 14 HTx 5 LVAD implantation). Patients who have been affected by events showed a statistically significant (p < 0,005) lower VO2 value (< 15 ml/Kg/min; %pVO2 < 55%), higher VE/VCO2 slope (<41), higher LV ESD (<52 mm) and higher RV EDD (<39 mm) than patients without events. Contrarily LVEF was not statistically significant different between patients with and without events. We have also found a statistically significant correlation between VE/VCO2 slope and RV EDD (R 0,35; p 0,0005).
Conclusion: outpatients CHFrEF prognostic stratification is still an hard challenge for cardiologist. The LVEF alone, moreover cornerstone of many different therapeutic choices, is lacking. Useful are those parameters that identify an advanced stage of the disease (extreme adverse LV remodelling, right ventricular involvement)

or provide a quantification of the system reserve (VO2 peak; VE/VCO2 slope). Also the correlation between VE/VCO2 slope and RV EDD supports the role of ventriculo-arterial unit in the clinical history of CHFrEF

P1791

Iron status and muscle-derived secretion of regenerative and pro-hypertrophic myokines (follistatin and decorin) in men with heart failure with reduced ejection fraction

MM Dziegala[1]; M Kasztura[1]; KA Kobak[1]; M Tkaczyszyn[1]; M Drozd[1]; K Wegrzynowska-Teodorczyk[2]; K Josiak[3]; J Bania[4]; L Kiczak[5]; W Banasiak[6]; P Ponikowski[3]; EA Jankowska[1]
[1]Wroclaw Medical University, Department of Heart Diseases, Laboratory for Applied Research on Cardiovascular System, Wroclaw, Poland; [2]University School of Physical Education of Wroclaw, Faculty of Physiotherapy, Wroclaw, Poland; [3]Wroclaw Medical University, Department of Heart Diseases, Wroclaw, Poland; [4]Wroclaw University of Environmental and Life Sciences, Department of Food Hygiene and Consumer Health, Wroclaw, Poland; [5]Wroclaw University of Environmental and Life Sciences, Department of Biochemistry, Pharmacology and Toxicology, Wroclaw, Poland; [6]Military Hospital of Wroclaw, Centre for Heart Diseases, Wroclaw, Poland

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Background: Disturbed iron status impairs the functioning of skeletal muscle in patients with heart failure (HF). Skeletal muscle has recently emerged as an important secretory organ producing various, mainly contraction-induced proteins (myokines). These bioactive factors trigger local responses and influence energy metabolism, hypertrophy and regeneration of the muscle.
Purpose: The aim of the study was to determine whether patients with HF and iron deficiency (ID) had the altered the secretion of follistatin, a myokine enhancing muscle regenerative potential, and decorin which exerts pro-hypertrophic effect. Further, we investigated whether the intravenous iron repletion influenced the exercise-induced production of these myokines.
Methods: Study population comprised of 53 men with heart failure with reduced ejection fraction (LVEF = 40%; mean age: ± 64 years; NYHA class I-II: 87%) and of 15 middle-aged healthy men. We assessed follistatin and decorin levels in plasma samples from peripheral blood from all patients by ELISA. Further, we analyzed samples taken from antecubital veins draining the forearm muscle before and after physical local exercise (standardized 5-minute handgrip exercise) for the myokines. Additionaly iron-deficient HF patients (serum ferritin < 100μg/L or serum ferritin = 100 μg/L and = 300 μg/L with Tsat < 20%) and were randomized in a 1:1 fashion (double-blind scheme) to receive either intravenous ferric carboxymaltose (FCM) or saline (comparator) (24-week dosing protocol according to CONFIRM-HF trial).
Results: There were no differences in both myokine levels measured in peripheral samples between HF patients with and without ID, and between HF patients and controls. There were no correlations between myokine concentrations in peripheral and forearm samples. Levels of follistatin and decorin assessed in the forearm samples both before and after handgrip were significantly lower in HF patients with ID as compared to those with preserved iron status (all $p < 0.001$). Further, lower levels of decorin in forearm samples of men with HF were associated both before and after exercise with lower mean handgrip strength ($R = 0.45$, $p < 0.01$; $R = 0.46$, $p < 0.01$). In HF patients during exercise a reduced netto decorin production correlated with higher netto lactate formation in forearm samples ($R = -0.38$, $p < 0.01$). Importantly, after FCM therapy the netto muscle production of follistatin in forearm samples were significantly increased in men with HF and ID treated with FCM as compared to those who received saline ($p < 0.01$).
Conclusions: Reduced follistatin and decorin secretion assessed in forearm blood, but not in peripheral blood, reflects the lower regenerative and pro-hypertrophic potential of muscle from patients with HF and ID. In patients with HF lower secretion of decorin during exercise is associated with altered muscle metabolic activity. Iron repletion therapy in patients with HF and ID partially restores the follistatin production during exercise.

P1792

Body composition and hydratation status in Heart Failure types

D Gonzalez[1]; A Orea-Tejeda[1]; R Sanchez-Santillan[1]; C Olivo-Villalobos[1]; G Davila-Said[1]; C Chavez-Mendez[1]; V Pelaez-Hernandez[1]; M Rivera-Rodriguez[1]; L Castillo-Aguilar[1]; K Balderas-Munoz[1]; A Figueroa-Herrera[1]
[1]Instituto Nacional de Enfermedades Respiratorias "Ismael Cosío Villegas", Heart Failure and Respiratory Distress Clinic, Mexico city, Mexico

Introduction : Patients with Heart Failure (HF) present different alterations in hydration status as well as a dismish of protein reserves wich increase the mortality and the hospitalization risk. However, the protein reserve has been unusually studied by the heart failure types.
Purpuse: To evaluate the hydration status and the protein reserve by heart failure type.
Materials and Methods: Cross-sectional study. 776 subjects older than 18 years old with a diagnosis of stable HF were included. The HF type was classified in: Heart Failure with reduced ejection fraction (HFrEF), Heart Failure with mid-range Ejection Fraction (HFmrEF), Heart Failure preserved Ejection Fraction (HFpEF). Patients with cancer diagnosis were excluded.
Results: Mean age 63.56, the 51.93% were men. Significant differences were observed between HErEF, HFpEF and HFpEF groups: sex (57.8 % vs. 59.2% vs. 43.6%, $p < 0.001$), body weight (66.3 ± 17.2 kg vs. 68.9 ± 17.6 kg vs 74.7 ± 23.8 kg, $p < 0.001$), mid upper arm circumference (28.1 ± 4.2 cm vs. 28.9 ± 4.6 cm vs. 29.8 ± 6.2 cm), total body water (56 ± 33.8% vs. 53.9 ± 8 % vs. 51.2 ± 8.7%, $p = 0.036$), third space (0.4 lt [-0.4 to 1] vs -0.3 lt [-0.8 to 0.8] vs 0.005 lt [-0.8 to 0.71], $p = 0.027$), lean body mass (8.6 ± 1.9 vs 9.2 ± 2.2 vs 9 ± 3.4, p= 0.106) and cachexia (65.9 % vs 55.6 % vs 49.5 %, $p = 0.003$).
Conclusions: Besides, subjects with HErEF have higher hydration status alterations and muscle depletion, those with HFmrEF present a similar and middle behaviour between HFrEF and HfpEF, wich disclose the degradation and poor prognosis.

P1793

Abdominal obesity as risk factor for endothelial dysfunction in heart failure and chronic obstructive pulmonary disease

C Chavez-Mendez[1]; A Orea-Tejeda[1]; R Sanchez-Santillan[1]; D Gonzalez-Islas[1]; L Castillo-Aguilar[1]; C Olivo-Villalobos[1]; G Davila-Said[1]; V Pelaez-Hernandez[1]; M Rivera-Rodriguez[1]; K Balderas-Munoz[1]
[1]Instituto Nacional de Enfermedades Respiratorias "Ismael Cosío Villegas", Heart Failure and Respiratory Distress Clinic, Mexico city, Mexico

Introduction: The prevalence of obesity in heart failure (HF) and Chronic Obstructive Pulmonary Disease (COPD) is high. Obesity affects the structure and endothelial function increasing the risk of cardiovascular events. Endothelial dysfunction (ED) is the imbalance between vasodilator and proinflammatory mediators and this one lead to atherogenesis. Waist circumference (WC) is a practical and non-invasive method that evaluates abdominal obesity (AO). Nevertheless, there is not enough evidence between the impact of AO on endothelial dysfunction.
Purpose: To determine if AO is a risk factor for ED in patients with HF and COPD.
Materials and methods: A cross-sectional study of 173 patients with HF and COPD diagnosis. The patients were divided into to groups; those with ED and those without. It was excluded patients with asthma, cancer and pulmonary fibrosis. Endothelial dysfunction was evaluated by photoplethysmography. Abdominal obesity was defined as waist circumference > 90 cm in males and > 80 cm in females.
Results: The mean age was 70.53 ± 12.02 years, 41.04% were men and 64.14% had cachexia. Patients with ED has lower arm circumference (27.91 ± 5.19 vs 30.89 ± 14.36, $p = 0.090$), compared with subject without ED. There was no difference in: fat mass, muscle mass, body fluids, impedance index, phase angle and force. Subjects with AO have 3 times the risk of developing ED compared to subjects without AO [RR 3.11, IC 95%; 1.07- 9.03, $p = 0.037$].
Conclusions: AO is a risk factor for ED in patients with HF and COPD.

P1794

Heart failure with atrial fibrillation: are greater elevations in natriuretic peptide levels temporary or permanent?

B T Santema[1]; CSP Lam[1]; AA Voors[1]
[1]University Medical Center Groningen, Cardiology, Groningen, Netherlands

Funding Acknowledgements: CVON2014-11 RECONNECT and FP7-242209-BIOSTAT-CHF

Background: Natriuretic peptides (NP) are elevated in heart failure (HF), but patients with atrial fibrillation (AF) and HF have even higher NP levels. These elevated NP levels in patient with concomitant AF could either be directly related to the hemodynamic changes during an episode of AF, to structural or functional cardiac remodeling due to sustained episodes of AF, or they could reflect that patients with AF have more advanced HF. In a post-hoc analysis of The BIOlogy Study to Tailored Treatment in Chronic Heart Failure (BIOSTAT-CHF) trial, we evaluated these three explanations.
Methods: Patients were categorized based on history and baseline electrocardiogram into three groups: (1) AF at time of NP measurement, (2) history of AF but in sinus rhythm (SR) at time of NP measurement and (3) SR at time of NP measurement and no previous documented episode of AF. The levels of N-terminal pro-B-type natriuretic peptide (NT-proBNP) were compared between the three rhythm groups. These levels were compared to the levels of growth differentiation

factor 15 (GDF-15); a biomarker that is well-established to reflect HF severity but is not known to be influenced by AF.
Results: A total of 1230 patients with HF with reduced ejection fraction (HFrEF) and 583 patients with HF with preserved ejection fraction (HFpEF) were studied. Similar trends were observed across the three rhythm groups, with stepwise increase in median NT-proBNP: lowest in the group with SR at baseline without a history of AF, intermediate in those with SR at baseline with a history of AF, and highest in those with AF at baseline (Figure 1). In contrast, the levels of GDF-15 were similar in patients with AF at baseline and those who only had a history of AF and were in SR at baseline.
Conclusion: These data suggest that the greater elevation in NP levels in HF patients with concomitant AF seem to be mainly caused by the immediate hemodynamic alterations during the actual episode of AF, and to a lesser extent to the chronic structural or functional cardiac remodeling as a result of sustained episodes of AF.

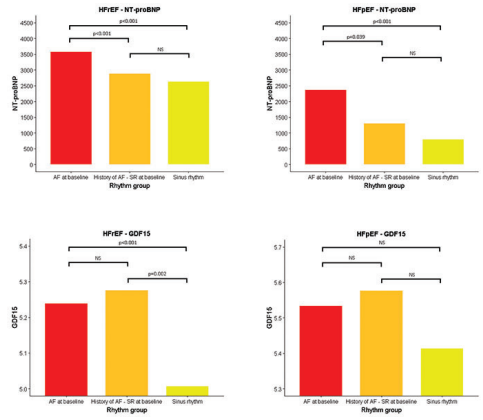

Figure 1

P1795

The cholesterol paradox may only be valid for heart failure patients without diabetes

FM Cunha[1]; J Pereira[2]; A Ribeiro[2]; S Silva[3]; JP Araujo[4]; A Leite-Moreira[5]; P Bettencourt[6]; P Lourenco[2]
[1]Hospital Center of Tras-os-Montes and Alto Douro, Department of Endocrinology, Vila Real, Portugal; *[2]Sao Joao Hospital, Department of Internal Medicine, Porto, Portugal*; *[3]Hospital CUF, Department of Internal Medicine, Porto, Portugal*; *[4]Sao Joao Hospital, Department of Internal Medicine - University of Porto Medical School, Porto, Portugal*; *[5]Sao Joao Hospital, Department of Cardiothoracic Surgery - University of Porto Medical School, Porto, Portugal*; *[6]Hospital CUF, Department of Internal Medicine - University of Porto Medical School, Porto, Portugal*

Funding Acknowledgements: Project DOCnet (NORTE-01-0145-FEDER-000003), NORTE 2020 under the PORTUGAL 2020 Partnership Agreement, European Regional Development Fund

Background: In heart failure (HF) patients, several paradoxes have been reported concerning traditional cardiovascular risk factors. In patients with diabetes mellitus (DM), a frequently encountered comorbidity in HF, such paradoxes not always hold true. This appears to occur with the blood pressure and the obesity paradoxes. The cholesterol paradox consists in HF patients with lower total cholesterol (TC) having a more ominous outcome than the ones with higher values. A differential prognostic impact of TC in HF patients according to DM has never been addressed.
Purpose: We aimed to study if the prognostic impact of TC was different according to DM status in a chronic HF population.
Methods: We prospectively recruited HF patients followed in a HF clinic. Patients with systolic HF diagnosed for at least 6 months, under optimized and stable evidence-based therapy were consecutively recruited. Patients were excluded if they were on renal replacement therapy, if they had hospitalizations or therapeutic adjustments in the previous 2 months and if the left ventricular ejection fraction was = 50%. Patients' comorbidities and medications in use were recorded, a complete physical examination was performed and a venous blood sample was collected in all patients. Patients were followed for up to 5 years and all-cause mortality was the endpoint under analysis. The prognostic impact of TC was analysed using the Kaplan-Meier method. Analysis was then stratified according to coexistence of DM. Multivariate models were built.
Results: We studied 262 chronic stable HF patients, 182 (72.1%) males, mean age 69 years, 98 (37.4%) were diabetic and 62.2% had severe left ventricular systolic dysfunction. Median BNP was 237.8pg/mL and median (interquartile range) TC was 162 (135-200)mg/dL); 96.9% of the patients were taking beta blockers and 93.5% were on an angiotensin converting enzyme inhibitor or an angiotensin II receptor blocker. Sixty-nine percent of the patients were taking statins. During the 5-year follow-up 121 (46.2%) patients died. Patients with TC>200mg/dL had better survival than those with lower TC (p log rank < 0.001); however this protective effect was only reproduced in the group of non-diabetic HF patients. In non-diabetic HF patients the multivariate (age-, haemoglobin-, creatinine-, BNP-, body mass index-, coronary artery disease- and statin use-) adjusted 5-year mortality HR was 0.34 (95% CI: 0.16-0.74) for those with TC>200mg/dL. In the group of HF patients with DM no significant survival benefit of TC>200mg/dL was reported [HR = 0.72 (95%CI: 0.31-1.66)].
Conclusions: Non-diabetic chronic HF patients with TC>200mg/dL have a 66% lower risk of dying in the upcoming 5 years. In chronic HF patients with DM, no protective effect of elevated TC appears to exist. The cholesterol paradox may not be valid in diabetic HF patients.

P1796

Fibroblast growth factor 21 is markedly elevated in patients with chronic heart failure and cardiac cachexia - a possible role of increased inflammation is suggested

M Refsgaard Holm[1]; HM Christensen[1]; J Rasmussen[1]; ML Johansen[1]; M Schou[2]; J Faber[1]; C Kistorp[1]
[1]Herlev Hospital - Copenhagen University Hospital, Department of Internal Medicine, Copenhagen, Denmark; *[2]Herlev Hospital - Copenhagen University Hospital, Department of Cardiology, Copenhagen, Denmark*

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Background/Introduction: Fibroblast growth factor 21 (FGF-21) is a novel regulator in glucose and lipid metabolism. Cardiac cachexia is a wasting syndrome with poor prognosis, which is prevalent 10-15 % of patients with heart failure with reduced ejection fraction (HFrEF). Cardiac cachexia is characterized by insulin resistance, increased systemic inflammation and wasting of muscle and fat mass. As elevated FGF-21 levels have been reported in patients with insulin resistance and systemic inflammation further research of the clinical significance of FGF-21 in cardiac cachexia is warranted.
Purpose: To assess circulating FGF-21 levels in relation to cardiac function, inflammation and wasting in patients with ischemic heart disease, HFrEF and cardiac cachexia.
Methods: We included 57 patients in a cross-sectional study among three groups. One group with HFrEF and cardiac cachexia (HF+cachexia, n = 19); a second group with HFrEF but without cachexia (HF%cachexia, n = 19); and a third group with prior myocardial infarction and left ventricle ejection fraction > 45 % (IHD, n = 19). The three study groups were matched by age and sex. Cardiac cachexia was defined as unintentional non-oedematous weight loss of > 5 % within the last 6 months. FGF-21 was measured in EDTA-plasma using a validated ELISA assay.
Results: Mean (±SD) age was 78.0 (±7.1) years with a male/female ratio of 15/4 in all groups. Patients with HFrEF and cardiac cachexia displayed markedly higher FGF-21 levels, NT-proBNP levels and systemic inflammation, as assessed by IL-6, compared with the two other groups: FGF-21 (median (IQR): HF+cachexia: 381 (232-577) pg/mL, HF%cachexia: 224 (179-309), IHD: 221 (156-308), p = 0.050; NT-proBNP (median (IQR): HF+cachexia: 2310 (1430-3860) ng/L, HF%cachexia: 1090 (508-2110), IHD: 423 (140-1100), p = 0.001; IL-6 (median (IQR): HF+cachexia: 5.3 (2.8-6.8) pg/mL, HF%cachexia: 2.8 (2.0-6.9), IHD: 2.6 (1.7-3.6), p = 0.042. Notably, FGF-21 showed no association to NT-proBNP (Ln) (ß = 0.128, p = 0.087). In multivariate linear regression analysis, adjusted for sex and age, FGF-21 (Ln) was independently associated with IL-6 and total cholesterol and inversely associated with muscle mass and HbA1c (IL-6 (Ln): ß = 0.304, p = 0.026; total cholesterol: ß = 0.270, p = 0.009; muscle mass: ß= -0.038, p = 0.024; HbA1c:ß= -0.426, p = 0.044).
Conclusions: We demonstrated markedly increased FGF-21 levels in patients with HFrEF and cardiac cachexia. Our data suggest that the elevated FGF-21 levels in cardiac cachexia are mediated by increased inflammation and wasting of muscle mass rather than impaired cardiac function. FGF-21 could, therefore, bear clinical implications in predicting cardiac cachexia.

P1797

Lower heart rate predicts spontaneous echo contrast presence in left heart chambers in patients with dilated cardiomyopathy

A Aurora Bakalli[1]; LG Ismail[2]; D Kocinaj[1]; X Krasniqi[1]
[1]University Clinical Center of Kosova, Prishtina, Kosovo Republic of; *[2]University Clinic of Cardiology, Skopje, Macedonia The Former Yugoslav Republic of*

Introduction: Spontaneous echo contrast (SEC) is "smoke-like" echo detected in heart chambers and is highly associated with embolic events.

Purpose: We aimed to determine predictors of left heart chamber SEC presence in sinus rhythm patients with dilated cardiomyopathy of mild to moderate systolic dysfunction.
Material and Methods: This was a prospective cross-sectional transesophageal echocardiography study which included 101 patients (70 m, 31 f, age 58.1 ± 12.7). Patients with atrial fibrillation, anticoagulation therapy, valvular heart disease, prosthetic valves, severe systolic dysfunction, acute myocardial infarction were excluded.
Results: SEC in left ventricle (LV) was significantly related to older age (r = 0.2), history of coronary artery disease (CAD) (r = 0.2), more advanced NYHA class (r = 0.289), lower heart rate (HR) (r=-0.237), larger LV inner dimensions (LVID) in diastole (r = 0.324) and systole (r = 0.44), lower LVEF (r=-0.443), higher wall motion score index (WMSI) (r = 0.295), lower average MAPSE value (r=-0.33). The overall logistic regression model revealed that lower HR (OR = 0.909; 95%CI 0.845-0.978; p = 0.011) and larger LVIDs (OR = 1.200; 95%CI 1.034-1.394; p = 0.017) were independent predictors for LV SEC presence.
SEC in left atrium (LA) was significantly related to male gender (r = 0.211), more advanced NYHA class (r = 0.276), lower HR (r=-0.2), higher packed cell volume (r = 0.332), higher count of red blood cells (r = 0.268), larger LVID in diastole (r = 0.398) and systole (r = 0.425), lower LVEF (r=-0.494), higher WMSI (r = 0.468), lower average MAPSE value (r=-0.305), larger LA diameter (r = 0.258) and it's normalized value for BSA (r = 0.256), larger LA area (r = 0.255), greater LAV/BSA (r = 0.210). Prediction model for LA SEC revealed that only lower LVEF was an independent predictor (95%CI (-0.079)-(-0.037)) (p = 0.0001).
SEC in left atrial appendage (LAA) was significantly related to longer duration of diabetes mellitus (r = 0.404), history of CAD (r = 0.284), lower HR (r=-0.238), high C-reactive protein (CRP) (r = 0.2), greater LV length in diastole (r = 0.238; p = 0.016), greater LA diameter (r = 0.252; p = 0.011) and it's normalized dimension for BSA (r = 0.284), greater LAA maximal area (r = 0.196), greater LAA dysfunction (r = 0.354). In a prediction model for SEC in LAA, lower HR (95%CI, (-0.030)-(-0.003); p = 0.018), greater LA dimension normalized for BSA (95%CI, 0.016-0.116; p = 0.010) and higher value of CRP (95%CI, 0.0026-0.031; p = 0.027) were responsible for LAA SEC presence.
Conclusion: Lower HR is an important predictor of SEC presence in left heart chambers. Additionally, lower LVEF, larger LVIDs and LA, and CRP predict SEC in left heart chambers in patients with dilated cardiomyopathy. This study calls for future research to determine the optimal heart rate in heart failure patients.

P1798

Thyroid hormones levels and their circadian changes in patients with persistent atrial fibrillation and chronic heart failure

YO Tsareva[1]; EA Mayskova[1]; YG Shwartz[1]
[1]*Saratov State Medical University, Saratov, Russian Federation*

Aim of study. We had been studied circadian changes in the levels of secretion of thyrotropin (TSH) and free triiodothyronine (T3) in patients with stable coronary heart disease (CHD) complicated by persistent atrial fibrillation (AF) and chronic heart failure (HF).
Materials. 133 patients with stable ?HD and HF (I-III classes by NYHA) were included. Persistent AF was detected in 79 patients. Persons with hypo - or hyperthyroidism were excluded. The average age of subjects was 64,1 ± 5,4 years. The serum levels of TSH and free T3 were determined twice a day (at 7 a.m. and 8 p.m.). Changes in the diurnal levels of hormones were defined as the difference between the morning and the evening concentrations, and also were calculated in percent (%).
Results: Most of included patients (89 persons - 66,9%) had a certain diurnal rhythm of TSH secretion, which had high values in the morning and low in the evening within the reference range. A part of the examined patients (33,3%) had the opposite tendency, and higher values of TSH were recorded in the evening. This phenomenon was called 'the inversion of TSH variation'.
In patients with inversion of TSH diurnal changes there was noticed a predominance of III-IV classes of angina pectoris on I-II classes (45% versus 22.3%), p < 0.04. Age differences in the two groups were not significant. There was tended to shorter duration of chronic heart failure in the group with the inversion of TSH in comparison with persons with "normal" direction of TSH biorhythm (3 years (1,0;5,0) vs 5 years (2,0;5,0), p < 0,05). In the group with inversion of TSH variation patients with non-congestive heart failure (NYHA I-II) prevailed over persons with NYHA III (42,4% vs 28.5%), p < 0.03.
In patients without rhythm disturbances the range of TSH circadian changes was wider than in patients with AF (18% vs 6.3%, p < 0.05). In the presence of NYHA III the range of TSH variation had tendency to be more widely (13%) than in patients with non-congestive HF NYHA I-II (8%), p < 0.05. Among patients with AF a certain narrowing of TSH diurnal changes was revealed in case of NYHA III opposite to the subgroup NYHA I-II (3% vs 6.7%, p < 0.05). Amplitude of variation of T3 had a narrower range in the subgroup NYHA III as well. The most significant differences in the changes of thyroid hormones levels were identified in patients with a recent episode of arrhythmia (less than 7 days before enrollment). In this group in case of combination with NYHA III the narrowest interval of variation of T3 was detected.
Conclusions: A part of patients with stable ?HD had the inversion of the circadian changes in TSH which combined with the clinical features of cardiovascular pathology. Significant narrowing of the range of circadian variation of TSH and T3 was observed in patients with ischemic heart disease and atrial fibrillation. Changes in the levels of TSH and T3 in chronic heart failure depended on the severity of HF and the presence of a rhythm disorder.

P1799

Sexual dysfunction in patients with heart failure: a therapeutic limitation for the patient or the physician?

J Ribeiro Agostinho[1]; F Veiga[1]; J Rigueira[1]; R Pires[2]; A Nunes-Ferreira[1]; I Aguiar-Ricardo[1]; R Santos[1]; N Andre[1]; I Goncalves[1]; M Mendes Pedro[1]; FJ Pinto[1]; D Brito[1]
[1]*Cardiology Department, Santa Maria Hospital, CHLN, CCUL, Lisbon University, Lisbon, Portugal*; [2]*Faculty of Psychology, CINEICC, University of Coimbra, Coimbra, Portugal*

On behalf of: RICA-HFTeam

Introduction: Erectile dysfunction (ED) is a common comorbidity in patients (pts) with cardiovascular disease, with major impact on their quality of life (QoL). Given the association between ED and the pharmacological therapy commonly used in heart failure (HF) with reduced left ventricular ejection fraction (LVEF), the management of ED in these pts may be challenging.
Objective: To evaluate the erectile function (EF) in pts with chronic HF and reduced LVEF, and its possible potential relation with the clinical severity, QoL and pharmacological therapy used to treat the syndrome.
Methods: Single centre prospective study that included men aged 18 to 70 years hospitalized for decompensate chronic HF. EF was assessed at discharge and at 9 ± 3 months of follow-up, using the validated Portuguese Version of the International Index of Erectile Function. ED is considered to be present when the test value is < 26, and can be classified as mild (25-17), moderate (16-11) and severe (10-6).
The relationship of EF with clinical features, medical therapy and QoL [(validated Portuguese Version of the Kansas City Cardiomyopathy Questionnaire (KCCQ)] was established by Spearman correlation, Mann-Whitney, Wilcoxon and Chi-square tests.
Results: 24 pts, 62.8 + 7.5 years, were included. The prevalence of hypertension (HTN), diabetes and ischemic heart disease, was 71%, 50%, and 38%, respectively. The median LVEF was 26.5%.
The prevalence of ED at the initial evaluation was 92% (mild in 3 pts, moderate in 6 and severe in 13), and 71% at the follow-up (mild in 2 pts, moderate in 3 and severe in 12) - P= N.S.
The EF evaluated in the follow-up associated with age (p < 0.01; r= -0.767), HTN (p= 0.30), maximum and minimum NTproBNP values recorded during hospitalization (p= 0.11, r= -0.54 and p= 0.38, r= -0.048, respectively), serum creatinine (p= 0.06, r= -0.416) and urea (p= 0.025, r= -0.488).
During the follow-up it was possible to increase significantly beta-blocker (p < 0.001) and ACEI/ARB doses (p= 0.006) - compared to pre-admission ones - and a significant improvement in LVEF (p= 0.001) and NYHA functional class (p= 0.002) was also observed. Erectile dysfunction had no relationship with these parameters, but it correlated with physical limitation (p= 0.022, r= 0.509) and frequency of symptoms (p= 0.024, r= 0.502) assessed by KCCQ.
Conclusions: Erectile function in patients with chronic HF correlated with NTproBNP values and erectile dysfunction showed impact on QoL. The progressive increase in doses of neurohormonal antagonists was not associated with a significant change in erectile function, suggesting that the beneficial effects of recommended HFrEF therapies prevail in this population. This should motivate medical therapy uptitration, regardless of the presence of erectile dysfunction.

P1800

Gender-specific differences of anxiety and depressive disorders in chronic heart failure

S Sviatlana Matskevitch[1]; ES Atroschenko[1]; MI Belskaya[1]; OG Shatova[1]; TA Troyanova-Shchutskaia[1]
[1]*Scientific and Practical Center "Cardiology" , Minsk, Belarus*

Purpose: To assess gender-specific differences of anxiety and depressive disorders in chronic heart failure (CHF).
Materials and Methods: A total of 102 men and 102 women (mean-age 59.9 ± 5.25 y.o.) with functional class (FC) II and III CHF of ischemic origin were examined. Both groups included 59.8% patients with FC II CHF (LVEF 51.9 ± 5.11%) and 40.2% patients with FC III CHF (LVEF 47.1 ± 6.58%). The assessment of the presence and severity of anxiety and depressive disorders was made using Scale HADS while CES-D questionnaire was used as a screening tool to establish depression. Life quality (LQ) was measured using MLHFO.

Results: Psychological testing (CES-D) showed that 70.6% of patients had signs of depression. Therefore, the presence and severity of depressive experience was also defined using HADS questionnaire and based on gender-specific differences. The signs of depression were shown in 22.5% of men (CES-D). As evidenced by HADS, anxiety and depressive experience was demonstrated in 30.4% of men, whereas isolated anxiety was seen only in 23.5% of cases, and depression in 17.6% of cases. 14.7% of men had both depression and anxiety, and LQ was 1.5 time poorer compared to those having no comorbidities. Thirty percent of men with FC II CHF showed anxiety and depressive experience (HADS), while 25% and 16.6% showed signs of isolated anxiety and depression, respectively. In FC III CHF, anxiety and depressive experience (HADS) were shown in 31% men, while isolated anxiety and depression was seen in 19% of cases. As for the women's group, 48% (CES-D) showed signs of depression. Based on HADS, anxiety and depressive experience was evident in 63.7% of women; signs of isolated anxiety were seen in 39.2% of cases and depression was noted in 41.2%. In addition, 21.6% of women had both depression and anxiety; in this group, LQ was 1.5 times poorer compared to those with no comorbidities. Some positive associations were established between LQ and depression (r = 0.59, ? <0.01) and anxiety (r = 0.54, ? <0.01) level. As for women with FC II CHF, anxiety and depressive experience (HADS) were seen in 56.7%, whereas the signs of isolated anxiety and depression were noted in 36.7% and 28.4% of cases, respectively. In FC III CHF, anxiety and depressive experience (HADS) were shown in 76.1%, and the signs of isolated anxiety and depression were seen in 45.2% and 61.9%, respectively. This group showed a correlation between LQ and depression (r = 0.56, ? <0.01) and anxiety severity (r = 0.40, ? <0.05). Signs of anxiety and depression were noted in 38.1% of FC III CHF women, and the life quality was poorer compared to isolated anxiety and depression (? <0.01).
Conclusion: In this regard, women showed anxiety and depressive disorders 2 times more frequently compared to men in CHF. In women's group, unlike men, the more aggravated CHF became, the more evident were the signs of anxiety and depressive disorders. In addition, women were shown to be more prone to depression.

P1801

Association of depression and inflammatory markers in patients with congestive heart failure after cardiac resynchronization therapy

GS Pushkarev[1]; YA Fisher[1]; AD Sapozhnikova[1]; AM Soldatova[1]; TN Enina[1]; VA Kuznetsov[1]
[1]Tyumen Cardiology Research Center, Tomsk National Research Medical Center, Russian Academy of Scienc, Tomsk, Russian Federation

Background: Depression is a severe mental illness associated with significant morbidity and mortality. More recently, inflammation has been implicated in the patho-etiology of depression. It is also known that inflammatory syndrome is of major importance in the pathogenesis of congestive heart failure (CHF) because of the activation of pro-inflammatory cytokines. Thus, the study of markers of inflammation in patients with CHF according to depressive symptoms (DS) is a pressing issue.
Purpose: To reveal the association between the severity of depression with inflammatory markers in patients with CHF after cardiac resynchronization therapy (CRT). Methods. The study included 54 patients (46 males and 8 females, mean age 55.3 ± 8.6 years) who underwent CRT. The Beck Depression Inventory was used to measure DS. DS was considered mild for a score between 10 and 18, significant - if more 19 and absent for a score less than 9. Plasma levels of interleukin (IL)-1ß, IL -6, IL -10, tumor necrosis factor a (TNF -a), C-reactive protein (CRP), myeloperoxidase were measured.
Results: The mean Beck Depression Inventory score was 12.3 ± 7.5. The absence of DS was detected in 24 (44.4%), mild DS in 20 (37.0%) and significant DS in 10 (18.5%) patients. CRP level was significantly higher in the group with significant DS (9.4 ± 3.3 mg/L vs 5.2 ± 3.6 mg/L in the group with mild DS, p = 0.02 and vs 4.5 ± 3.5 mg/L in the group without DS, p = 0.008). Significantly higher myeloperoxidase level was in the group of patients with significant DS compared to patients without DS (170.9 ± 248.5 pg/mL vs 47.4 ± 11.4 pg/mL, p = 0.03). No significant differences were found in IL-1ß, IL -6, IL -10 and TNF –a in the groups.
Conclusion: Patients with significant DS had higher levels of CRP and myeloperoxidase.

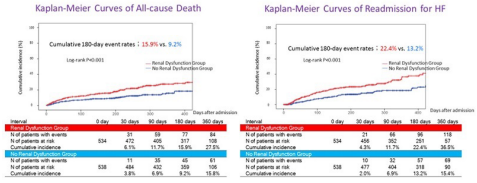
P1802

Relationship of renal dysfunction with prognosis of acute decompensated heart failure

R Reo Hata[1]; Y Kawase[1]; T Tada[1]; K Kadota[1]
[1]Kurashiki Central Hospital, Cardiology, Kurashiki, Japan

Purpose: The prevalence of renal dysfunction (RD) in patients hospitalized for acute decompensated heart failure (ADHF) is high, which seems to be related to their high in-hospital mortality; the purpose is to investigate the relationship of RD with prognosis of ADHF

Methods: We retrospectively analyzed 1072 consecutive patients hospitalized for ADHF and divided them into two groups based on levels of estimated glomerular filtration rate (eGFR): 578 patients with eGFR <45 ml/min/1.73m2 (RD group) and 593 patients with eGFR = 45 ml/min/1.73m2 (non-RD group). The clinical outcome measures were defined as all-cause death and readmission for heart failure. Subgroup analysis of the RD group was performed to further stratify the risk of all-cause death.
Results: The 180-day cumulative rates of all-cause death and readmission for heart failure were significantly higher in the RD group than in the non-RD group (15.9% vs. 9.2%, p <0.01; 22.4% vs. 13.2%, p <0.01). Multivariate Cox proportional hazards model showed that over 80 years of age (hazard ratio [HR], 1.66; 95% confidence interval [CI], 1.08 to 2.56; p = 0.02), hyponatremia (<135 mEq/L) (HR, 1.71; 95% CI, 1.08 to 2.71; p = 0.02), and prior ischemic heart disease (HR, 1.53; 95% CI, 1.02 to 2.29; p = 0.04) were independent predictors of all-cause death.
Conclusion: Our findings suggest that RD is strongly related to poor prognosis of ADHF. Elderly, hyponatremia, and a history of ischemic heart disease were negative predictors of all-cause death in ADHF patients with RD.



Cumulative incidence of event rate

P1803

Potassium value in heart failure and atrial fibrillation patients

O A Otilia Tica[1]; O Tica[2]; MI Popescu[1]
[1]University of Medicine of Oradea, Cardiology, Oradea, Romania; [2]University of Medicine of Oradea, Oradea, Romania

Introduction: Hyperkalemia is a common electrolyte disorder among patients with heart failure (HF) and atrial fibrillation (AF). Hyperkalemia is associated with poor clinical outcomes.
Aim: To prove the prevalence and clinical outcomes in hyperkalemia compared to hypokalemia in patients with heart failure and atrial fibrillation.
Methods - A total of 374 patients admitted consecutively in our clinic were evaluated at admission, during hospitalization and after discharge periodically. Patients included had the discharge diagnosis from our clinic: atrial fibrillation and heart failure. The patients were divided into 2 groups, depending on whether they have atrial fibrillation, heart failure and hyperkalemia(serum potassium >5.1 mEq/l) or hypokalemia (potassium serum < 3.5 mEq/l). The follow-up period of 1.8 years performed included surveillance, blood test (potassium level and creatinine value) and a cardiology examination (EKG, echocardiography, and clinical examination). Furthermore, hyperkalemia group was classified into mild, moderate and severe for better analyze outcomes based on severity of hyperkalemia.
Results: In our study, hyperkalemia was present in 173 patients (46.25%) with mean admissions serum sodium 5.8 ± 3.4 mg/dl. Hypokalemia was found in 89 (23.79%) patients, and 117 (31.28%) have normal potassium value. Patients with hyperkalemia had significantly higher in-hospital mortality (p = 0.027) and longer hospital stays (p = 0.002) compared to hypokalemia, but no difference in readmission rate was observed between groups (p = 0.502). Among hyperkalemia groups, severe hyperkalemia had worse clinical outcomes, with highest in-hospital mortality (17.11%) and longest length of stays (9.6 ± 4.1 days).
Conclusions: - Hyperkalemia was a relatively common condition found in patients hospitalized for HF and AF. It was associated with higher in-hospital mortality and longer hospital stays. Hyperkalemia has poorer clinical outcomes and is proven to be an ominous sign in patients with HF and AF.

P1804

Mini mental state exam for evaluation of cognitive function in patients with CHF treated with sacubitril / valsartan compared with controls taking conventional therapy: a retrospective cohort study.

R De Vecchis[1]; C Ariano[2]; G Di Biase[3]; M Noutsias[4]
[1]Preventive Cardiology and Rehabilitation Unit, DSB 29 " S. Gennaro dei Poveri Hospital", Napoli, Italy; [2]Division of Geriatrics, "Casa Sollievo della Sofferenza" Hospital, S.Giovanni Rotondo, Italy; [3]Division of Geriatrics, Clinic "S. Maria del Pozzo", Somma Vesuviana, Italy; [4]Division of Cardiology, Angiology and Intensive Medical Care, University Hospital Halle, Martin-Luther-University Halle, Halle, Germany

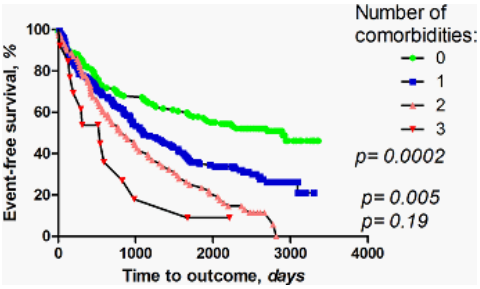
Introduction: Sacubitril, a neprilysin inhibitor, is present in the combination molecule called sacubitril / valsartan, used for therapeutic purposes as an agent able to slow down degradation of endogenous natriuretic peptides, thereby achieving an enhancement of their beneficial cardiovascular effects. However, sacubitril might also favor, through neprilysin inhibition at the level of central nervous system, missing degradation and consequent intracerebral accumulation of beta-amyloid, thus promoting neuronal dysfunction and cognitive impairment in patients with chronic heart failure(CHF) treated with sacubitril/valsartan.
Methods: A retrospective cohort study was undertaken to detect the effects on cognitive function exerted by sacubitril / valsartan in CHF patients. The clinical sheets of these patients were examined as regards the information provided in the specific questionnaire (Mini Mental State exam, MMSE), routinely administered during clinical visits carried out in the Heart Failure Units at two centers from May 15 to November 30,2017. The cases, i.e., CHF patients in the sacubitril/ valsartan group, had to have a clinical history of at least three continuous months of administration of sacubitril/valsartan. Control group, i.e. the group of CHF patients free from sacubitril/valsartan therapy, had to be composed of patients with similar mean age, educational level and percentage distribution of male sex compared to cases, as well as similar severity of clinical picture, that is CHF patients had to belong to NYHA classes II-III in both groups, and their comorbidities had to show a substantial overlap as regards nosographic type and clinical severity in the betwen-group comparison.
Results Mean MMSE score in sacubitril /valsartan group (no.51 patients) was 21.70 ± 3.33(mean $\pm$ SD) , whereas mean MMSE score in control group (no.51 patients) was 20.60 ± 3.77(mean $\pm$ SD) ($p = 0.1215$ using independent samples t-test). Thus, according to usual criteria, a similar mild-to moderate impairment in cognitive performance was found in the comparison of the two groups.
Conclusions: The alleged harmful influence of sacubitril/ valsartan on cognitive function has not been proven in our retrospective study. Indeed, patients taking therapy with sacubitril /valsartan for at least three months have shown a mean MMSE score not significantly different from that exhibited by controls.

P1805

The impact of comorbidities in heart failure patients

J Jan Benes[1]; M Kotrc[1]; P Jarolim[2]; J Kautzner[1]; V Melenovsky[1]
[1]IKEM, Prague, Czech Republic; [2]Brigham and Women's Hospital, Department of Pathology and TIMI-group, Boston, United States of America

Background: Diabetes mellitus (DM), chronic obstructive pulmonary disease (COPD) and chronic kidney disease (CKD) are prevalent in heart failure (HF) patients. The goal of the study was to determine the impact of DM, COPD and CKD on quality of life and outcome of a well-treated cohort of HF patients.
Methods: A total of 397 patients with stable systolic HF were followed for 1135 (IQRs 379-2005) days. Clinical, laboratory and echocardiographic evaluations were performed at study entry. During follow-up, 250 pts (62.9%) experienced an adverse outcome (death, urgent heart transplantation, implantation of mechanical circulatory support).



Event-free survival

Results: 16.4% of patients had COPD, 33.4% DM and 34.5% CKD. 40.3% of patients had no comorbidity, 38.0% were diagnosed with one, 18.4% with two and 3.2% with three comorbidities. Patient with more comorbidities were older, had longer HF history and more often CAD as the underlying HF etiology ($p < 0.0001$). They were using larger diuretic dose ($p = 0.0003$) and were less likely treated with ACE-inhibitors/angiotensin receptor blockers ($p = 0.003$). No difference in LV ejection fraction, LV end-diastolic diameter, blood pressure and heart rate was observed. Patients with more comorbidities reported similar quality of life assessed by MLHFQ ($p = 0.48$). With increasing comorbidities, no significant difference in BNP ($p = 0.06$), but sharp increase in GDF-15 ($p < 0.0001$) was observed. All three comorbidities were associated with impaired survival (Fig.1), the effect of comorbidities on outcome was independent and additive ($p < 0.0001$).

Conclusion: Comorbidities in HF patients are unrelated to cardiac function and are not associated with impaired quality of life, but they additively portend a poor prognosis.

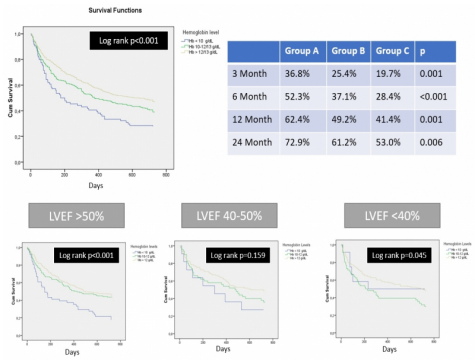
P1806

Heart Failure and Anemia: importance of hemoglobin in prognosis

J G Julio Gil Goncalves Pereira[1]; I Pires[1]; L Abreu[1]; H Antunes[1]; ML Goncalves[1]; B Marmelo[1]; JM Santos[1]; D Moreira[1]; R Silverio[2]; LF Santos[1]; J Costa Cabral[1]
[1]Hospital Sao Teotonio, Cardiology, Viseu, Portugal; [2]Hospital Sao Teotonio, Internal Medicine, Viseu, Portugal

Introduction: Reduced hemoglobin (HB) has been shown to be associated with a worse overall outcome in patients with heart failure (HF).
Purpose: The objective of this study is to evaluate which patients hospitalized for HF present with anemia. Assessment of the impact of anemia in the outcome is evaluated, namely the mortality/hospital readmission rate (M/Ra) at 3, 6, 12 and 24 months (M).
Methods: A retrospective study was performed on all patients admitted for HF. Clinical data, blood work and echocardiogram imaging were evaluated. Patient follow-up was maintained for 24 months. The study population was divided into 3 groups: Group A with HB < 10g/dL; Group B with HB 10-12 g/dL (in women) and 1013g/dL (in men); Group C with HB > 12g/dL (in women) and >13 g/dL (in men).
Results: The study population included 1052 patients.
When evaluating in-hospital mortality, there was no statistical difference (7.0% vs 8.8% vs 6.0%, p = 0.187). However, when evaluating the occurrence of the combined endpoint, there is a significant difference, already detected at 3-month follow-up. That difference was especially evident in the group with preserved ejection fraction. The image contains the survival curve and M/Ra rates as well as the survival curves for each specific group of patients depending on left ventricular ejection fraction (LVEF).
Conclusion: In this population, it is confirmed that anemia is particular frequent in older patients with chronic kidney disease. Anemia does not seem to affect in-hospital mortality. However, there was a higher mortality and readmission rate in the group with lower hemoglobin levels throughout follow-up. Anemia also seems to play a particularly more important role in prognosis in patients with preserved ejection fraction.

	Group A	Group B	Group C	p
Male	46.5%	43.8%	55.1%	0.004
Age	80±7 yo	78±9 yo	76±10 yo	<0.001
Diabetes	42.6%	37.7%	33.3%	0.131
Hypertension	69.3%	64.6%	68.3%	0.490
Dyslipidemia	26.7%	30.3%	30.0%	0.778
Coronary disease	12.9%	13.8%	15.0%	0.798
Cerebrovascular disease	11.9%	5.4%	7.5%	0.092
Chronic Kidney disease	40.0%	31.3%	17.3%	0.029
Chronic Obstructive Pulmonary disease	19.3%	18.3%	14.8%	0.472
Atrial Fibrillation	48.0%	49.3%	55.7%	0.115

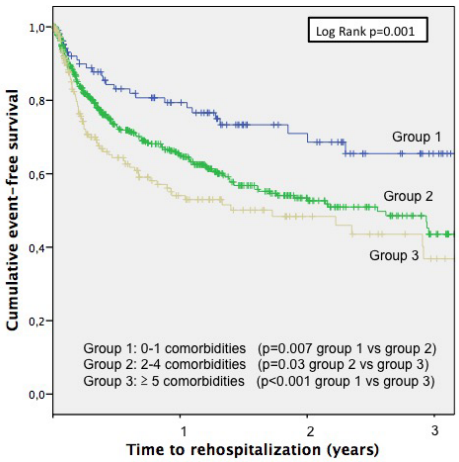


P1807

Can the number of Comorbidities predict readmissions for Heart Failure patients?

MF Maria Ferre[1]; R Lopez-Vilella[1]; I Sanchez-Lazaro[1]; I Husillos[1]; L Martinez-Dolz[1]; L Almenar[1]
[1]*Hospital Universitario y Politécnico La Fe, Valencia, Spain*

The aim of this study was to evaluate whether the comorbidities in patients hospitalized for acute heart failure predicts readmission rates for heart failure (HF).
Methods: A prospective cohort study of 901 consecutive patients admitted to our centre for acute heart failure was conducted. All hospital readmissions within 3 years of discharge were reviewed.
We collected different comorbidities such as: diabetes mellitus, hyperlipidaemia, hypertension, kidney disease, atrial fibrillation and anaemia.
We divided the study population in three groups: 1) patients with 0 or 1 comorbidities, 2) patients with 2, 3 or 4 comorbidities and 3) patients with 5 or more comorbidities.
Kaplan-Meier was used to analyse readmission rates for HF.
Results: The study population had a mean age of 74 ± 11 years. 53% of the patients were men. More than half of the population (53%) had HF with preserved ejection fraction (EF).
The majority of the patients (66%) were in group 2, followed by 22% of patients in group 3 and 12% of patients in group 1.
During the 3-years follow-up, the readmission rate for all the population was 32%. According to the subgroups, the readmission rate was 25% in group 1, 32% in group 2 and 38% in group 3 (p = 0.06).
The median time period to readmission was higher in the group with less comorbidities, being 927 days compared to 764 days in group 2 and 631 days in group 3.
The readmission rate was lower in group 1 being 17% at 6 months, 21% at 12 months and 29% at 24 months compared with group 2 (26%, 33% and 47% at 6, 12 and 24 months respectively) and group 3 (36%, 46% and 52% at 6, 12 and 24 months respectively) (p = 0.001).
Conclusions: Presence of comorbidities in heart failure patients is associated with a high readmission rate for heart failure. Thus, we recommend closer monitoring in these patients in order to avoid readmissions.



Time to rehospitalization.

P1808

Diabetes mellitus type 2 contribution to chronic heart failure in patients with permanent atrial fibrillation along with coronary artery disease

N Natalia Koziolova[1]; E Polyanskaya[1]; S Berestneva[1]; P Karavaev[1]
[1]*Medical Academy, Perm, Russian Federation*

Aim: to evaluate diabetes mellitus type2 (DM2T) contribution to chronic heart failure (CHF) in patients with permanent atrial fibrillation (AF) along with coronary artery disease (CAD) and arterial hypertension depending on glycated hemoglobin (HbA1c) Methods and materials: 48 patients with CHF, and ischemic permanent AF, and DM2T were examined. Average age was 64,2+8,9 years. HbA1c was evaluated in all the patients, as well as NT-proBNP, left ventricle ejection fraction (LV EF), E/e' (via echo). Patients were divided into 3 groups depending on HbA1c. The 1st group included patients with HbA1c 6-7,9%, (n = 13, 27,1%). The 2nd group - HbA1c = 8-10% (n = 21, 43,8%). The 3rd group consisted of patients with HbA1c >10% (n = 14, 29,1%).
Results: NT-proBNP was significantly higher in group 3, than in group 1 and group 2 (pmg < 0,001); it consisted of 846,8+74,1 ng/mL, 489,6+54,8 ng/mL, 421,4+32,7 ng/mL, respectively (p1-2, p1-3, p2-3 < 0,001). LV EF presented as moderately reduced in all the groups and did not differ between of them: group 1 - 54,8+6,7%, group 2 - 53,7+6,1%, group 3 - 49,5+7,2%. Reliable difference was found in diastolic dysfunction by average transmitral flow velocity E/e': group 1 - 13,9+2,0, group 2 - 15,3+1,6, group 3 - 16,2+1,8 (pmg= 0,0001; p1-2 = 0,0005, p1-3 < 0,001, p2-3 = 0,007).
Correlation analysis showed direct moderate interconnection between NT-proBNP and HbA1c (r = 0,53, p = 0,007), and direct severe interconnection between E/e' and HbA1c (r = 0,73, p < 0,001).
Conclusion: in patients with DM2T and permanent AF, there was indicated a progressive increase of HF severity (estimated by NT-proBNP and E/e' in echo with moderately decreased LV EF) along with increase of HbA1c

P1809

Novel truncating titin gene variants in hungarian patients with cardiomyopathies identified by next-generation sequencing

B Csanyi[1]; V Nagy[1]; L Hategan[1]; J Borbas[1]; A Tringer[1]; I Nagy[2]; Z Hegedus[3]; T Forster[1]; R Sepp[1]
[1]*University of Szeged, 2nd Department of Internal Medicine and Cardiology Center, Szeged, Hungary*; [2]*Biological Research Centre of Szeged, Institute of Biophysics, Bioinformatics Group, Szeged, Hungary*; [3]*Biological Research Centre of Szeged, Institute of Biophysics, Szeged, Hungary*

Funding Acknowledgements: Supported by GINOP-2.3.2-15-2016-00039

Background: The sarcomere protein titin, encoded by the TTN gene, is responsible for the passive elastic properties of cardiac muscle. Mutations affecting the TTN gene may play a role in the development of various cardiomyopathies.
Aim: The aim of our study was to screen for genetic variants in TTN gene using Next- Generation Sequencing (NGS) in a cohort of Hungarian patients with cardiomyopathy.
Patients and Methods: A total of 148 patients with proven diagnosis of a cardiomyopathy were screened. The patient cohort included 103 patients with hypertrophic cardiomyopathy (HCM, 58 males, avg. age 50 ± 17 years), 21 patients with dilated cardiomyopathy (DCM, 10 males, avg. age 43 ± 21 years), 9 patients with left ventricular non-compaction cardiomyopathy (LVNC, 3 males, avg. age 58 ± 20 years) and 15 patients with arrhythmogenic right ventricular cardiomyopathy (ARVC, 8 males, avg. age 48 ± 10 years). Genotyping was performed by NGS and validated by capillary sequencing.
Results: Genetic screening detected 143 TTN non-common (minor allele frequency <1%), possibly disease causing variants that led to amino acid change or 'splice site' variation. Out of these, there were 8 (5%) variants which had truncation effect (all novel). In 6 cases frameshift (p.Glu13828fs, p.Glu16261fs, p.Glu19847fs, p.Lys22311fs, p.Thr18527fs, p.Val18616fs) and in further 2 cases nonsense variants (p.Gln34219 *, p.Ser8519 *) were identified. These potentially pathogenic variants occurred primarily in patients with DCM (4/21, 19%) and LVNC (4/9, 44%). The further 135 variants were predominantly likely benign or variants of uncertain significance (VUS).
Summary: Our results suggest that due to the size of the TTN gene, many variants can be detected, which can often be classified as VUS or benign. The identification of novel truncating pathological variants in DCM and LVNC patients, further strengthen the predominant role of titin in the pathogenesis of DCM and LVNC.

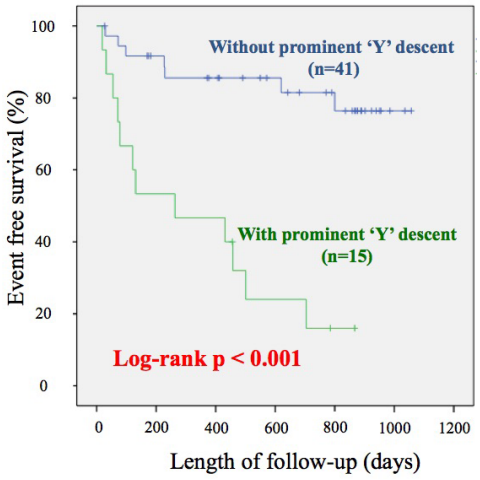
P1810

The prominent Y descent of right atrial pressure waveform was related to poor outcome in heart failure patients

K Kazushi Sakane[1]; R Horai[1]; D Maeda[1]; K Akamatsu[1]; M Ozeki[1]; T Fujisaka[1]; K Sohmiya[1]; N Ishizaka[1]; M Hoshiga[1]
[1]*Osaka Medical College, Cardiology, Osaka, Japan*

Background: The 'Y' descent of right atrial (RA) pressure occurs at the beginning of right ventricle (RV) diastolic phase following the 'V' wave. The presence of prominent 'Y' descent is known to represent poor RV compliance and volume overload. However its prognostic importance remains uncertain.
Methods: Among 250 patients who were admitted with acute decompensated heart failure, 56 patients underwent right heart catheterization (RHC) under clinically compensated status after conventional heart failure treatment. We defined prominent 'Y' descent of RA waveform that 'Y' descent was deeper than 'X' descent, and investigated its related clinical factors and prognostic importance.

Results: Among 56 patients, 15 patients (26.8%) were observed prominent 'Y' descent of RA pressure waveform. In patients with prominent 'Y' descent, the prevalence of atrial fibrillation (AF) was higher (92.3% vs. 34.8%, p = 0.001), plasma BNP levels were higher (274.3 ± 254.3pg/mL vs. 163.2 ± 102.3, p = 0.006), and the history of previous cardiac surgery were more frequent (46.7% vs. 18.8%, p = 0.05) compared to patients without prominent 'Y' descent. During the mean follow up period of 553 ± 341 days, patients with prominent 'Y' descent were more likely to have experienced major adverse cardiac events (MACE; death, heart failure re-hospitalization, LVAD implantation) than those without prominent 'Y' descent (80.0% vs. 18.9%, p <0.001, Figure).
Conclusion: The presence of prominent 'Y' descent as assessed by RHC was associated with AF prevalence, BNP and poor prognosis in patients with heart failure even in clinically compensated status. To evaluate the RA pressure waveform is useful to identify the high risk group of heart failure patients and it is hopefully applicable by less invasive method such as monitoring of jugular pulse waveform.



Figure

P1811

Defining heart failure with mid-range ejection fraction

S Del Prado Diaz[1]; G Alonso Salinas[1]; AM Martin Acuna[1]; JM Vieitez[1]; M Abellas[1]; A Lorente[1]; A Pardo Sanz[1]; M Plaza Martin[1]; M Pascual Izco[1]; E Gonzalez[1]; M Castillo Orive[1]; I Rayo[1]; S Fernandez Santos[1]; JL Zamorano[1]
[1]*University Hospital Ramon y Cajal de Madrid, Department of Cardiology, Madrid, Spain*

Introduction: European Heart Failure Guidelines published in 2016, defined a new classification based on left ventricular ejection fraction (LVEF).

Clinical characteristics

Characteristic	HFrEF	HFmrEF	HFpEF	P value
No of patients (%)	115 (57.5%)	36 (18%)	49 (24,5%)	
Age	73.8	72.5	77.9	NS
Male sex -no (%)	72.20 %	69.40 %	24.5 %	<0,05
Hypertension	60 %	58.30 %	71.4 %	NS
Dyslipemia	40 %	47.2 %	49 %	NS
Diabetes (non-insulin-depent)	28.7 %	13.9 %	6.1 %	<0,001
Diabetes (insulin-dependent)	10.4 %	22.2 %	30.6 %	<0,001
COPD	20.9 %	25.5 %	26.5 %	NS
Peripheral artery disease	7 %	13.9 %	8.3%	NS
Stroke	11.3 %	13.8 %	12.2 %	NS
Atrial fibrilation/Flutter	50.4 %	52.8 %	73.5 %	NS
Mitral regurgitation III_IV	20%	22%	10%	<0,05

Methods: A series of 200 patients followed at Heart Failure Unit was analysed with the aim of defining characteristic of mid-range group (40-49%), and comparing with preserved (= 50%) and reduced (< 40%) LVEF.
Results: In the series, only 18% of patients was in mid range group, facing 57,5% with severely depressed EF and 24,5% with preserved EF. HFmrEF was the younger group, and similarly to HFrEF, masculine sex was more frequently (69,4 and 72,5%), opposite to HFpEF group where 75% were women.
Regarding risk factors, there were no differences in hypertension and dyslipemia, however there were significant predominance of non-insulin-dependence diabetic patient in HFrEF and insulin-dependence diabetic patients in HFpEF group. Relative to prevalence of atrial fibrillation/flutter it was significantly higher in HFpEF (73,5%). The presence of significative mitral regurgitation was predominant in reduced and mild-range EF above preserved EF (20% vs 22% vs 10%), and the prevalence of RVdysfunction was higher in HFrEF than HFmrEF (9% vs 4%).
There were no differences related to renal function, BNP, all causes admissions nor exitus in this series.
Conclusions: In the subgroup HFmrEF it was remarkable the prevalence of males and younger age, higher prevalence of mitral regurgitation and fewer right ventricle dysfunction. Nowadays, mild range ejection fraction represents a grey area as far as characteristics, etiology and prognostic, to be researched next years.

P1812

Clinical profile and prognosis in a spanish cohort of elderly patients with mid range ejection fraction managed in a hospital-based heart failure care program

A Olmo Sanchez[1]; J A Jose Satue[1]; J Belinchon Paraiso[1]; S Gonzalo Pascua[1]; J Marrero Frances[1]; A De La Rosa[1]; A San Martin Prado[1]; A Zapatero Gaviria[1]
[1]*University Hospital of Fuenlabrada , Fuenlabrada, Spain*

Objective : The aim of this study is to compare clinical profile and prognosis of Mid Range Ejection Fraction Heart Failure (MREF- HF) patients managed in our Internal Medicine Hospital Based HF Care Program with reduced and preserved ejection fraction Heart Failure patients.
Patients and methods : 323 consecutive patients with heart failure admitted into our internal medicine ward between june 2011 and may 2017 were prospectively recruited. Demographic data, cardiovascular risk factors, clinical, biochemical and echocardiography findings, Barthel and Charlson scores, and treatments at discharge were registered in our electronic health records (EHR). Follow up was performed after discharge through ambulatory consult and telephonic interview Patients were classified as MREF-EF when ejection fraction (EF) was 40-49%, reduced EF (HFrEF) when EF <40% and preserved EF (HF-PEF), when EF was = 50%.Statistical análisis was performed with IBM SPSS statistics version 20.
Results : 34/323 patients had MREF-HF (10,5% of all). Male sex percentage is greater in MREF-HF (50%) than in HF-PEF (32,3, p 0,041%) and HFrEF (34,2%, no statistically significant). Mean age and Body Mass Index (BMI) are similar in MREF-HF and HF-PEF(78,47 years (SD 8,43) vs 79,77 years (SD 8,33) , and 31,56 kg/m2 (SD 6,43) vs 30,9 kg/m2(SD 5,95) respectively. Hypertension (91,2%), dyslipidemia (76,5%), diabetes (55,9%) and atrial fibrillation (64,7%) are found in similar percentages in MREF-HF and HF-PEF. There are more tobacco users (47,1%) and Chronic Obstructive Pulmonary Disease (COPD, 26,5%) in MREF-HF than in HF-PEF patients (p 0,034 and 0,048 respectively), also with a greater percentage of patients with pulmonary hypertension (73,5%), but not significantly. Mean NT-pro BNP is greater in MREF-HF patients (1907,5 pg/mL) than in HF-PEF (1679 pg/mL) and lower than HF-rEF (3150 pg/mL), with statistical significance (p 0,043 in Kruskal-Wallis test). Patients with MREF-HF had a similar prognosis to HF-rEF patients, with a follow-up mortality of 41,2 % and 42,1% respectively, greater than HF-PEF patients (35,1%), but without reaching statistical significance.
Conclusions: : 10% of Elderly patients managed in our Internal Medicine Hospital-based heart failure care program had Mid Range Ejection fraction (MREF-HF). They are usually hypertensive and obese patients in atrial fibrillation, with many other comorbidities as patients with HF-PEF, but there are more frequently tobacco users, with COPD and Pulmonary Hypertension; they also have a higher mean NT-pro BNP and a worse prognosis after discharge than patients with HF-PEF. More studies are needed to better determine clinical phenotype and prognosis in MREF-HF elderly patients

P1813

Assistant professor and cardiology clinical nurse specialist

A Angela Massouh[1]; H Abu Saad Huijer[1]; P Meek[2]; H Skouri[1]
[1]*American University of Beirut AUB, School of Nursing, Beirut, Lebanon*;
[2]*University of Colorado Denver, College of Nursing, Denver, United States of America*

Funding Acknowledgements: University Research Board grant from the American University of Beirut

Background: Self-care is recognized as a common means for improving outcomes of heart failure (HF); yet failed self-care remains common and more prevalent in developing countries like Lebanon and the Middle East and North Africa (MENA) region. Studies to date have not addressed what predicts successful self-care in

Lebanon and the MENA region. Until we understand self-care behaviors from a cultural perspective, failed self-care will remain common, with tremendous socioeconomic costs and burdens to the individual, family, and society. Knowledge from this study will facilitate clinician understanding of what factors affect the performance or lack thereof of self-care in Lebanon and the MENA region and aid in designing tailored behavioral modification interventions targeting improved HF self-care.
Purpose: The primary purpose of this study was to describe self-care behaviors and the relationships among clinical and sociodemographic characteristics, functional ability, and psychological status and self-care in a sample of Lebanese patients with HF.
Methods: Self-care was measured in a sample of 100 participants with confirmed HF (76% males; mean age of 67.59 years) recruited from a major tertiary medical center in Lebanon. Self-care was measured using the Arabic translated version of the Self-Care of HF Index (A-ScHFI), which provides scores on self-care maintenance, management, and confidence.
Results: Provider-directed self-maintenance behaviors were expectedly high in this sample and included compliance with medication and appointment keeping. Abiding by physician directives is a characteristic of collectivist cultures like Lebanon. Behaviors low in this population were symptom monitoring and exercising. Taking an extra water pill had one of the lowest scores and this is attributed to either providers not prescribing diuretics to use as necessary or not educating patients on how to adjust their diuretic dose. About a quarter of the participants were unable to detect changes in their symptoms. Lebanese HF patients participated in self-care behaviors mainly in response to an acute deterioration. This indicates an acute model of HF self-care, where participants are unable to connect chronic symptoms with their HF and hence do not perform routine self-care.
Higher HF knowledge, higher confidence, and lower New York Heart Association class predicted better self-care maintenance. Higher HF knowledge score, higher maintenance, no recent hospitalization, and being unemployed predicted better self-care confidence. Self-care management was predicted by confidence alone.
Conclusion: HF self-care in Lebanon is suboptimal. To effectively address HF self-care practices, healthcare professionals need to understand facilitators and barriers to self-care identified in this study. Higher HF knowledge, self-care confidence, and social support were consistently associated with better self-care in this population.

P1814
Role of right ventricle in heart failure

S Del Prado Diaz[1]; G Alonso Salinas[1]; AM Martin Acuna[1]; M Plaza Martin[1]; M Abellas[1]; A Lorente[1]; JM Vieitez[1]; E Gonzalez[1]; S Fernandez Santos[1]; M Castillo Orive[1]; I Rayo[1]; JL Zamorano[1]
[1]*University Hospital Ramon y Cajal de Madrid, Department of Cardiology, Madrid, Spain*

Introduction: Heart failure traditionally has been classified according to left ventricle ejection fraction (LVEF), in fact, in the last European heart failure guidelines, it was reclassified in three types; however, the great forgotten in this issue has been the right ventricle (RV).
Methods: It was designed a registry to evaluate RV impact in heart failure. For this aim it was recorded echocardiographic data, laboratory analysis, functional class and symptoms, and related with RV function.
RV dysfunction was assessed according to ESC recommendation for chamber quantification by echocardiogram.
Results: A series of 198 patients followed in a tertiary Hospital Heart Failure Unit was included. 28% of patients presented some degree of RV dysfunction: 9.1% mild, 13.6% moderate and 7.1% severe dysfunction.
NYHA functional class was directly related to RV dysfunction ($p = 0.016$), just like the RV dysfunction degree and regardless of left ventricle function. The presence of RV dysfunction was associated with pulmonary hypertension. Nevertheless, it was not statistically significant related to LVEF, nor different types of LV dysfunction.
Patients with RV dysfunction showed tendency to more deteriorated glomerular filtration ($p = 0.06$) and higher urea levels ($p = 0.06$), without significant differences in creatinine levels. Regarding liver values, transaminases were higher (AST 23,9 vs 24,8; ALT 22,8 vs 26,1) but it has no achieved significant statistical difference. BNP presented clear tendency to be lower in normofunctional right ventricles (608 vs 839, $p = 0.09$).
It was remarkable the large prevalence of atrial fibrillation or flutter in RV dysfunction and it increased with RV dysfunction severity ($p < 0.05$).
Regarding symptoms, in RV dysfunction paroxysmal nocturnal dyspnea was more frequent ($p = 0.035$), however it was not related with orthopnea.
Relative to treatment, diuretic dose needed was higher in RV dysfuncion (95.2 mg vs 76.3 mg, $p < 0.05$)
Conclusion: RV plays and important role in heart failure, both in functional class, as in symptoms and treatment.

P1815
Heart failure associated to the hemoglobinopathy

K Khadija Khay[1]; Z Qechchar[1]; H Mechal[1]; A Kone[1]; H Bendahou[1]; A Quessar[1]; K Hachim[1]; R Habbal[1]
[1]*Ibn Rochd University Hospital, cardiology, Casablanca, Morocco*

Introduction: Due to the increased longevity of patients with hemoglobinopathy, cardio-vascular complications are more and more evident, such as rhythm and conduction disorders, heart failure, vascular involvement and pulmonary artery hypertension.
The aim of our work is to detect the repercussions of these hemoglobinopathies on the cardiovascular system.
Material and Methods: Prospective study including patients with sickle cell anemia and thalassemia followed in adult and pediatric hematology department at Ibn Rochd University Hospital in Casablanca and whose age is greater than 14 years. This is a study conducted between May and October 2017. All patients had a complete clinical examination with electrocardiogram and echocardiography.
Results: A total of 46 patients were included, with predominantly younger patients, the mean age is 23 years. 63% of our patients had thalassemia (55% homozygous thalassemia), 30.5% had sickle cell disease and 6.5% had sickle-thalassemia.
Only one patient was hypertensive and 4 smokers.
In our series, one patient had left ventricular systolic dysfunction with 48% of LVEF and a longitudinal strain at -16.
Diastolic heart failure was present in one case with elevated LV filling pressures. Three patients were in right heart failure with pulmonary arterial hypertension, one with homozygous sickle cell disease, one with heterozygous sickle cell disease and the other with sickle-thalassemia.
The right ventricle was dilated in 2 cases with impaired function in a case of homozygous sickle cell disease. Left ventricular was dilated in 14 cases, or 30% of cases.
The longitudinal global strain was altered in 2 cases, one of which had a LVEF lowered.
Conclusion: Heart failure in hemoglobinopathy remains a common complication that is a prognostic factor in this type of patients.

Chronic Heart Failure - Other

P1816
Riociguat in transthyretin cardiac amyloidosis - experiences from a prospective heart failure registry

F Franz Duca[1]; C Zotter-Tufaro[1]; C Binder[1]; AA Kammerlander[1]; B Boerries[1]; H Agis[2]; R Kain[3]; J Mascherbauer[1]; D Bonderman[1]
[1]*Medical University of Vienna, Cardiology, Vienna, Austria*; [2]*Medical University of Vienna, Oncology, Vienna, Austria*; [3]*Medical University of Vienna, Pathology, Vienna, Austria*

Background: Transthyretin cardiac amyloidosis (TTR CA) is a rare disease and represents the prototype of a restrictive cardiomyopathy. A vast majority of affected patients present with advanced heart failure and face significant morbidity and mortality. However, an effective therapy is still lacking and a diagnosis of CA precludes patients from participation in standard heart failure clinical trials.

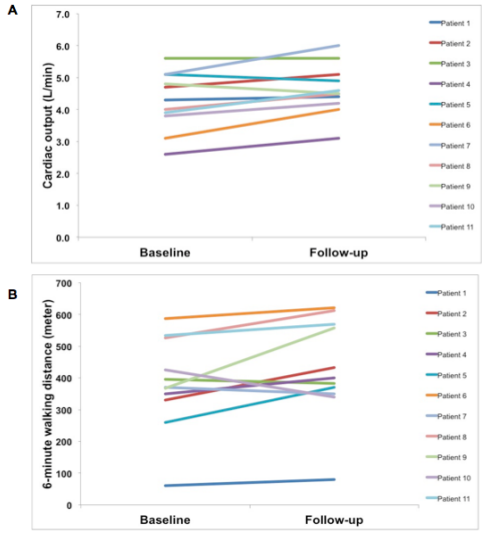


Figure 1

The soluble guanylate cyclase - stimulator riociguat, already approved for the treatment of pre-capillary pulmonary hypertension, has also been shown to have favorable hemodynamic effects in heart failure.

Purpose: We aimed to test the safety and efficacy of riociguat in a case-series of patients with TTR CA.

Methods: TTR CA was diagnosed either by histological assessment of endomyocardial biopsy samples with Congo red staining and subsequent immunohistochemical typing or non-invasively in accordance with current recommendations.

Parameters of interest were change in invasively measured hemodynamics, exercise capacity, quality of life as well as safety and tolerability.

Results: Between August 2014 and June 2017, 11 patients with wild-type TTR CA and 2 patients with mutations of the TTR gene (His108Arg) were included into our study. 2 patients discontinued with the study and the remaining 11 patients completed all procedures.

Median age of the study population was 75.0 years (IQR: 69.0 - 83.0) and 9 (81.8%) were male. The majority of the patients were in New York Heart Association (NYHA) class = III (n = 6, 54.6%), and NT-proBNP values were markedly elevated with a median of 2923pg/mL (IQR: 1773 - 7912). Median 6-MWD was 370m (IQR: 330 - 526).

Cardiac output improved significantly from 4.3L/min (IQR: 3.8 - 5.1) to 4.5L/min (IQR: 4.2 - 5.1) (p = 0.022, Figure 1) whereas diastolic pressure gradient decreased (baseline: 0.0mmHg, IQR: -2.0 - 3.0; follow-up: -1.0mmHg, IQR: -3.0 - 1.0; p = 0.049).

6-MWD increased from 370m (IQR: 330 - 526) at baseline to 400m (IQR: 350 - 570) at follow-up (p = 0.045, Figure 1B) Correspondingly, NYHA class improved significantly (baseline: NYHA class = III: n = 6, 54.6%; follow-up: n = 0, 0.0%; p = 0.031). However, NT-proBNP did not change from baseline 2923pg/mL (IQR: 1773 - 7912) to follow-up: 2584pg/mL (IQR: 1804 - 7255) (p = 0.929). Overall health status improved significantly from 50% (IQR: 40.0 - 50.0) at baseline to 60% (IQR: 50.0 - 75.0) at follow-up (p = 0.021).

Conclusion: The present case series of TTR CA patients suggests beneficial effects of riociguat administration in this patient population. However, further studies of stronger design are warranted to explore the therapeutic potential of riociguat in TTR CA.

P1817

Impact of hyperkalaemia on managing patients with cardiorenal disease; a healthcare professional perspective

N Navneet Kalsi[1]; H Purcell[2]; P Kalra[3]; P R Kalra[1]
[1]Portsmouth Hospitals NHS Trust, Cardiology, Portsmouth, United Kingdom; *[2]Cardiorenal Forum, London, United Kingdom*; *[3]Salford Royal Hospital, Renal Medicine, Manchester, United Kingdom*

Funding Acknowledgements: This survey was supported by an educational grant from Vifor Pharma UK Ltd.

Background: Renin-angiotensin-aldosterone system (RAAS) antagonism is of prognostic benefit in cardiac and renal disease. The incidence of associated hyperkalaemia (potassium >5.5mmol/L) is unknown. Guidelines advocate target doses of RAAS inhibitors in heart failure, but concerns about hyperkalaemia may limit their use. Little data exists documenting potassium levels clinicians treat and how this impacts on RAAS blockers.

Purpose: This survey describes how healthcare professionals' perceive the burden of hyperkalaemia and the impact on RAAS blockade.

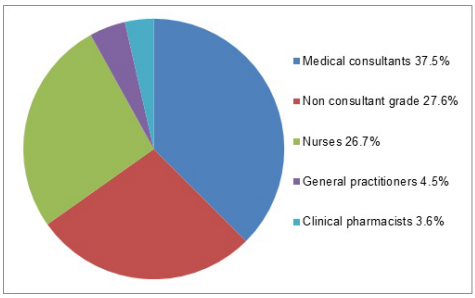
Methods: Healthcare practitioners from the British Journal of Cardiology and UK Cardiorenal Forum databases participated in an anonymised online survey.

Results: 112 complete responses were received (37% attended the Cardiorenal Forum). UK respondents totalled 81%. 74% work in hospitals: cardiac care 55.4%, renal medicine 24.1%, or other clinical domains.

Table 1.

	Number of respondents	Average potassium level (mmol/L) necessitating action	Mode of response range
Cardiology all grades Consultant only	62 18	5.7 5.7	5.5 (SD 0.4) 6.0 (SD 0.3)
Nephrology all grades Consultant only	27 15	5.8 5.7	6.0 (SD 0.4) 6.0 (SD 0.3)
Other practitioners	23	5.7	6.0 (SD 0.5)

Respondent cited values of hyperkalaemia prompting treatment.



Respondent characteristics by profession

Across all respondents, the serum potassium cited as requiring treatment ranged from = 4.8 to 6.6mmol/L (mean 5.7mmol/L). Little difference in opinion existed between those in cardiology and nephrology (Table 1). Higher values of hyperkalaemia were cited by nephrologists. Reasons given for consideration of intervention included concerns regarding cardiac stability (31.5%) and deterioration in renal function (15.7%).

70% of professionals felt hyperkalaemia would affect use of RAAS blockers in up to 25% of patients, with 10% having this concern for over half of their patients. Respondents ranked the European Society of Cardiology Heart Failure Guidelines as most influential when prescribing neurohormonal blockade. When considering which factors influence the initiation and choice of RAAS inhibitor, the priority was renal over cardiac function.

Long-term benefits are proven for RAAS blockers, but it's recognised that hyperkalaemia limits their use and impacts on prognosis. Successful interventions to manage hyperkalaemia, rather than avoidance of the drugs is perceived as beneficial in cardiorenal patients. Respondents identified the need for newer agents, such as orally active potassium binders.

Conclusions: Minimal differences between cardiologists and other prescribers exist when managing hyperkalaemia in cardiorenal patients. Healthcare professionals identify a need for alternatives in therapies that will facilitate RAAS blockade to maximal prognostic benefit.

P1818

Starting with the patient: designing an electronic application with patient and caregiver feedback to promote heart failure self-care in the home setting

C Catherine Demers[1]; S Wali[1]; L Nguyen[1]; G Mulvale[1]; E Mckay[2]; L Mbuagbaw[1]; K Keshavjee[3]
[1]*McMaster University, Medicine, Hamilton, Canada*; [2]*Ux Design Edge, Burlington, United States of America*; [3]*InfoClin, Toronto, Canada*

Background: Heart failure (HF) affects over 1% of Canadians and is associated with growing healthcare costs. Readmission rates represent 70% of these costs. Despite an overall decline in HF-related hospitalizations, up to 50% of patients are readmitted within 3 months. Self-care is key to HF management and potentially leads to improved clinical outcomes. Self-care includes daily weight and symptom monitoring, as well as adjusting diuretics according to their current weight. Less than 50% of patients regularly weigh themselves, as they view HF self-care as both challenging and intimidating.
Purpose: Mobile health (mHealth) applications (apps) can support self-care. However, technology is often poorly adopted due to factors such as literacy, numeracy, and mild cognitive impairment. To optimize the potential of a mHealth app we must ensure these barriers are addressed in its design. Our pilot study supports the use of a paper-based standardized diuretic decision tool (SDDST) to promote self-care in older individuals with HF. The purpose of this study is to convert our paper-based SDDST into a user-centered mHealth app by using participant (HF patients, informal caregivers/CPs) input throughout its design process.
Methodology: We recruited patients with a confirmed diagnosis of HF (male and female, age > 60), and their CPs. HF patients were categorized according to their self-care adequacy measured with the Self-Care Heart Failure Index (SCHFI) (score < 70 suggests poor self-care). Patients were separated into three groups, 1) Patients with adequate self-care, 2) Patients with inadequate self-care without a CP or 3) Patients with inadequate self-care with a CP. We completed standardized, semi-structured interviews with patients and CPs using a Persona-Scenarios methodology. Thematic data analysis was conducted following verbatim transcription and using NVivo, version 10. This study has received ethics approval.
Results: We have interviewed 9 patients (5 male, 4 female, mean age: 74) and 5 CPs. Six themes were identified: 1) Challenges with technology, 2) Communication and assistance with circle of care, 3) App customization, 4) Complexity of self-care, 5) Usefulness of HF information and 6) Cost and long-term use. These themes were a reflection of the challenges patients and their CPs face and how they felt the tool would either help or hinder them with self-care. We found participants were supportive in using the HFApp when the inclusion of volunteers and nurse assistance was mentioned.
Conclusion: Our solution proposes to engage patients and CPs in the design process. Patient and CP feedback will lead to the development of a simple, cost-effective and user-centered mobile application that will promote self-care in the home setting following hospital discharge.

P1819

Identification of preclinical predictors of systolic dysfunction in an elderly outpatient population without a diagnosis of heart failure: rationale and design of PULSE-HF study

ME Esquerro[1]; R Zamora[2]; ER Perna[3]; G Cursack[4]; D Caruso[5]; FP Manghi[6]; C Majul[7]; C Engel[8]; S Volman[1]; L Pereyra[1]
[1]*Novartis Argentina S.A., Buenos Aires, Argentina*; [2]*Hospital de Clinicas Jose de San Martin, Department of Internal Medicine, Buenos Aires, Argentina*; [3]*J.F. Cabral Cardiology Institute, Heart Failure Clinic, Coronary Intensive Care Unit, Corrientes, Argentina*; [4]*Sanatorio Esperanza, Santa Fe, Argentina*; [5]*MClin Res, Head of the Clinical Research Department, U.A. Dr. César Milstein, Buenos Aires, Argentina*; [6]*Centro de Investigaciones Metabólicas (CINME), Buenos Aires, Argentina*; [7]*Centro de Especialidades Médicas (CEMEDIC), Buenos Aires, Argentina*; [8]*Centro Cardiovascular, Salta, Argentina*

Background: Heart failure (HF), especially in the elderly population, poses diagnostic challenges due to its overlap with other co-morbidities and lack of direct access to echocardiography. The signs and symptoms of HF in the elderly are characterized by poor sensitivity and specificity, and the classical signs of HF are not present in approximately 30-40% of patients, which makes an early detection of HF difficult in this population. To our knowledge, no clinical score exists to screen systolic dysfunction in an elderly outpatient population.
Purpose: PULSE-HF, aims to develop a simple predictive score for systolic dysfunction and HF in an outpatient elderly at-risk population, suitable for the everyday clinical setting. The primary objective is to develop a clinical score to predict systolic dysfunction (left ventricular ejection fraction [LVEF] = 40%) and evaluate its diagnostic precision compared with echocardiogram. The secondary objectives include assessment of prevalence of reduced and preserved ejection fraction (EF) (LVEF = 40% and = 50%, respectively); identification of independent predictors for preserved EF and eventually a score derivation; and assessment of the association between N-terminal pro B-type natriuretic peptide (NT-proBNP) and reduced EF.
Methods: PULSE-HF, a cross-sectional, phase IV study that will enrol 800 elderly (aged = 70 years) at-risk outpatients without a diagnosis of HF, at 15 centres in Argentina. No study drug will be administered to patients during the study. The study will consist of two visits. At Visit 1, information on demographics, comorbidities, concomitant medications and disease characteristics will be collected. In addition, at Visit 1, patients will undergo a physical examination and cognitive (Mini-Cog test), functional (VIDA questionnaire and Edmonton scale) and emotional (geriatric depression scale) assessments, along with an evaluation of falls, incontinence and other geriatric parameters. Patients will receive recommendations for any outstanding assessments that cannot be performed at Visit 1 and the reports of such assessments will be collected at Visit 2, which will be within 3 months of Visit 1. No further assessments will be performed at Visit 2.
The primary analyses will be based on multivariate logistic regression model. Any adverse events occurring during the course of the study will be reported to the local health authority.
The study has enrolled 583 patients until Dec 2017 and the interim analysis results of the first 400 patients are expected in May 2018.
Conclusion: This study aims to develop a clinical score to predict systolic dysfunction and HF in an elderly at-risk outpatient population without a diagnosis of HF to assist screening programmes for HF. This clinical score may also assist clinicians in the early recognition of HF in the elderly, and can help to optimize treatment and lead to an improved prognosis.

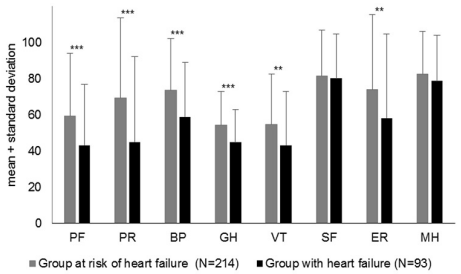
P1820

Health-related quality of life, depressive symptoms and satisfaction with life in population with and at risk of heart failure

N Natasa Sedlar[1]; M Lainscak[2]; D Omersa[3]; J Farkas[4]
[1]*National Institute of Public Health, Ljubljana, Slovenia*; [2]*General Hospital Murska Sobota, Department of Internal Medicine, Murska Sobota, Slovenia*; [3]*General Hospital Jesenice, Jesenice, Slovenia*; [4]*General Hospital Murska Sobota, Department of Research, Murska Sobota, Slovenia*

Funding Acknowledgements: Heart failure epidemiology in Slovenia: prevalence, hospitalizations and mortality, J3-7405 - financially supported by the Slovenian Research Agency

Background: Measuring health-related quality of life (HRQOL), depression and satisfaction with life is important to understand the impact of heart failure (HF) on patients' lives. Despite the numerous studies evaluating HRQOL and subjective well-being in patients with HF, little is known about subjective experiences among people at risk of HF.



PF: physical functioning; PR: physical role functioning; BP: bodily pain; GH: general health perception; VT: vitality; SF: social functioning; ER: emotional role functioning; MH: mental health;
** p<0.01 and *** p<0.001

SF-12 scales in both groups.

Purpose: The aim of our study was to compare levels of health-related quality of life, depressive syptoms and satisfaction with life in population with and at risk of heart failure.
Methods: A cross-sectional study assessing the prevalence of HF in general population aged 55 years or more has been conducted in city of Murska Sobota. Overall, 702 persons were screened with NT-proBNP and 307 had concentration = 125 pg/mL; they underwent detailed diagnostic visit with echocardiography, history and physical examination and electrocardiogram. HF diagnosis was based on 2016 European Society of Cardiology guidelines. We also assessed HRQOL (the Short-Form 12 Health Survey, SF-12), depressive symptoms (Patient Health Questionnaire, PHQ-9) and satisfaction with life (Satisfaction With Life Scale, SWLS). Differences on the subscales were assessed with the Mann–Whitney U-test.
Results: HF was confirmed in 93 persons and 214 were at risk of HF. Compared to the group at risk of HF, the group with HF reported significantly (p <0.001) lower scores on all four SF-12 physical health domains (physical functioning, role

limitations due to physical problems, bodily pain, general health) and two SF-12 mental health domains: vitality (p = 0.002) and role limitations due to emotional problems (p = 0.004). They also reported significantly more depressive symptoms (p <0.001), while there were no significant differences between the groups with respect to social functioning, experienced psychological distress and self-rated satisfaction with life. In both groups, depressive symptoms and satisfaction with life were significantly (moderately) negativelly associated with all HRQOL domains.
Conclusions: HRQOL is generally worse in patients with HF than in those at risk of HF, while its association with depressive symptoms was found for both groups. Longitudinal studies assessing trajectories of change in HRQOL and subjective well-being in patients developing HF are needed.

Acute Heart Failure - Pathophysiology and Mechanisms

P1821
Different outcome and fibrosis marker profiles suggest different pathomechanisms for peripartum cardiomyopathy in German and South African patients

F Feriel Azibani[1]; TJ Pfeffer[2]; M Ricke-Hoch[2]; W Dowling[1]; O Briton[1]; J Baard[1]; J Anthony[3]; S Stella[2]; D Hilfiker-Kleiner[2]; K Sliwa[1]
[1]University of Cape Town, Medicine, Cape Town, South Africa; *[2]Hannover Medical School, Cardiology and Angiology, Hannover, Germany*; *[3]University of Cape Town, Obstetrics & Gynaecology , Cape Town, South Africa*

Background Peripartum cardiomyopathy (PPCM) is heart failure with reduced systolic LV function in the last month of pregnancy or in the first 6 postpartal months in previously healthy women. Multiple pathomechanism trigger the disease suggesting different disease entities in Caucasian and African patients
Purpose We compared collagen metabolism related blood markers in PPCM cohortes from Germany (G) and South Africa (SA)
Methods and Results German (G-PPCM, n = 80) and South African (SA-PPCM, n = 74) PPCM patients were divided according to their LVEF at 6-months follow-up: poor outcome: < 35%, partial recovery: 35%-50%, full recovery: >50%. We observed lower mean baseline LVEF but a higher 6 months recovery rate and lower mortality rate in the G-PPCM (LVEF 24 ± 9%, recovery rate: 71%, mortality rate: 0) compared to the SA-PPCM (LVEF 30 ± 9%, full recovery rate: 36%, mortality rate: 11%). Age and parity were similar in both collectives. Healthy pregnancy state matched women from Germany (G-controls, n = 60) and South Africa (SA-controls, n = 28) served as controls.
Serum levels of type I (PINP) and type III (PIIINP) N-terminal procollagen propeptide, soluble ST-2 (sST-2) and plasma levels of Galectin 3 (Gal3) were measured by ELISA at diagnosis (baseline) and after 6 months follow up (FU). Gal3 was elevated in G- and SA-PPCM patients at baseline compared to controls ($p < 0.001$) and were normalised after 6 months, with no differences between the two cohorts. SST2 was elevated significantly in G-PPCM patients ($p < 0.01$), and tended to be higher in SA-PPCM patients compared to their respective controls. In patients with poor outcome from both collectives Gal3 levels were significantly higher at baseline compared to patients with total recovery ($p < 0.01$). Furthermore Gal3 ($p < 0.001$) and sST2 ($p < 0.01$) levels at baseline were significantly higher in non-survivors compared to survivors of the SA-PPCM cohort.
PINP and PIIINP differed between G- and SA controls and the kinetics of both markers differed between SA- and G-PPCM patients. In SA-PPCM, baseline PINP and PIIINP levels were similar to SA-controls, whereas 6 months FU PINP and PIIINP levels were significantly reduced. The PINP/PIIINP ratio was lower in non-recovered compared to recovered SA-PPCM patients ($p < 0.01$) and baseline PINP/PIIINP ratio was significantly decreased in the non-survivors versus survivors ($p < 0.05$).
In G-PPCM baseline PINP levels were higher compared to G-controls ($p < 0.01$), whereas PIIINP levels were not elevated. At 6 months FU both markers were similar to controls and no correlation was seen between the ratio of PINP/PIIINP with regard to the recovery status in the G-PPCM cohort.
Conclusion: Baseline cardiac function was lower in the G-PPCM patients compared to the SA-PPCM patients but the outcome in the G-PPCM was better. In addition, fibrosis related biomarkers differ substantially between the two cohorts supporting the hypothesis of different pathomechanisms of PPCM in G and SA-PPCM patients

P1822
Change of iron status and its association with prognosis in patients with acutely decompensated heart failure

K Kenji Kajitani[1]; K Nagao[1]; A Tamura[1]; T Kobayashi[1]; H Yukawa[1]; K Aida[1]; T Kanazawa[1]; Y Kobayashi[1]; N Takahashi[1]; E Nakagawa[1]; H Ito[1]; F Hayashi[1]; T Makita[1]; I Tsukasa[1]; M Tanaka[1]
[1]Osaka Red Cross Hospital, Department of Cardiovascular Center, Osaka, Japan

Background: Iron deficiency (ID) in chronic heart failure (HF) is common and infusion iron therapy has been proved to improve functional capacity in patients with reduced ejection fraction (EF). However, change of iron status in the acute phase of HF and its association with prognosis remain unclear. The purpose of this study is to analyze the change of iron status and its association with prognosis in the patients with acutely decompensated heart failure (ADHF).
Methods: We prospectively evaluated iron parameters on admission and at discharge among 201 ADHF patients without iron therapy. ID was defined as ferritin < 100 μg/L or ferritin 100-299 μg/L with transferrin saturation < 20%.
Results: Proportion of ID on admission was 73 %, which was decreased to 55% at discharge (P = 0.01). Factors independently associated with ID on admission were gender female and reduced EF. During the hospitalization, 13 patients died. ID on admission was not related to in-hospital death (P = 0.7). During the median follow-up of 320 days, 21 cardiac death and 52 readmission for HF occurred. Cumulative 1-year incidence of composite endpoint of cardiac death and admission for HF was 33% in the patients with ID at discharge and 31% in the patients without ID at discharge (log-rank P = 0.9). During the hospitalization, ferritin level was increased in the 75% of patients, whereas it was decreased in the remaining 25% of patients. Patients with decreased ferritin level were associated with worse prognosis as compared with those with increased ferritin level (log-rank P = 0.02). Decrease in ferritin level during the hospitalization was independently associated with poor prognosis (adjusted hazard ratio: 2.8, 95% confidence interval: 1.5-5.4, P = 0.003)
Conclusion: ID is very common and iron status dynamically changes in the patients with ADHF. Not only temporal iron status, but also its transition should be evaluated during the acute phase of HF.

Acute Heart Failure - Epidemiology, Prognosis, Outcome

P1824
Performance measurement has a different prognostic implication in de novo vs. acute decompensated heart failure

MS Ahn[1]; BS Byungsu Yoo[1]; JW Son[1]; JY Kim[1]; SW Park[1]; SH Baek[2]; ES Jeon[3]; MC Cho[4]; DJ Choi[5]; SC Chae[6]
[1]Wonju College of Medicine, Yonsei University, Division of Cardiology, Department of Internal Medicin, Wonju, Korea Republic of; *[2]The Catholic University of Korea, Cardiology, Seoul, Korea Republic of*; *[3]Samsung Medical Center, Seoul, Korea Republic of*; *[4]Chungbuk National University Hospital, Cheongju, Korea Republic of*; *[5]Seoul National University Bundang Hospital, Seongnam, Korea Republic of*; *[6]Kyungpook National University Hospital, cardiology, Daegu, Korea Republic of*

Background: Guideline driven therapy (GDT)can reduce morbidity and mortality in patients with HF and treatment guideline adherence is an important predictor of clinical deterioration. There is a paucity of data on the differential effects of adherence to treatment on outcomes according to acute HF classification such as de novo or acute decompensated HF. This study assessed the differential relationship according to heart failure classification between performance measures at hospital discharge and relevant patient clinical outcomes, including 60day and 1 year heart failure hospitalization, all-cause mortality and a composite end point of both.
Method and Results: Korean Heart failure registry (KorAHF) is a prospective observational multicentre cohort study, which have been consecutively enrolled since March 2011. Among 5,625 patients in the KorAHF, 2,769 patients with left ventricular systolic dysfunction who survived hospitalization and were not candidate for heart transplantation were separately analyzed as de novo HF and acute decompensated HF. Modified validated performance measures were defined as follows: use at discharge of ACEI, ARB or ß-blocker. An additional performance measure for MRA and anticoagulation were developed using a population definition similar to that used for ACE inhibitor/ARB. In de novo heart failure, adherence to ACEI or ARB was significantly associated with 60days rehospitalization (odds ratio (OR), 0.54; 95% confidence interval (CI), 0.31-0.93), mortality (OR, 0.37; 95% CI, 0.21-0.65) and composite end point (OR, 0.48; 95% CI, 0.31-0.73). That was not associated with 1 year rehopitalization (OR, 0.75; 95% CI, 0.49-1.15) but with 1 year mortality(OR, 0.58; 95% CI, 0.38-0.87) and composite end point (OR, 0.61; 95% CI, 0.43-0.87). The adherence to beta blocker was associated with all outcomes except 60day mortality. In acute decompensated heart failure, adherence to ACEI or ARB did not influence to all 60 day rehospitalization(OR, 1.08; 95% CI, 0.73-1.59), composite end point (OR, 0.83; 95% CI, 0.60-1.15), 1 year rehospitalization (OR, 1.31; 95% CI, 0.97-1.78), death (OR, 0.81; 95% CI, 0.59-1.11) and composite end point (OR, 1.07; 95% CI, 0.81-1.42). That was only associated with 60 day mortality (OR, 0.57; 95% CI, 0.36-0.90). Adherence to beta blocker had a constant significant effect on the outcome except 60 day rehospitalization. The adherence to MRA and anticoagulation had no effect on clinical outcomes in both group.
Conclusion: The adherence to treatment performance measures has a difference effect on the prognosis according to the heart failure classification. ACEI or ARB at discharge has a prognostic implication in de novo heart failure but its effect is weak in acute decompensated heart failure. Beta blocker has a constant effect on the prognosis regardless of heart failure classification.

P1825

Inequalities in mortality due to heart failure in chile: a gender-based analysis

J Martinez[1]; F Diaz[2]; H Verdejo[3]; M Sanhueza[1]
[1]Catholic University Clinical Hospital, Santiago, Chile; *[2]Universidad Andres Bello, Faculty of Nursing, Santiago, Chile*; *[3]Pontifical Catholic University of Chile, Faculty of Medicine, Santiago, Chile*

Background: Heart Failure (HF) is one of the leading cause of death and re-hospitalization in older people worldwide. Several studies had shown that gender inequality increases mortality rates in HF patients. However, there is limited evidence of its impact in Latin American countries.
Aim: To assess the impact of gender inequality in mortality due to HF in Chilean patients.
Methods: Cross-sectional study. We reviewed all country-wide deaths during 2015 of subjects 20 years and older using the national mortality database. Mortality due to HF was identified by the following ICD-10 codes: I500 (congestive heart failure), I501 (left ventricular heart failure), and I509 (non-specified heart failure). We analyzed sociodemographic and clinical variables stratified by gender. We assessed the prevalence of deaths due to HF by age, educational level, and rural/urban area of living. Odds ratios (OR) and 95% confidence intervals were calculated through multivariate logistic models.
Results: During the study period, there were 103,327 deaths in people older than 20 years in Chile. From those, 1,156 (1.12%) had HF as the primary cause of death. The number of women who died due to HF was higher than men (55.5% vs. 44.6%; p <0.002). Women were older (83.2 vs. 76.2 years; p <0.001), had less education (less than 8 years of schooling 88.5% vs. 77.4% p <0.001), and a larger percentage died in rural areas (16.2% vs. 10.9%; p <0.01) when compared with their male counterparts. Factors associated with mortality by HF in multiple logistic regression analysis were: women older than 80 years old (OR 2.81 IC95%; 2.19-3.61; p <0.001), women with less than 8 years of education (OR 1.99 IC95%; 1.43-2.78; p = 0.005) and living in rural areas (OR 1.72 IC95%; 1.21-2.47; p = 0.003).
Conclusion: Older and less educated women are features associated with higher mortality due to HF. While the reported mortality of HF is probably underestimated, this research is the first approach to assess the epidemiologic impact of inequalities in the Chilean population with HF.

P1826

Predictors of high killip class on admission in st-segment elevation myocardial infarction

K Kevin Domingues[1]; MJ Vieira[1]; D Durao[1]; M Leal[1]
[1]Hospital of Santarem, Cardiology, Santarem, Portugal

On behalf of: Investigators of the National Registry of Acute Coronary Syndrome of the Portuguese Society of Cardiology

Introduction: Heart failure (HF) is a common complication of ST-segment elevation myocardial infarction (STEMI). The Killip-Kimball classification (KK) is a system used in this setting, which takes into account physical examination and the development of heart failure in order to predict and stratify the risk of mortality. KK class is expectedly dependent on several factors, however, it is unknown which are the predictors of an elevated KK class on admission.
Aim: To determine predictors of high KK class on admission in STEMI patients.
Methods: A retrospective study of patients inserted the National Registry of ACS of the Portuguese Society of Cardiology was performed. The sample was divided in two groups: patients with KK class = 1 (KK = 1) and patients with KK class >1 (KK>1). Demographic and clinical data were analysed.
Results: A total of 7274 patients were included, predominantly men (75.4%), with a mean age of 64 ± 14 years. Most patients (85.5%) presented in KK = 1 (II 8.6%; III 2.3%; IV 3.6%).
There was a higher incidence of KK>1 in the female gender (36.3% vs 22.6%, p < 0.001), older patients (71 vs 63 years old, p < 0.001), patients with longer time from the beginning of symptoms to the first medical contact (median 143 vs 128 minutes, p = 0.008), anterior infarcts (59.6% vs 46.5%, p < 0.001) and in patients with atrial fibrillation (13.4% vs 4.0%, p < 0.001). Higher creatinine and glycaemia were both associated with a higher incidence of KK>1, as well as previous medication with commonly used cardiovascular drugs (including aspirin, clopidogrel, beta-blockers, ACE-inhibitors, statins, diuretics) and antidiabetic drugs (both oral and insulin).
In the multivariate analysis, including sex, age, comorbidities, time from the beginning of symptoms to the first medical contact, previous medication, blood tests and haemodynamic parameters on admission as variates, age >75 years old (p < 0.001; OR 1.82, CI95 1.46-2.27), prior heart failure (p < 0.001, OR 2.91, CI 1.75-4.85), previous medication with statins (p = 0.018; OR 1.29, CI 1.05-1.60), creatinine >2 mg/dL (p < 0.001; OR 2.25, CI95 1.44-3.52) and glycaemia >200 mg/dL (p < 0.001; OR 2.16, CI95 1.74-2.68) were independent predictors of KK>1 on admission.
On the contrary, sinus rhythm on admission (p < 0.001; OR 0.45, CI95 0.33-0.60) and right coronary artery as culprit (p = 0.010; OR 0.66, CI95 0.48-0.91) were independently associated with a lower incidence of KK>1.
Conclusion: In this study of STEMI patients, age >75 years old, previous medication with statins, creatinine >2 mg/dL and glycaemia >200 mg/dL were independent predictors of KK>1 on admission. On the contrary, sinus rhythm on admission and right coronary artery as culprit were independently associated with a lower incidence of KK>1.

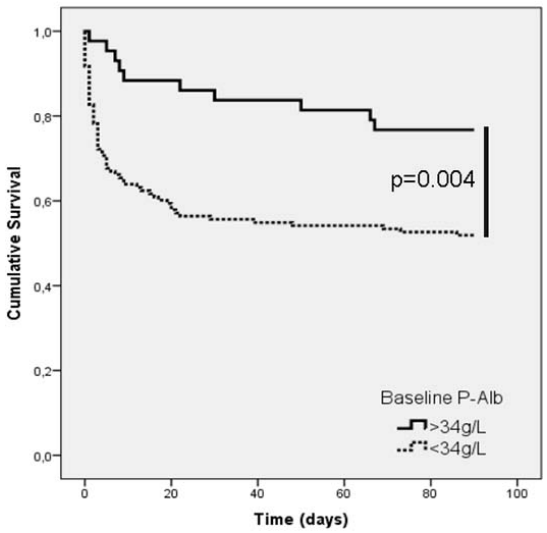
P1827

Frequency and prognostic significance of hypoalbuminemia in cardiogenic shock

T A J Toni Antti Juhani Jantti[1]; T Tarvasmaki[1]; V-P Harjola[1]; J Parissis[2]; K Pulkki[3]; A Sionis[4]; J Silva-Cardoso[5]; L Kober[6]; M Banaszewski[7]; J Spinar[8]; V Carubelli[9]; S Disomma[10]; A Mebazaa[11]; JP Lassus[1]
[1]Helsinki University Central Hospital, Helsinki, Finland; *[2]Attikon University Hospital, dHeart Failure Clinic and Secondary Cardiology Department, Athens, Greece*; *[3]Eastern Finland Laboratory Centre, Kuopio, Finland*; *[4]Hospital de la Santa Creu i Sant Pau, fIntensive Cardiac Care Unit, Cardiology Department, Barcelona, Spain*; *[5]Sao Joao Hospital, CINTESIS, Porto Medical School, Porto, Portugal*; *[6]Rigshospitalet - Copenhagen University Hospital, hDivision of Heart Failure, Pulmonary Hypertension and Heart Transplantation, Copenhagen, Denmark*; *[7]Institute of Cardiology, Warsaw, Poland*; *[8]University Hospital Brno, Brno, Czech Republic*; *[9]Civil Hospital of Brescia, Brescia, Italy*; *[10]Sant' Andrea Hospital, Rome, Italy*; *[11]Hospital Lariboisiere, Paris, France*

On behalf of: CardShock study group
Funding Acknowledgements: This study was supported by grants from the Finnish Foundation for Cardiovascular Research and Aarne Koskelo Foundation.

Background: The prevalence of hypoalbuminemia, early changes of plasma albumin levels and their effects on mortality in cardiogenic shock are unknown.
Methods: Prospective multinational observational study enrolling consecutive patients in cardiogenic shock. Plasma albumin was measured from serial blood samples in 178 patients. Clinical characteristics, course of hospital stay including treatment and procedures were registered. The main outcome was all-cause 90-day mortality.
Results: Hypoalbuminemia (plasma albumin < 34g/L) was very frequent (75%) at baseline in patients with cardiogenic shock. Patients with hypoalbuminemia had higher mortality than patients with normal albumin levels (48% vs. 23%, p = 0.004). Odds ratio for death was 2.4 [95% CI 1.5-4.1] per 10 g/L decrease in baseline plasma albumin. The association remained independent in regression models adjusted for risk prediction scores developed for cardiogenic shock (CardShock score, IABP-SHOCK II score) and variables associated with hypoalbuminemia at baseline in this study.
In serial measurements, albumin levels declined at a similar rate between 0h and 72h in both survivors and nonsurvivors. In contrast, the rate of albumin decline was greater for patients with normal plasma albumin at baseline (p < 0.001). The rate of albumin decline was not associated with outcome.
Conclusion: Hypoalbuminemia is a frequent finding early in cardiogenic shock, and plasma albumin levels decline during hospital stay. Low plasma albumin at baseline, but not change in albumin, is associated with mortality independently of other previously described risk factors. Thus, plasma albumin should be part of the initial evaluation in patients with cardiogenic shock.



Kaplan-Meier curves of 90-day mortality

P1828

C-terminal fragment of IGFBP-4 is independently associated with mortality in patients hospitalized due to acute heart failure

AB Postnikov[1]; AA Konev[1]; AV Kharitonov[2]; PN Datskevich[2]; FN Rozov[2]; J Lassus[3]; VP Harjola[3]; AG Katrukha[1]
[1]HyTest Ltd, Turku, Finland; *[2]Moscow State University, Faculty of Biology, Moscow, Russian Federation*; *[3]Helsinki University Central Hospital, Heart and Lung Center, Helsinki, Finland*

Background: Insulin-like growth factor binding protein-4 (IGFBP-4) fragments are products of proteolytic cleavage mediated by pregnancy-associated plasma protein A (PAPP-A). IGFBP-4 fragments have been proposed as biomarkers of major adverse cardiovascular events risk in patients with acute coronary syndrome. In addition, IGFBP-4 fragments have been shown to predict cardiac and all-cause mortality in patients with type 1 diabetes. Recently carboxy-terminal fragment of IGFBP-4 (CT-IGFBP-4) was shown to provide incremental prognostic information on cardiovascular events and mortality in patients with ST-elevation myocardial infarction. As progressive heart failure (HF) is a major cause of morbidity and mortality following acute myocardial infarction, we suggest that CT-IGFBP-4 could also be utilized as a biomarker for prognosis of HF outcomes.
Purpose: In this study the prognostic value of CT-IGFBP-4 for all-cause mortality was evaluated in emergency patients with acute HF.
Methods: CT-IGFBP-4 was measured at admission in Li-heparin plasma samples of 156 emergency patients with acute HF. A specific immunoassay utilizing monoclonal antibodies recognizing proteolytic neo-epitopes of CT-IGFBP-4 was used. Cross-reaction of the immunoassay with intact IGFBP-4 was less than 2%. One year all-cause mortality was recorded. ROC curve and Cox proportional hazard ratio analysis were performed to evaluate prognostic value of CT-IGFBP-4.
Results: During one year of follow-up 52 (33.3%) patients died. 52% of deaths (27 of 52 cases) occurred during the first month of observation. The concentration range of CT-IGFBP-4 of the study cohort was 9.4-1121 ng/mL. CT-IGFBP-4 was significantly elevated in non-survivors at both one month ($p = 0.0003$) and one year ($p = 0.0018$) periods. CT-IGFBP-4 predicted all-cause mortality at one month and one year follow-up periods: the areas under the ROC curves were 0.753 and 0.727, respectively. The optimal cut-off value of CT-IGFBP-4 for predicting all-cause mortality was 92.5 ng/mL that corresponded to 81% sensitivity and 58% specificity. Also the Cox hazard analysis revealed CT-IGFBP-4 as a predictive factor of one month and one year mortality. The unadjusted hazard ratio (HR) for CT-IGFBP-4 = 92.5 ng/mL was 6.15 (95% confidence interval [CI]: 2.12-17.79, $p = 0.0008$) for one month and 4.20 (95% CI: 2.11-8.39; $p < 0.0001$) for one year of follow-up. After adjustment for multiple clinical and echocardiographic variables CT-IGFBP-4 was an independent risk biomarker (HR 5.39 [95% CI: 2.11-13.76, $p = 0.0004$] and HR 3.26 [95% CI: 1.63-6.51, $p = 0.0008$] for one month and one year mortality, respectively).
Conclusion: CT-IGFBP-4 independently predicted all-cause mortality in patients with acute HF, suggesting that PAPP-A/IGFBP-4 might be involved in the pathogenesis of HF.

P1829

Risk factors for 30-day all-cause readmissions in patients with acute dyspnoea

K Cerlinskaite[1]; T Javanainen[2]; R Cinotti[2]; R Visinskiene[3]; A Kavoliuniene[4]; J Celutkiene[1]; A Mebazaa[2]
[1]Vilnius University, Clinic of Cardiac and Vascular diseases, Centre of Cardiology and Angiology, Vilnius, Lithuania; *[2]Hospital Lariboisiere, Inserm UMR-S 942 and Anesthesia and Critical Care Department, Paris, France*; *[3]National Health Insurance Fund Under the Ministry of Health, Vilnius, Lithuania*; *[4]Department of Cardiology, Medical Academy, Lithuanian University of Health Sciences, Kaunas, Lithuania*

On behalf of: GREAT (Global Research on Acute Conditions Team) Network
Funding Acknowledgements: The work was supported by the Research Council of Lithuania, grant Nr. MIP-049/2015 and approved by Lithuanian Bioethics Committee, Nr. L-15- 01.

Introduction: Patients with acute dyspnoea are at high risk of vulnerable phase readmission after initial episode, but the risk factors for early readmissions have yet to be established.
Purpose: To determine predictors of 30-day all cause readmissions in both acute heart failure (AHF) and non-AHF patients with acute dyspnoea.
Methods: Prospective multicentre observational cohort study enrolled 1404 consecutive patients admitted with acute dyspnoea due to AHF and non-AHF. Present analysis included 30-day survivors who were divided into AHF and non-AHF groups. Cox regression analysis was used to determine independent predictors for 1 month all-cause readmissions.
Results: Of 1284 patients (median age 70 (62-78) years) included, 707 (55%) patients had AHF, and 577 (45%) had non-AHF (pneumonia 95(16%), pulmonary embolism 82(14%), etc.) dyspnoea. In AHF group 169 patients (24%) were readmitted in 1 month, in non-AHF group - 147 (25%) ($p < 0.05$). Median time to first 30-day readmission was 6 (1-16) and 6 (1-16.5) in AHF and non AHF groups, respectively ($p < 0.05$). In AHF group 30-day all-cause readmissions were mainly caused by impaired renal function and inadequate HF treatment, while in non-AHF group acute myocardial infarction (27 (5%) and pleural effusion (18 (3%) were the most important factors (Table 1). 19 readmitted patients (11%) died in 3 months vs 25 non-readmitted patients (5%) in the AHF group ($p = 0.004$); 23 readmitted patients (16%) died in 3 months vs 21 non-readmitted patients (5%) in the non-AHF group ($p < 0.001$).
Conclusions: Main predictors of readmission appear to be different in patients with acute dyspnoea due to AHF and non-AHF. Targeting the potential risk factors of readmissions in both groups could improve long-term outcome.

Predictors of 30-day readmissions

	Variable	HR (95% CI)	p value
Non-AHF group	Age per 1 year	1.02 (1.01-1.04)	0.000486
Dyslipidemia	0.45 (0.27-0.75)	0.002367	
Heart rate at admission > 90 b.p.m.	1.63 (1.16-2.28)	0.004714	
Psychotropic drugs at discharge	2.63 (1.42-4.9)	0.002225	
Acute myocardial infarction	2.71 (1.44-5.09)	0.001959	
Pleural effusion	2.66 (1.33-5.29)	0.005399	
AHF group	ACE inhibitors or ARBs at admission	0.65 (0.47-0.89)	0.00666
Creatinine at admission > 130 μmol/l	1.55 (1.12-2.15)	0.00817	
Beta blockers at discharge	0.71 (0.51-0.99)	0.0494	

HR - hazard ratio, CI - confidence interval

P1830

Prognostic factors for one-year mortality in patients with acute heart failure with and without chronic kidney disease: Differential impact of beta-blocker and diuretic treatments.

K Matsushita[1]; T Minamishima[1]; K Sakata[1]; T Satoh[1]; H Yoshino[1]
[1]Kyorin University School of Medicine, Tokyo, Japan

Funding Acknowledgements: The Japan Society for the Promotion of Science (KAKENHI 26461086 and 17K09523; to KM) and the Kyorin Univ. Sch. Med. (No. B102090002; to KM)

Background: Multifactorial pathways are implicated in heart failure (HF) and chronic kidney disease (CKD), complicating the pathogenic features of cardiorenal syndrome. Consequently, the pathophysiology and treatment of acute decompensated HF with CKD remain ill defined.
Purpose: Here we compared the prognostic factors for one-year mortality in patients with acute decompensated HF with and without CKD.
Methods: We retrospectively studied 392 consecutive patients with acute decompensated HF. CKD was defined as an estimated glomerular filtration rate of < 60 mL/min/1.73 m2. Potential risk factors for one-year mortality were selected using univariate analyses; subsequently, multivariate Cox regression analysis with forward stepwise selection was performed with variables showing a statistical value of $P < 0.10$ in the univariate analyses to identify significant factors. Kaplan-Meier survival curves and log-rank testing were used to compare one-year mortality between groups.
Results: Across the study cohort, 65% of patients had CKD, and the one-year mortality rate was 9.2%. There were no significant differences between patients with and without CKD with respect to left ventricular ejection fraction, ratio of early transmitral velocity to tissue Doppler mitral annular early diastolic velocity, and discharge prescription rates of renin–angiotensin–aldosterone system inhibitors, beta blockers, calcium channel blockers, and diuretics. In the HF with CKD group, older age, lower systolic blood pressure at admission, discharge medications without beta-blockers, and discharge medications without diuretics were independent risk factors for one-year mortality. In contrast, coexisting chronic obstructive pulmonary disease and higher C-reactive protein levels were independent risk factors for one-year mortality in the HF without CKD group. Kaplan-Meier survival curves

showed that discharge medications with no beta-blockers or diuretics correlated with significantly lower survival rates in patients with CKD (P < 0.001 in both groups, log-rank test), but not in patients without CKD (P = 0.822 and P = 0.374, respectively, log-rank test).
Conclusions: There were significant differences in the prognostic factors for one-year mortality between patients with acute HF with and without CKD. In particular, differential prognostic impacts of beta-blocker and diuretic treatments were demonstrated. Elucidation of the mechanisms underlying these findings could lead to more effective individualized therapeutic strategies for patients with HF.

P1831

Acute decompensated heart failure- predictive factors for all-cause in-hospital mortality

H B Hui Beng Koh[1]; SS Lim[1]; J Jaafar[1]; MA Sulong[1]; IS Sabian[1]; N Jaafar[1]; AA Abdul Rahim[1]; A Mohd Ghazi[1]; CK Teoh[1]; D Chew[1]
[1]National Heart Institute, Cardiology, Kuala Lumpur, Malaysia

Background: Heart failure is an important cause of morbidity and mortality. Its prevalence is on the rise not only due to increasing average life expectancy but also higher survival from cardiac events.
Purpose: Risk stratification, by identifying predictive factors for in-hospital mortality in patients presented with acute decompensated heart failure (ADHF), is vital so that prudent treatment can be instituted early.
Methods: A retrospective observational cohort study based on patient first admission to National Heart Institute from 2009 to 2015, using descriptive, cross tabulation, univariate and multivariate logistic regression analysis.
Results: 2,785 patients were admitted for ADHF. 124 had in-hospital mortality. Independent predictors for in-hospital mortality were background atrial fibrillation (OR 1.857, p = 0.021), stroke (OR 2.762, p = 0.009), elevated NT-Pro BNP (OR 3.534, p = 0.005), hyponatraemia (OR 1.962, p = 0.006), raised urea (OR 2.713, p = 0.001) and impaired LVEF <40% (OR 1.997, p = 0.045). Other non-independent predictors for in-hospital mortality were SBP = 100mmHg, HR >100, Stage 4 CKD and hyperuricaemia. Medications independently reduced in-hospital mortality- beta blocker (BB) (OR 0.299, p = 0.011), Angiotensin Converting Enzyme inhibitor (ACEI)+BB (OR 0.212, p = 0.007), Angiotensin Receptor Blocker (ARB)+BB (OR 0.274, p = 0.038), BB + Mineralocorticoid Receptor Antagonist (MRA) (OR 0.185, p <0.001), ACEI+BB+MRA (OR 0.149, p <0.001), ARB+BB+MRA (OR 0.048, p <0.001). Background hypertension showed an independent predictor for reduced in-hospital mortality (OR 0.506, p = 0.009). Initial SBP = 140mmHg upon admission was associated with lowered in-hospital mortality (OR 0.322, p <0.001), whereas SBP = 100mmHg was associated with increased in-hospital mortality. However, this was non-independent after adjusted for multivariate analysis. At presentation, patients with background hypertension had significantly more disease-modifying heart failure medications, less atrial fibrillation, less hyponatraemia, less SBP presentation of = 100mmHg. They however, had more pre morbid history of stroke and had more patients with Urea > 7. There were numerically more patients with LVEF <40% in the non hypertensive group versus hypertensive group, however it was not significant.
Conclusions:
Identification of predictors will help risk stratify ADHF patients to reduce in-hospital mortality. Background hypertension was found to independently reduce in-hospital mortality. It could be due to the presence of more disease-modifying heart failure medications already prescribed to hypertensive patients, thus lowering their in-hospital mortality. Other factors may have played some roles in explaining why background hypertension was associated with reduced in-hospital mortality. Prompt initiation of oral disease-modifying heart failure medications are crucial to reduce in-hospital mortality amongst patients presenting with acute decompensated heart failure.

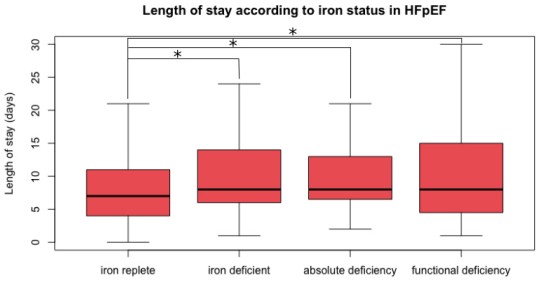
P1832

Iron deficiency predicts longer hospital stay in patients with heart failure and preserved ejection fraction, but not in those with reduced ejection fraction

A L Anna Louise Beale[1]; J Stirnemann[2]; N Garin[2]; D Carballo[2]; D M Kaye[3]; P Meyer[2]; S Carballo[2]
[1]Monash University, Melbourne, Australia; *[2]Geneva University Hospitals, Geneva, Switzerland*; *[3]The Alfred Hospital, Melbourne, Australia*

Funding Acknowledgements: No sources of funding to declare.

Background: Iron deficiency (ID) is gathering recognition as an important determinant of outcomes in heart failure, with evidence suggestive of a pathophysiological role in myocardial remodelling. Existing data on the prognostic and therapeutic use of iron predominantly relates to heart failure with reduced ejection fraction (HFrEF).
Purpose: This study investigated the associations between ID and length of hospital stay, dyspnoea class, biomarker levels, and echocardiographic indices of diastolic function in patients with HFrEF and heart failure with preserved ejection fraction (HFpEF).
Methods: Consecutive patients admitted with acute decompensated heart failure were included between December 2014 and August 2017 at a single Swiss tertiary centre. Demographic information, blood tests, echocardiography results and metrics regarding hospital stay and readmission were extracted from the patients' hospital record. Patients were classified as having 'absolute' ID if they had a ferritin level <100ng/mL; or 'functional ID' if they had a ferritin 100-200ng/mL in conjunction with a transferrin saturation <20%.



Length of stay in HFpEF

Results: Of the 503 patients recruited with ejection fraction data available, 160 (33%) had HFrEF, 270 (55%) had HFpEF, and 57 (12%) had HFmrEF. Reflecting other reported heart failure cohorts, HFpEF patients were older, female predominant, had a higher prevalence of hypertension and atrial fibrillation, and lower levels of natriuretic peptides than those with HFrEF. Other key comorbidities did not differ between groups. The prevalence of ID was 58% in HFpEF, 60% in HFmrEF, and 55% in HFrEF patients with iron results available. HFmrEF patients were excluded from further analyses due to a low number with iron studies. Haemoglobin level was significantly higher in HFrEF at 129 ± 20g/mL, compared to 121 ± 23g/mL in HFpEF. In patients with HFpEF, ID was significantly associated with female sex and a longer length of hospital stay of approximately 2 days (9 ± 6 vs. 11 ± 7.7 days, depicted below). HFpEF patients with functional ID had a higher C-reactive protein (CRP), and were older than those without ID or with absolute ID. No such associations were seen in the HFrEF cohort. No association was found between ID and dyspnoea class or diastolic function in either group.
Conclusions: This study highlights a high prevalence of ID in all heart failure phenotypes, along with an increased length of stay of 2 days in ID HFpEF patients compared to iron replete HFpEF patients. This may indicate an enhanced role for ID in HFpEF, which could be due to the detrimental effects of ID on exercise tolerance and myocardial remodelling in HFpEF. Furthermore, inflammation plays an important role in both HFpEF and ID, and may mediate the link between the two, as suggested by the elevated CRP in HFpEF patients with functional ID. Further studies in larger cohorts of patients from diverse ethnic backgrounds are warranted to increase the generalisability of these results.

P1833

Higher loop diuretic dose administered at admission for acute heart failure predicts worse 1-year outcomes

J Justas Simonavicius[1]; R Zeimaite[2]; A Rimkus[2]; Z Abramikas[2]; P Budrys[1]; A Mikalauskas[1]; V Juknevicius[1]; A Mebazaa[3]; J Celutkiene[1]
[1]Vilnius University, Clinic of Cardiac and Vascular Diseases, Centre of Cardiology and Angiology, Vilnius, Lithuania; *[2]Vilnius University, Faculty of Medicine, Vilnius, Lithuania*; *[3]University Paris Diderot , U942 Inserm, Hospital Lariboisiére, Paris, France*

On behalf of: The GREAT network

Introduction: Observational studies related treatment with high loop diuretic (LD) dose to worse long-term prognosis in chronic heart failure (HF); prognostic significance of LD dose in acute HF (AHF) is less certain.
Purpose: This study was designed to investigate the relation between LD dose administered to AHF patients in an emergency department (ED) and composite end-point of 1 year rehospitalisation and mortality.
Methods A prospective two-centre observational cohort study consecutively enrolled dyspnoeic patients admitted to an ED. Single centre data were included in the present analysis because medical records regarding LD doses were not available in the collaborating institution. 414 subjects were diagnosed with AHF; 1 year follow-up of mortality and rehospitalisation was available in 230 subjects that underwent outcome analysis. Patients were divided into quartiles (Q) based on LD dose administered at an ED (70% intravenous (IV), 26% oral (PO), 4% IV and PO

administration): Q1 (mg of furosemide) (= 60 mg) was compared with Q2 (61-80 mg), Q3 (81-100 mg) and Q4 (<100 mg).
Results: Patients treated with the highest LD dose were younger (mean age Q1 vs Q4 was 70 vs 65 years [p < 0.05]) and predominantly male (83%), their systolic (SBP) and diastolic (DBP) blood pressure at admission was lower (SBP Q1 vs Q4 was 139 vs 127 mmHg; DBP Q1 vs Q4 was 82 vs 74 mmHg [p < 0.05]). 21.7% of patients died; 51.4% were rehospitalised in 1 year. In an univariate analysis Q4 was identified as a predictor of 1-year rehospitalisation and mortality (Q1 vs Q4 unadjusted odds ratio (OR) 2.44, 95% confidence interval (CI) 1.06-5.64 [p < 0.05]) (Table). Other univariate predictors were included in a multivariate analysis, where furosemide dose >100 mg retained its predictive value (adjusted OR 2.98, 95% CI 1.01-8.80; p < 0.05) along with anaemia (Table).
Conclusion. Higher loop diuretic dose administered at admission for AHF is an independent predictor of 1-year rehospitalisation and mortality in AHF patients.

	Univariate analysis		Multivariate analysis	
Variable	OR	95% CI	OR	95% CI
Furosemide dose (mg) : ≤60[a] vs >100	2.44*	1.06-5.64	2.98*	1.01-8.80
Sodium (mmol/l): <134 vs ≥134[a]	3.17*	1.05-9.59	2.53	0.75-8.60
Haemoglobin (g/l): <120 vs ≥120[a]	1.93*	1.08-3.44	2.34*	1.10-4.50
Hs Troponin I: (ng/l): <35[a] vs ≥35	2.05*	1.15-3.63	1.64	0.83-3.23
Creatinine (μmol/l): <120[a] vs ≥120	1.79*	1.02-3.14	1.39	0.69-2.80

a- referent; * - p < 0.05; OR - odds ratio; CI - confidence interval; Hs: high sensitivity

P1834

Mitral regurgitation worsens prognosis in acute heart failure

J Jack Stewart[1]; A Baltabaeva[1]; O Lazariashvili[1]
[1]*Ashford and St Peter's Hospitals NHS Trust, Cardiology, Chertsey, United Kingdom*

Funding Acknowledgements: Metanoic Health Ltd.

Introduction
Acute Heart Failure (AHF) is a well recognised and growing healthcare problem with 1 year mortality typically reported around 30%. Mitral regurgitation (MR) is a highly prevalent valvular disease, but it's impact on heart failure and the potential benefits of intervention are currently unclear.
Purpose: We have aimed to assess the prognostic impact of MR in patients admitted with AHF or exacerbation of chronic HF (ECHF) in a single-centre, prospective, cross-sectional study.
Methods: All patients admitted to a large district general hospital with AHF and/or ECHF over the period of 1 year were assessed and approached for recruitment to the study. Those recruited had standard clinical assessment, biochemistry including bedside B-type natriuretic peptide levels and bedside transthoracic echocardiography within 48 hours of recruitment. Demographic and comorbidity data was also recorded including history of heart failure and MR. Geometric and functional parameters of cardiac function were assessed according to international guidelines with a specific focus on valvular disease characteristics. All-cause mortality was documented at 6 months post discharge.
MR was categorised as mild, moderate, moderate-severe and severe according to international guidelines.
Subsequent recategorisation was performed with patients divided into Mild MR and Significant MR (moderate severity MR and above).
For statistical comparison values were categorised and analysed using Chi-square testing. Kaplan-Meier survival plots were created to demonstrate differences in survival.
Results: 617 patients met the inclusion criteria of whom 500 were consented and 448 patients were included in the study. 6 month mortality is currently available for 356 patients. Of these patients, 151 (42%) had known MR at admission. MR of at least trace severity was found in all patients (100%). Clinicians felt that worsening of MR was the likely cause of decompensation of HF in only 15 patients (4.2%).
6 month mortality was higher than previously reported data at 29%.
Patients with significant MR demonstrated significantly increased 6-month mortality when compared to mild MR (p < 0.05).
Additionally, patients with known MR prior to admission demonstrated significantly increased mortality at 6 months compared to those without (p < 0.05).
Conclusion: Significant MR is associated with reduced 6 month survival in acute heart failure. Known MR is also a predictor of impaired long term survival, irrespective of whether or not this is the cause of acute decompensation.

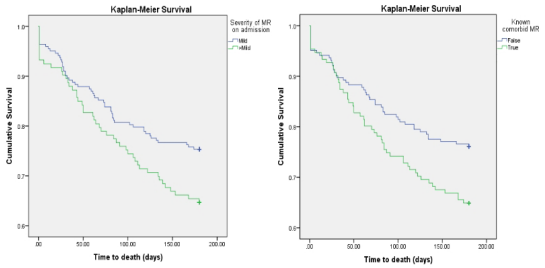


Figure 1. Kaplan-Meier Survival Plots

P1835

Precipitant of hospitalisation predicts mortality in acute heart failure

J Jack Stewart[1]; O Lazariashvili[1]; A Baltabaeva[1]
[1]*Ashford and St Peter's Hospitals NHS Trust, Cardiology, Chertsey, United Kingdom*

Funding Acknowledgements: Abbott Vascular ltd

Introduction: Acute Heart failure (AHF) has a poor prognosis with mortality similar to or worse than 5 of the most common cancers. The ability to prognosticate for individual patients is of significant benefit and clear understanding of precipitants of hospitalisation may provide useful information for targeted treatment.
Purpose: We aimed to assess how precipitants of hospitalisation in acute heart failure (AHF) can predict of outcome in patients with AHF presenting to the emergency room of a large district general hospital in a single-centre prospective cross-sectional study.
Methods: All patients admitted to a large district general hospital with AHF over 1 year underwent standard clinical assessment, biochemistry and transthoracic echocardiography. Patients admitted with AHF as a non primary driver of admission were excluded from the study. Parameters of cardiac function were assessed according to international guidelines. Precipitants of AHF were recorded according to the CHAMP classification as outlined in the ESC guidelines, with additional categories for 'Medication withdrawal' (MW) and 'Unclear precipitant' (U). All-cause mortality was documented at 6 months post discharge. Chi-square analysis was used to demonstrate or refute statistical excess in mortality.
Results: 617 patients met the inclusion criteria of whom 500 were consented and 448 were included in the study. 6-month mortality is currently available for 356 patients. 49 (14.6%) had acute ischaemia (C) as precipitant of HF admission, 5 (1.5%) - hypertensive crisis (H), 94 (28%) - arrhythmias (A), 41 (12.2%) - mechanical cause (M), 6 (1.8%) - lung disease (P), 18 (5.3%) - MW and 123 (36.6%) had U.
Overall 6-month mortality was 29.1%.
Patients with hospitalisation precipitated by medication withdrawal had significantly increased mortality at 6 months (p < 0.05). Patients in whom precipitant was unclear had significantly increased mortality at 6 months (p < 0.05).
Patients with AHF precipitated by pulmonary disease had significantly increased mortality at 6 months compared to the rest of the cohort (p < 0.05).
Patients with an arrhythmogenic precipitant of AHF had the best outcome, with significantly reduced mortality at 6 months compared to the rest of the cohort (p < 0.0001).
6-month mortality in AHF precipitated by acute ischaemia, hypertensive crisis or mechanical disease was not statistically significantly different from the rest of the cohort.
Conclusions: Aetiology of decompensation offers significant prognostic information to clinicians and patients. The prevalence of non-compliance and physician led withdrawal is relatively high and associated with poor 6-month prognosis, as is worsening of HF with no clear precipitant. Arrhythmias are significant contributors to HF admissions but demonstrate good 6-month survival. Inpatient treatment could be focussed on patients with greater risk, with the outpatient setting reserved for those with better prognosis.

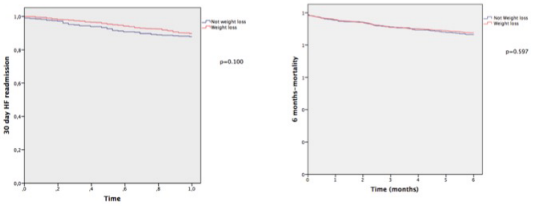
P1836

Body weight loss during hospitalization for acute heart failure and short and long term prognosis

I Gomez[1]; R Agra Bermejo[1]; A Varela Roman[1]; DA Pascual-Figal[2]; J Alvarez Garcia[3]; J Delgado Jimenez[4]; F Worner Diz[5]; R Vazquez Garcia[6]; L Alonso-Pulpon[7]; F Fernandez-Aviles[8]; J Cinca[3]; JR Gonzalez-Juanatey[1]
[1]University Hospital of Santiago de Compostela, Cardiology Department, Santiago de Compostela, Spain; *[2]Hospital Clínico Univeristario Virgen de la Arrixaca, Cardiology Department, Murcia, Spain*; *[3]Hospital de la Santa Creu i Sant Pau, Cardiology Department, Barcelona, Spain*; *[4]University Hospital 12 de Octubre, Cardiology, Madrid, Spain*; *[5]Hospital Arnau de Vilanova, Cardiology, Lleida, Spain*; *[6]University Hospital Puerta del Mar, Cardiology, Cadiz, Spain*; *[7]University Hospital Puerta de Hierro Majadahonda, Cardiology, Madrid, Spain*; *[8]University Hospital Gregorio Maranon, Cardiology, Madrid, Spain*

On behalf of: REDINSCOR II
Funding Acknowledgements: Centro de Investigación Biomédica en Red de Enfermedades Cardiovasculares (CIBERCV)

Introduction: Congestion is recognized as the major cause for hospitalization in the vast majority of patients with heart failure (HF) and contributes to adverse outcomes. Nevertheless, a significant proportion of the patients admitted to the hospital for acute decompensated heart failure (ADHF) is discharged with unresolved congestion. Despite the fundamental role congestion plays in AHF limited data exist regarding the association between changes in weight and outcomes following a hospitalization for AHF



outcomes

Purpose: The aim of the study was to evaluate the relationship between body weight change during HF hospitalización and outcomes.
Methods: The analysis included patients admitted for acute heart failure regardless of ejection fraction enrolled in the REDINSCOR II Registry, in whom body weight was avalaible at baseline and discharge. The primary endpoint was all-cause mortality or heart failure readmission at 30- day, 6 months and 1- year.
Results: The final analysis included 1391 patients; 981 with weight loss (71.1%) and 402 with no weight loss (28,9%). The median change in body weight during hospitalization was -2,74 ± 4,9 Kg in weight loss group and 1,2 ± 4,2 kg in no weight loss group. There were no differences between groups in age, sex, cardiovascular risk factors, NT-proBNP levels , renal disfunction , left ventricular ejection fraction or in utilization of guideline-directed medical therapies. The 30 -day mortality was 4,2% in weight loss group vs 4,5% in no weight loss group (p = 0,818), the 6 month mortality was 12,1% vs 13,3% (p = 0,544) and 1 year mortality was 18,6% vs 20,3% (p = 0,479) respectively. The Kaplan Meier Curves showed that these differences were not statistically significant. There was no statistically significant association between inhospital body weight loss and 30-day, 6 month and 1 year heart failure readmission
Conclusions: Only about 70% of patients admitted for acute heart failure experience weight loss during index hospitalization. Weight loss was no associated with a better post-discharge and one year prognosis.

P1837

Impact of end-stage chronic kidney disease on short- and long-term outcomes of acute heart failure patients

A Vinikovas[1]; R Rasa Zeimaite[2]; D Verikas[3]; D Kablucko[4]; K Stasaitis[5]; A Mebazaa[6]; A Kavoliuniene[5]; J Celutkiene[4]
[1]University Hospital Santariskiu Klinikos, Vilnius, Lithuania; *[2]Vilnius University, Vilnius, Lithuania*; *[3]Lithuanian University of Health Sciences, Faculty of Medicine, Kaunas, Lithuania*; *[4]Vilnius University, Clinic of Cardiac and Vascular diseases, Center of Cardiology and Angiology, Vilnius, Lithuania*; *[5]Lithuanian University of Health Sciences, Department of Cardiology, Kaunas, Lithuania*; *[6]University Paris Diderot , U942 Inserm, Hospital Lariboisiére, Paris, France*

On behalf of: GREAT network

Introduction: Chronic kidney disease (CKD) is the most frequent comorbidity in heart failure patients. However, importance of end-stage CKD in acute heart failure (AHF) is not entirely clear.
Aim: We aimed to evaluate the impact of end stage CKD (eGFR < 30 ml/min) on mortality (M) and rehospitalization (R) rates due to cardiovascular (CVR) and non-cardiovascular reasons (NCVR) in 1, 3, and 12 months in AHF patients.
Methods: A prospective two-centre observational cohort study enrolled 726 (mean age 72 years, 43% female) AHF patients admitted to an emergency department. Data of 679 patients (those without eGFR data were excluded from the study), including patient history, follow-up data and glomerular filtration rate (eGFR) was grouped into normal eGFR group (<90 ml/min), end-stage eGFR (< 30 ml/min) and analysed using binary logistic regression, SPSS v.20. Normal eGFR group was used as a reference. Odds ratio (OR) were also adjusted to age, gender, LVEF, anemia and systolic blood pressure.
Results: 96 patients (14.1%) represented normal eGFR group, 82 (12.1%) - end-stage eGFR group, 501 patient had eGFR between 30 and 90 ml/min. The results are presented in the table below (p < 0.05 are marked with an asterisk *). End-stage renal disease increases the chance to die due to cardiovascular reasons in 3 and 12 months after discharge by 3.5 times for acute heart failure patients. The chance of being rehospitalized due to the cardiovascular reasons increases twice in the long-term period - 12 months. Adjusted OR did not show independent association.
Conclusion: Acute heart failure patients with end-stage renal disease die and are readmitted due to cardiovascular reasons more frequently in 3 and 12 months after hospitaliazation. However, no independent association could be demonstrated.

Results

	1 month	3 months	12 months			
Outcomes	OR (C.I. 95%)	Adjusted OR (C.I. 95%)	OR (C.I. 95%)	Adjusted OR (C.I. 95%)	OR (C.I. 95%)	Adjusted OR (C.I. 95%)
Readmissions due to CVR	1.223 (0.6; 2.4)	2.315 (0.5; 9.5)	1.554 (0.8; 2.9)	1.690 (0.4; 6.8)	1.909* (1.0; 3.4)	2.529 (0.6; 10.3)
Readmissions due to NCVR	1.395 (0.6; 3.1)	1.304 (0.2; 5.9)	1.580 (0.7; 3.1)	1.950 (0.4; 8.1)	0.946 (0.4; 1.9)	0.970 (0.2; 4.1)
Deaths due to CVR	1.437 (0.4; 4.8)	0.968 (0.1; 16.9)	3.429* (1.1; 10.1)	0.789 (0.1; 12.2)	3.328* (1.4; 7.7)	0.907 (0.1; 5.7)
Deaths due to NCVR	2.447 (0.5; 10.1)	0.086 (0.01; 18.2)	1.375 (0.4; 3.9)	0.681 (0.1; 5.5)	1.704 (0.6; 4.4)	0.996 (0.1; 6.1)
Composite end-point (M+R) due to CVR	1.155 (0.5; 2.2)	0.658 (0.1; 2.5)	1.326 (0.6; 2.5)	0.685 (0.1; 2.5)	1.815 (0.9; 3.3)	0.484 (0.1; 2.0)
Composite end-point (M+R) due to NCVR	1.914 (0.8; 4.3)	0.436 (0.1; 3.4)	2.012 (0.9; 4.0)	0.504 (0.1; 3.7)	1.288 (0.6; 2.5)	0.351 (0.1; 2.6)

P1838

Different characteristics and treatments of patients hospitalized to acute heart failure in the department of cardiology or medicine

C Lombardi[1]; A Roncolato[1]; A Ravera[1]; E Sciatti[1]; V Carubelli[1]; I Bonadei[1]; AI Castrini[1]; E Gorga[1]; E Vizzardi[1]; M Metra[1]
[1]University of Brescia, Cardiology, Department of Medical and Surgical Specialties, Radiological Sciences, and Public Health, Brescia, Italy

Background: pts may have a different diagnostic and therapeutic patway depending on the hospitalization department.
Purpose: analyse the different characteristics of pts admitted to the ED for AHF and to describe the differences in treatment and outcome according to the hospitalization department.
Methods: we retrospective analysed 426 pts admitted to the ED. We evaluated the characteristics and therapeutic management compared Cardiology (CD) vs Medicine (MD) departments. Results (table 1): 134 pts were admitted in CD, 276 in MD. Pts in CD were more male and younger with lower EF and higher NT-pro BNP. Previous history of MI or devices was higher in CD. More than 80% of pts had iv furosemide in both departments. Inotropes and vasodilators were more given in CD. The average duration of the hospitalization in MD was 13 days vs 11 in CD. Death for CV occurred in 7% in CD and in 5% in MD. Conclusion: The results demonstrate

different characteristics and treatment strategies between pts hospitalized for AHF Medicine or Cardiology

Table 1

Characteristics	Cardiology n = 134	Medicine n = 276	P value
Male; n = (%)	99 (73)	144 (52)	<0.001
Age; years	74±11	82±8	<0.001
Previous MI; n = (%)	59 (44)	96 (45)	0.004
PM / ICD; n = (%)	46 (34)	82 (30)	0.05
Alzheimer; n = (%)	1 (1)	17 (6)	0.01
NT-proBNP	7232±11665	6351±9345	0.03
Ejection fraction; (%)	37(12)	41(13)	0.001
Inotropic drugs n = (%)	9 (7)	7 (3)	0.03
Vasodilators n = (%)	23 (17)	13 (5)	<0.001
Nitrates; n = (%)	20 (15)	68 (25)	0.02
ACE-I n = (%)	54 (40)	83 (30)	0.15
ARBs; n = (%)	14 (10)	32 (12)	0.002
MRA n = (%)	75 (60)	65 (25)	< 0.001
B-Blockers; n = (%)	100 (75)	166 (60)	0.06
Furosemide; n = (%)	117 (87)	214 (76)	0.78
Furosemide dose (mg)	125±118	104±111	0.11
days of hospitalization (n)	11±9	13±7	0.03
CV death during hospitalization n = (%)	10 (7)	13 (5)	0.26

Comparison of patients hospitalized in Department of Cardiology and the patients admitted to Department of Medicine.

P1839

Age and gender-related differences in clinical presentations, managements, and outcomes in taiwanese patients with acute decompensated heart failure

H-Y Hung-Yu Chang[1]; M-C Fong[1]; A-N Feng[1]; Z-C Chiang[1]; C-W Hsueh[1]; W-T Lai[1]; W-H Yin[1]
[1]*Cheng-Hsin General Hospital, Taipei, Taiwan ROC*

Introduction: Data of the Taiwan Society of Cardiology-Heart Failure with reduced Ejection Fraction (TSOC-HFrEF) registry had provided insights into the characteristics and management of hospitalized decompensated systolic HF patients in Taiwan. We aimed to evaluate the age and gender-related differences in the TSOC-HFrEF registry patients.
Methods: A total of 1509 patients hospitalized for acute decompensated HFrEF were recruited in 21 hospitals in Taiwan between 2013 and 2014. Baseline characteristics, medical history, presenting symptoms, medications, and one-year outcomes were collected and analyzed. Patients were divided by age and by gender for analysis.
Results: Of the 1509 patients included in this registry, 416 (27.6%) were women, mean age 70.1 years; 1093 (72.4%) were men, mean age 61.7 years; 271 (18.0%) were older than 80 years and 300 (19.9%) were younger than 50 years. Older patients more frequently had atherosclerotic cardiovascular disease, valvular heart disease, diabetes, atrial fibrillation, chronic kidney disease, hypothyroidism, cardiac implantable electronic device compared with younger patients. Women more frequently had valvular heart disease, diabetes, cancer with history of chemotherapy, hyperthyroidism, and less frequently coronary heart disease, dilated cardiomyopathy, obstructive lung disease, or sleep apnea compared with men.
Older patients and women were unlikely to received guideline-directed medical therapy at discharge. One-year re-hospitalization rates (38.5%) were similar in both genders and age groups. One-year morality rates were higher in older patients but similar in both gender groups. Non-cardiovascular death was significantly higher in women compared with men (7.9% vs. 4.5%, p = 0.042).
Conclusion: Significant age and gender differences exist in etiology and co-morbidities. Individual factors should be considered for setting personalized and patient-centered HF management.

P1840

Acute renal failure as a predictor for in-hospital death in acute heart failure patients

LCSP Luiz Carlos Passos[1]; TM Trindade[2]; WN De Carvalho[2]; AGQ De Jesus[2]; EL Garrido[3]; NFC De Oliveira[4]; EOM Andrade[3]; YM Lira[4]; AMP De Lima[2]; VRS Souza[3]
[1]*Federal University of Bahia, Internal Medicine, Salvador, Brazil*; [2]*Ana Nery Hospital, Salvador, Brazil*; [3]*Federal University of Bahia, Faculty of Nursing, Salvador, Brazil*; [4]*Bahiana School of Medicine and Public Health, Salvador, Brazil*

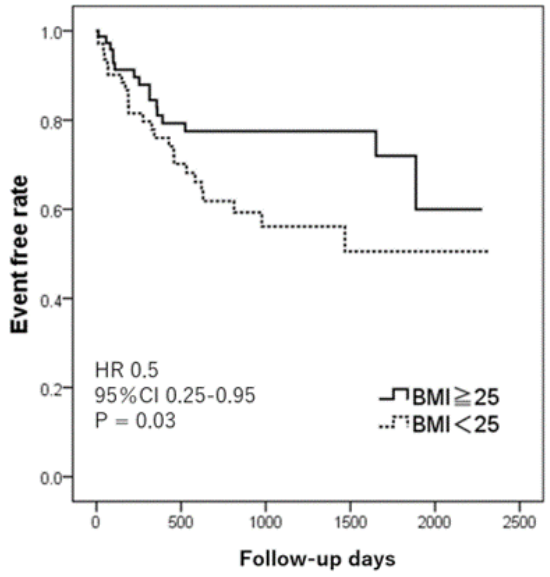
Background/Introduction: The development of acute heart failure involves complex features and worsening renal function has been reported as a factor for longterm poor prognosis. Cardiorenal syndrome has been reported as a panel in which both cardiac and renal dysfunction coexist.
Purpose: The aim of this study was to investigate if acute renal failure developed during hospital stay was a predictor for worse prognosis among acute heart failure patients.
Methods: Cohort data from 295 patients admitted in a tertiary cardiac referral centre for acute decompensated heart failure treatment between 2016 and 2017. All the data were collected from medical records. Heart failure was defined according the European Society of Cardiology guidelines.
Results: The mean of age was 55.2 years among non-acute renal failure patients and 57.4 among its acute renal failure counterparts (P = 0.3). The mean of Left Ventricular Ejection Fraction (%) (31.8% vs 30.5%) and the prevalence of previous comorbidities such as hypertension (60% vs 65%; P = 0.3), diabetes mellitus (28.3 vs 29.7; P = 0.8) and coronary artery diease (11% vs 16%; P = 0,3) showed no diferences between the groups. On the other hand, acute renal failure patients had higher incidences of infection (12% vs 38.9%; P < 0.001), hyperkalemia (30% vs 71.4%; P= < 0.001), intensive care unit admission (34 vs 61.1%; P= < 0.001) and sudden cardiac arrest, (1% vs 12.6%; P= < 0.001) during hospital stay. Moreover, acute renal faliure patients had a longer average length of hospital stay (10.5 vs 20 days; P < 0.001) and higher in-hospital lethality (8% vs 23.4%; P < 0;001). Conclusion: Acute renal failure was a predictor for worse outcomes such as intensive care unit, sudeen cardiac arrest, length of hospital stay and in-hospital lethality.

P1841

Clinical characteristics and mid-term outcomes of non-elderly obese patients with acute decompensated heart failure in Japan

M Ito[1]; H Wada[1]; K Sakakura[1]; T Ibe[1]; Y Ugata[1]; S Momomura[1]; H Fujita[1]
[1]*Jichi Medical University Saitama Medical Center, Cardiology, Saitama, Japan*

Background/Introduction: Obesity is the well-known risk factor for cardiovascular diseases including heart failure (HF). However, previous reports suggested better clinical outcomes in obese patients with HF and higher body mass index (BMI) levels of HF patients were significantly associated with younger age. The impact of obesity on clinical outcomes in non-elderly HF patients should be elucidated.
Purpose: The purpose of this study was to investigate the clinical characteristics and the mid-term outcomes of the obesity patients with HF among Japanese non-elderly population.
Methods: Consecutive 155 non-elderly acute decompensated HF patients (< 60-year-old) who admitted to our institution between 2009 and 2013 were included. Those patients were divided into the two groups according to the BMI: the obesity group (BMI = 25 kg/m2, n = 81) and the non-obesity group (BMI < 25 kg/m2, n = 74). The primary composite outcome of this study was defined as re-admission due to HF and all-cause death.
Results: The prevalence of hypertension was significantly greater in the obesity group (87.7%) than in the non-obesity group (63.5%) (P < 0.001). The levels of plasma B-type natriuretic peptide (BNP) were significantly lower in the obesity group (758.4 ± 765.8 pg/ml) than in the non-obesity group (1099.2 ± 968.0 pg/ml) (P = 0.03). The apnea-hypopnea index (AHI) was greater in the obesity group (25.5 ± 19.2 /hour) than in non-obesity group (14.0 ± 13.1 /hour) (P < 0.01). The primary composite outcome (re-admission due to HF and all-cause death) was less frequently observed in the obesity group as compared to the non-obesity group (Hazard ratio [HR] 0.50, 95% confidence interval [CI] 0.26-0.95, P = 0.03).
Conclusions: The mid-term outcomes in non-elderly HF patients with obesity were better as compared to non-elderly HF patients without obesity which supports obesity paradox in this specific population.



Kaplan-meier event-free curve

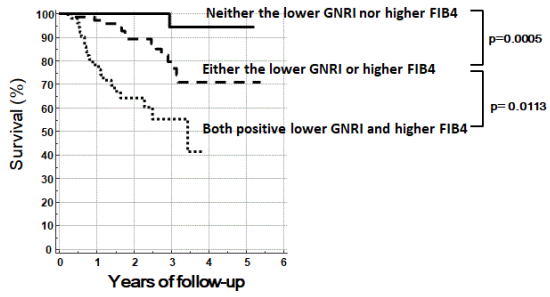
Acute Heart Failure - Diagnostic Methods

P1842

Prediction of all cause death in patients with acute decompensated heart failure using the combination of the fibrosis-4 index and geriatric nutritional risk index.

Y Sato[1]; O Nakagawa[1]; M Kumada[1]; M Tsukiyama[1]; Y Okazaki[1]; Y Koh[1]; T Iida[1]; N Fukushima[1]; A Miyaoka[1]
[1]*Toyonaka Municipal Hospital, Cardiology, Toyonaka, Japan*

Background: Malnutrition is associated with poor outcome in acute decompensated heart failure(ADHF)patients. Liver stiffness(LS), assessed by Fibrosis-4 index(FIB4), is known as indication of liver congestion in patients with HF. Aim of this study was to investigate the prognostic value of combining objective nutritional index and LS for long-term mortality prediction in ADHF patients.
Methods: We retrospectively enrolled 165 ADHF patients between 2012 and 2015. Objective nutritional indexes were evaluated by Geriatric Nutritional Risk Index(GNRI), Controlling Nutrition Status(CONUT)and prognostic nutritional index(PNI). LS was also valuated by FIB4. The primary outcome was all cause death(ACD).
Results: During a follow-up period of 2.5 ± 1.2 years ,35 patients had ACD. At multivariate Cox analysis, GNRI(p = 0.0001) and FIB4(p = 0.0012)were independently associated with ACD. Kaplan-Meier analysis revealed that patients with both positive lower GNRI (< 90: determined by ROC analysis)and higher FIB4(>2.22: determined by ROC analysis) had a significantly greater risk of ACD than those with either positive the lower GNRI or higher FIB4 (38% vs 20% p = 0.0005, adjusted HR 3.1126 [1.5092 to 6.4196]). Furthermore, patients with either positive the lower GNRI or higher FIB4 also had a significantly greater risk of ACD than those with neither positive the lower GNRI nor higher FIB4 (20% vs 2% p= 0.0113, adjusted HR 8.7554 [3.0942 to 24.7745]).
Conclusion: The combination of GNRI and FIB4 index would be useful for the prediction of ACD in HF patients.



Figure

P1843

Neutrophil gelatinase-associated lipocalin predicts long-term outcomes of worsening renal function in patients with acute heart failure

Y Horiuchi[1]; N Wettersten[1]; P Murray[2]; A Maisel[1]
[1]*University of California San Diego, Division of Cardiovascular Medicine, San Diego, United States of America*; [2]*University College Dublin, Department of Nephrology, Dublin, Ireland*

Funding Acknowledgements: Abbott Laboratories and Alere, Inc.

Background: Neutrophil gelatinase-associated lipocalin (NGAL) is a marker of renal tubular damage. Prognostic values of NGAL have not been fully elucidated in patients with acute heart failure (AHF).
Purpose: We aimed to investigate prognostic values of NGAL in relation to renal glomerular function in AHF.
Methods: We retrospectively analyzed 927 patients enrolled in the prospective, international, multicenter Acute Kidney Injury NGAL Evaluation of Symptomatic heart Fallure Study (AKINESIS). The endpoint of this analysis was a composite of death, HF hospitalization or emergent visit requiring intravenous diuretic therapy within one year. Worsening renal function (WRF) was defined as an increase in creatinine = 0.3 mg/dl or 50% of the first creatinine during the first 5 days.
Results: Sixteen patients lacking admission NGAL values were excluded leaving 911 patients for analysis. The composite endpoint occurred in 45% of patients with admission NGAL = 150 ng/dl versus 34% in those with NGAL < 150 ng/dl (p < 0.001). Patients with an NGAL < 150 ng/dl had better outcomes regardless of eGFR < or = 60 ml/min/1.73m2 (Figure 1). The composite endpoint correlated better with NGAL values than developing WRF (31% in low NGAL with WRF, 35% in low NGAL without WRF, 44% in high NGAL with WRF and 45% in high NGAL without WRF, p = 0.005, Figure 2). In multivariate Cox regression analysis, a high level of NGAL predicted one-year adverse outcomes.
Conclusions: In patients with AHF, admission NGAL has long-term prognostic utility beyond renal function and the development of WRF during hospitalization.

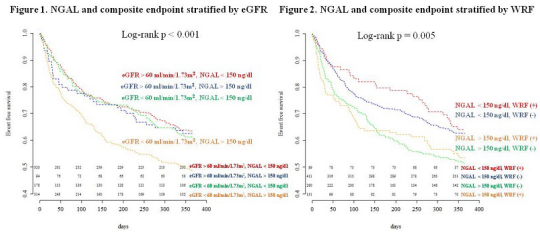


Figure 1 and 2

P1844

Serial high sensitivity cardiac troponin I measurements in acute heart failure patients

Y Horiuchi[1]; N Wettersten[1]; P Murray[2]; A Maisel[1]
[1]*University of California San Diego, Division of Cardiovascular Medicine, San Diego, United States of America*; [2]*University College Dublin, Department of Nephrology, Dublin, Ireland*

Funding Acknowledgements: Abbott Laboratories and Alere, Inc.

Background: Troponin elevation is common in acute heart failure (AHF) and is associated with worse outcomes. However, previous studies mainly used older-generation less sensitive assays and conflicting results exist, especially in terms of long-term outcomes.
Purpose: We aimed to investigate the association between serial measurements of high-sensitivity cardiac troponin I (hs-cTnI) and outcomes in AHF.

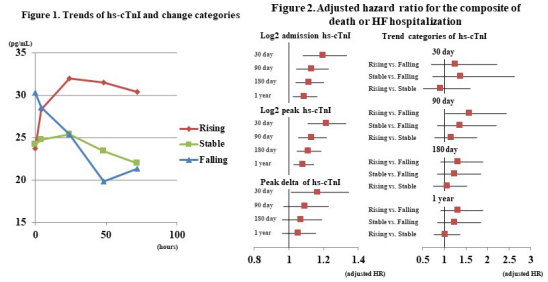


Figure 1 and 2

Method: The Acute Kidney Injury NGAL Evaluation of Symptomatic heart fallure Study (AKINESIS) was a prospective, international, multicenter study of AHF. hs-cTnI was measured at admission, 4-hours, day 1, 2, 3 and discharge. We retrospectively analyzed 849 patients for the relationships between admission, peak, peak delta and trend categories of hs-cTnI and a composite endpoint of death or HF hospitalization within 30, 90, 180 days and 1 year. Peak delta was the absolute change from log2-transformed admission to peak values of hs-cTnI. Trend categories included rising, falling and stable patterns. Rising was at least one value = 20% higher than admission hs-cTnI. Falling was at least one value = 20% lower than admission hs-cTnI with the last measured value less than admission. Stable was all values within 20% of admission value.

Results: The mean age was 68 ± 14 years, 62% were male and 47% had a history of coronary artery disease (CAD). Patients with hs-cTnI = median (25.6 pg/mL) were more likely to be male with CAD and impaired renal function. Rising, falling and stable trends occurred in 42%, 31% and 25% of patients, respectively (Figure 1). Higher admission and peak hs-cTnI were associated with worse short and long-term outcomes independent of confounding factors, although their risk ratios declined at long-term follow-up (Figure 2). Similar findings were observed with peak delta and trend categories, which were not statistically significant at long-term follow-up.

Conclusion: Higher admission and peak hs-cTnI were associated with short- and long-term worse outcomes. Changes of hs-cTnI may have short-term prognostic implications.

P1845 Prolonged QTc interval in ECG predicts long-term mortality in ICU patients

T Javanainen[1]; R Cinotti[1]; K Cerlinskaite[1]; S Ishihara[1]; E Akiyama[1]; N Vodovar[1]; E Gayat[1]; A Mebazaa[1]

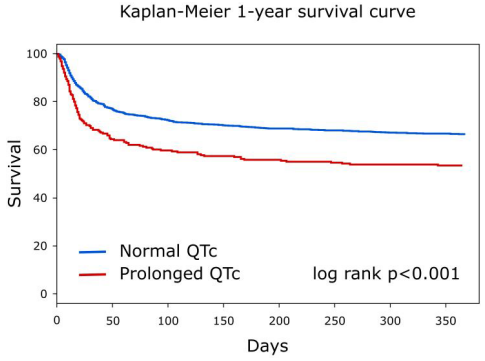
[1]*Hospital Lariboisiere, Inserm UMR-S 942 and Anesthesia and Critical Care Department, Paris, France*

Background: Prolonged QTc interval in ECG is a common finding in Intensive Care Unit (ICU). It has been associated with higher mortality in population based studies, but there is little information about the association with long-term mortality in critically ill patients.

Table

	Normal QTc (n = 1176)	Prolonged QTc (n = 421)	p-values
Age, years (SD)	59 (17)	63 (15)	<0.001
Male gender, n (%)	700 (60)	312 (74)	<0.001
Charlson Comorbidity index, n (%)	2.9 (2.3)	3.5 (2.4)	<0.001
SAPS II, n (%)	48 (19)	52 (19)	0.003
Cardiogenic shock, n (%)	63 (5)	34 (8)	0.059
Acute cardiac arrest, n (%)	80 (7)	52 (12)	0.001
Amiodarone treatment, n (%)	196 (17)	121 (29)	<0.001
Neuroleptic administration, n (%)	133 (11)	40 (10)	0.351
hs-TnI, ng/L (IQR)	30 (7-199)	60 (16-340)	<0.001

Baseline characteristics.



Figure

Purpose: The aim was to investigate the association between prolonged QTc and long-term prognosis in ICU patients.

Methods: FROG-ICU (NCT 01367093) is a prospective, observational study conducted in 21 ICUs in 14 European hospitals. In this sub-study, patients with at least one ECG available during the first 3 days after ICU admission were included. QT was measured digitally on standard 12-lead ECG, and it was corrected with Bazett's formula. Prolonged QTc was defined as QTc = 450ms in male and QTc = 460ms in female patients. For 1-year mortality analysis, adjusted cox model was formed including Simplified Acute Physiology Score II (SAPS II), Charlson Comorbidity Index, gender, amiodarone treatment, hs-TnI at inclusion and acute cardiac arrest or cardiogenic shock as cause for ICU admission.

Results: Of the 2087 FROG-ICU patients, 1597 (77%) were included in this study. 421 (26%) patients displayed with prolonged QTc. These patients were older (63 (± 15) vs. 59 years (± 17), p < 0.001), more often male (312 (74%) vs. 700 (60%), p < 0.001) and had more comorbidities. Amiodarone administration and acute cardiac arrest as cause for ICU admission were more common in prolonged QTc patients (Table) and hs-TnI was higher (60 ng/l (16-340) vs. 30 ng/l (7-199), p < 0.001). 1-year mortality was higher in patients with prolonged QTc (182 (43%) vs. 373 (32%), p < 0.001, Figure). In adjusted mortality analysis, prolonged QTc remained predictor of 1-year mortality (HR 1.29-IC95% (1.08-1.55), p = 0.006).

Conclusions:

Prolonged QTc during the first 3 days after ICU admission is a marker of long-term mortality in ICU patients.

P1846 Multiple soluble neprilysin concentration testing and its prognostic value in patients with at least moderate functional mitral regurgitation and hospitalized for acute decompensated heart failure.

K Kamil Janikowski[1]; A Sakowicz[2]; T Pietrucha[2]; M Lelonek[1]

[1]*Medical University of Lodz, Department of Noninvasive Cardiology, Lodz, Poland*; [2]*Medical University of Lodz, Department of Medical Biotechnology, Lodz, Poland*

Funding Acknowledgements: The study was carried due to research funding young scientists and doctoral students of the Faculty of Medicine of Medical University of Lodz

Background: The prognosis of patients (pts) hospitalized due to acute decompensated heart failure (ADHF) is still poor. One of the independent factors that worsen the prognosis of ADHF population is functional mitral regurgitation (FMR), regardless of the left ventricular ejection fraction (LVEF). The predictive value of soluble neprilysin concentration (sNEP) is unclear in this population.

Purpose: Evaluation of the prognostic value of sNEP in pts hospitalized for ADHF, related to FMR, in 6-month follow-up.

Methods: In a single-centre, prospective, non-interventional study we analyzed 55 pts hospitalized for ADHF (73% male, mean age 72 ± 12 yrs, median LVEF: 30% and ischemic etiology in 44%). All of them were referred due to exacerbation to III-IV NYHA class of previously confirmed chronic heart failure with peripherial oedema and required administration of intravenous diuretics. During hospitalization blood samples were collected at three time points: on admission, in the second day and at discharge. The population was divided into 2 groups related to FMR:

- with at least moderate FMR (30 pts, 73% men, mean age 73 ± 11 yrs, median LVEF: 30%, 53% of ischemic etiology, 55% of HFrEF);
- and non-FMR group (25 pts, 33% men, mean age 71 ± 12 yrs, median LVEF: 30%, 32% of ischemic etiology).

FMR was diagnosed based on transthoracic and/or transesophageal echocardiography and 2017 ACC expert consensus concerning management of mitral regurgitation. All FMR pts were disqualified by the Heart Team from invasive treatment of FMR. During 6-month follow-up all pts were treated with OMT for the heart failure.

Telephone calls concerning HF hospitalizations (HFh) and/or death were conducted 7 days, 1 month, 3 (3M) and 6 months (6M) after discharge.
Results: Of all 36% (n = 19) pts were rehospitalized for HF and 12 pts died (2 during the initial hospitalization) within 6M observation.
FMR subpopulation: HFh concerned 39% (n = 11) in 3M and 43% (n = 12) of pts in 6M. After 3M and 6M the mortality rate was 18% (n = 5) and 25% (n = 9), respectively. ROC-analysis showed the best significant predictive value of sNEP on admission for HFh in two time points - 3M and 6M (in both cases: AUC>0.7, p < 0.05). There were no significant predictive values for the results performed in the second day of hospitalization and at discharge.
non-FMR subpopulation: HFh were observed in 20% pts (n = 5) during 3M and in 28% (n = 7) during 6M. No one died in 3M and 3 pts died in 6M. ROC analysis revealed that sNEP results for HFh in 3M were statistically significant only at discharge (AUC>0.7, p < 0.05). sNEP peak results demonstrated a significant predictive value only for HFh during 6M (AUC>0.7, p < 0.05).
In each analysis NT-proBNP revealed no significant predictive value.
Conclusions: In the studied population hospitalized for ADHF, in contrast to NT-proBNP, sNEP has a good predictive power for HF hospitalizations, it seems that better for FMR pts than for non-FMR ones.

P1847
Higher natriuretic peptide levels is associated with higher hs-cTnT, CA-125, hsCRP and lower eGFR, hemoglobin and sodium levels in patients with acute decompensated heart failure

Y Yuksel Cavusoglu[1]; ME Altinbas[1]; S Eraslan[1]
[1]*Eskisehir Osmangazi University, Eskisehir, Turkey*

Purpose: Plasma levels of natriuretic peptide have been shown to correlate with clinical and hemodynamic parameters in heart failure (HF), and referred as a potent predictor of poor prognosis. A variety of clinical parameters such as cardiac troponin, high sensitive C-reactive protein (hsCRP), hemoglobin or sodium levels are also known to be of prognostic significance in patients with HF. The aim of this study was to assess possible associations between natriuretic peptide levels and other well-established clinical markers in patients with HF.
Methods: A total 446 patients admitted to hospital with the diagnosis of acute decompensated HF, NYHA II-IV, LVEF < 40% and >18 years of age were included in this study. N-terminal pro B-type natriuretic peptide (NT-proBNP), high sensitive cardiac troponin T (hs-cTnT), carbohydrate antigen 125 (CA-125), hsCRP, estimated glomerular filtration rate (eGFR), hemoglobin and sodium levels have been analyzed for the assessment of possible correlations and associations.
Results: Mean age of study population was 67 ± 12 years. Mean EF was 25.4 ± 7.9%, NT-proBNP was 7667 ± 9876 pg/mL, CA-125 was 86.2 ± 125.5 U/mL, hs-cTnT was 0.22 ± 0.86 ng/mL, creatinine level was 1.41 ± 0.88 mg/dL, eGFR was 62.9 ± 32.4 mL/min/1.73 m2, hsCRP was 27.4 ± 39.1 mg/dL, sodium was 138.2 ± 4.7 mEq/L and hemoglobin level was 12.4 ± 2 gr/dL. There were a significant positive correlation between NTproBNP and hs-cTnT levels (r=,252, p < 0.001), CA-125 levels (r=,303, p < 0.001), or hsCRP levels (r=,261, p < 0.001). Also significant negative correlations were found between NTproBNP and eGFR levels (r=-,451, p < 0.001), hemoglobin levels (r=-,453, p < 0.001) or sodium levels (r=-,219, p < 0.001). Furthermore, median NTproBNP levels were found to be significantly higher in patients with high hs-cTnT (<0.014 ng/mL) as compared to those with normal hs-cTnT levels (4531 [1716-12047] pg/mL vs 651 [327-1768] pg/mL, p < 0.001, respectively), in patients with anemia as compared to those without anemia (6594 [2535-19250] pg/mL vs 1740 [581-4397] pg/mL, p < 0.001, respectively), in patients with hyponatremia (sodium < 135 mEq/L) as compared to those with normonatremia (6779 [2650-19513] pg/mL vs 2986 [976-7966] pg/mL, p < 0.001, respectively), in patients with high hsCRP (<3.5 mg/dL) as compared to those with normal hsCRP levels (3800 [1254-11250] pg/mL vs 1841 [588-3732] pg/mL, p < 0.001, respectively), and as expected, significantly higher in patients with an eGFR < 60 mL/min/1.73 m2 as compared to those with an eGFR >60 mL/min/1.73 m2 (6654 [2723-15898] pg/mL vs 1482 [554-3665] pg/mL, p < 0.001, respectively).
Conclusions: The results of this study showed that in decompensated HF patients, higher NTproBNP level as a marker of nörohormonal activation is associated and correlated with higher hs-cTnT, CA-125, hsCRP levels and lower eGFR, hemoglobin and sodium levels.

P1848
Soluble ST2 Levels Predicts Length of Stay in Patients with Acute Heart Failure

H Gunes[1]; H Kaya[2]; E Aksu[1]; H Nacar[1]; M Kerkutluoglu[1]; MA Tatlisu[3]
[1]*Kahramanmaras Sutcu Imam University, Kahramanmaras, Turkey*; [2]*Cumhuriyet University, Cardiology, Sivas, Turkey*; [3]*Numune Hospital, Cardiology, Sivas, Turkey*

Introduction: The increased length of stay of patients with acute heart failure increases costs and morbidity. The association of ST2 levels with mortality and morbidity in patients with heart failure has been established.

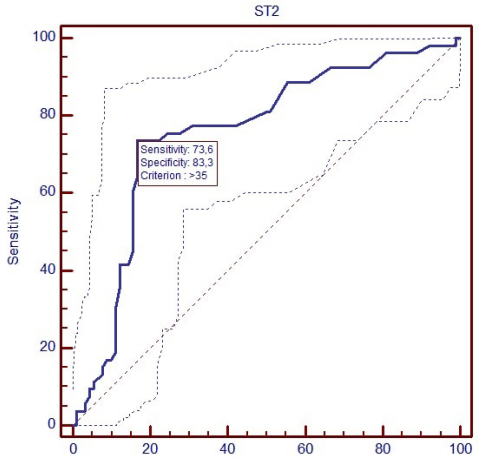


Figure 1
Purpose: We aimed to investigated the relationship between ST2 levels in patients with acute decompensated heart failure and the length of stay.
Methods: This study included 143 patients who were hospitalized for acute decompensated heart failure. The average length of stay was 4 days. Patients were divided into 2 groups: group 1 consisted of patients who stayed 4 days or less; group 2 consisted of patients who stayed more than 4 days.
Results: The serum ST2 levels were greater in the group 2 as compared to the group 1 (32 (3-68) versus 47 (9-298)) (P < 0.001). The optimal cutoff level of ST2 in the prediction of length of stay was >39 U/mL, with a specificity of 95.8% and a sensitivity of 96% (area under the curve, 0.979; 95% confidence interval [CI], 0.953-0.992). In the multivariate logistic regression model, ST2 levels of >35 U/mL on admission (OR = 10.750, 95% CI: 4.218-27.395 , p < 0.001), were also associated with a longer length of stay after adjustment for variables was found to be statistically significant in univariate analysis and correlated with ST2 levels.
Conclusion: In our study, the ST2 levels were found to be an independent marker for the length of stay in patients with acute decompensated heart failure.

P1849
Heart rate reduction and galectin 3 levels in patients with decompensated heart failure

D Darabantiu[1]; R Lala[1]; A Pop Moldovan[1]; L Pilat[1]; RM Christodorescu[2]
[1]*Vasile Goldis Western University, Arad, Romania*; [2]*University of Medicine & Pharmacy Victor Babes, Timisoara, Romania*

Premises and Purpose: In patients with heart failure and low ejection fraction heart rate and galectin 3 levels have an important prognostic value. The objective of this study was to assess the influence of heart rate reduction with ivabradine on galectin 3 levels in patients with decompensated systolic heart failure.
Material and Methods: This prospective study included 35 consecutive patients (P) (28 males, 7 females) (group 1), with LV systolic dysfunction (LVEF < 40%), hospitalized for heart failure decompensation, in whom heart rate reduction therapy with ivabradine was initiated. The control group (group 2), consisted of 29 hospitalized heart failure patients (18 males, 11 females) treated with guideline-recommended therapy but without ivabradine. At baseline and after 6 months of follow-up clinical and echocardiographic parameters (systolic and diastolic function) were collected. Also, both at baseline and after 6 months, galectin-3 levels were determined (Novus Biologicals assay-ELISA method). Data were expressed as mean ± standard deviation or percentages, comparisons between baseline and follow-up data were done with Student's paired t test, differences between groups with Fisher's exact test.
Results: Mean age was 60 ± 12 years in group 1 and 69 ± 10 years in group 2 , heart failure etiology was ischemic in 19 group 1 P (54 %) vs 16 group 2 P (55%). Diastolic function improved in group 1, E/e' ratio decreased significantly in group 1 (from 14.7 ± 5 to 11 ± 4) and remained stable in group 2 (11.5 ± 3 to 11.6 ± 4), while e' velocity increased in group 1 (from 5.5 ± 1.7 to 7.2 ± 1.6) and did not change in group 2 (from 7.3 ± 1.6 to 6.8 ± 1.3). At baseline left ventricular ejection fraction was 26 ± 8% in group 1 and 34 ± 10% in group 2, while after 6 months it increased in group 1 (31 ± 8%) and remained stable in group 2 (34 ± 9%). At 6 months as compared to baseline heart rate decreased from 96 ± 12 b/min to 72 ± 13 b/min

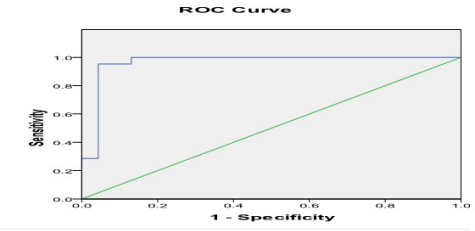
in group 1 and from 91 ± 20 b/min to 76 ± 26 b/min in group 2 ($p < 0.001$ for both differences). Betablocker therapy was given in 94% of group 1 P and 96% of group 2 P, and there were no differences regarding to ACE-inhibitor/ARB or spironolactone administration between the 2 groups. In group 1 galectin 3 levels changed nonsignificantly after 6 months (from 9.7 ± 7 ng/ml to 10.8 ± 3 ng/ml) ($p = 0.3$), and increased significantly in group 2 (from 8.5 ± 6 ng/ml to 11 ± 3 ng/ml) ($p = 0.03$). A decrease in galectin-3 level was observed in 11 P from group 1 (31%) and 8 P from group 2 (27%), while an increase more than 100% from baseline level was noted in 12 P from group 1 (34%) and 12 P from group 2 (41%).
Conclusions: In patients with systolic heart failure heart rate reduction with ivabradine does not decrease significantly galectin 3 levels at 6 months despite an improvement in systolic and diastolic LV function.

P1850

What is the importance of serum free testosterone in prediction of heart failure in patients with acute myocardial infarction?

M Mohammad El Tahlawi[1]; A Al Alfi[1]; M Alzaki[1]; M Aboueleinein[1]
[1]*Zagazig University Hospitals, Cardiology, Zagazig, Egypt*

Background: Testosterone is a potent coronary vasodilator; an effect mediated by a calcium channel antagonist action
The pro-fibrinolytic activity of testosterone was noted and confirmed by several subsequent studies.
The serum testosterone levels were found to be decreased significantly In early hours of MI.
Aim of work: This study is conducted to find out if serum testosterone can help in prediction of heart failurein patients with myocardial infarction.
Patients & Methods: This is an observational prospective case control study.
Inclusion criteria:
Male patients presenting with ST elevation myocardial infarction.
Presentation during the first 24 hours of onset of the chest pain.
Exclusion criteria:
Female patients.
Patients with non S-T segment elevation myocardial infarction
Patients on renal dialysis as serum testosterone levels flactuating before, during and after dialysis.
Patients with previous history of CABG.
Patients on anti-androgenic agents for prostrate and testicular cancer.
Patients on prolonged use of anabolic steroids.
Patients not willing for informed consent.
The included patients were subjected to:
Detailed history taking.
Thorough physical examination.
12 leasds ECG.
Measuring Serum free testosterone (between 6-9 AM) next to admission).
Echocardiography.
Assessment of patients' height & weight to calculate their BMI.
The studied patients have been divided into two groups (based on their ejection fraction):
Group I: this group included patients with ejection fraction (EF) < 50%.
Group II: this group included patients with ejection fraction = 50%.
Statistical analysis:
Data from the patients was collected and subjected to statistical analysis using test of significance.
Results: The studied included 44 patients with 21 patients in group I and 23 patients in group II.
There was high significant difference between both groups regarding testosterone level (10.58 ± 4.82 vs. 24.62 ± 4.51 " P value= 0.001").
There was significant positive correlation between testosterone level and EF with P value = 0.001.
With ROC curve data of free testosterone level in this study, the optimal cutoff of free testosterone level was 17.6. Area under the curve is 0.965, the sensitivity is 95.2% and the specificity is 95.7%.
Conclusion: free testosterone is considered a good predictor biomarker of heart failure after ST elevation myocardial infarction.



ROC curve of free testosterone level

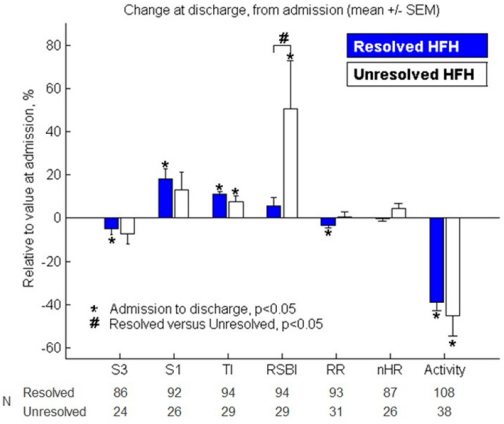
P1851

Readmissions or death are more likely when device-derived rapid shallow breathing index worsens during heart failure hospitalization

J Lindenfeld[1]; RS Gardner[2]; V Averina[3]; P Thakur[3]; Q An[3]; J Boehmer[4]
[1]*Vanderbilt University, Nashville, United States of America*; [2]*Golden Jubilee National Hospital, Clydebank, United Kingdom*; [3]*Boston Scientific, St. Paul, United States of America*; [4]*Penn State Hershey Medical Center, Hershey, United States of America*

Funding Acknowledgements: Boston Scientific

Background: A multisensor algorithm has been demonstrated to predict heart failure (HF) events in patients with implanted devices with high sensitivity and low false positive rate. However, it is not known how the individual sensors change from hospital admission to discharge and whether it can be indicative of readmissions or death within 30 days.
Methods: The MultiSENSE study followed 900 HF patients with CRT-D for up to 1 year. Devices were modified to enable the collection of first (S1) and third (S3) heart sounds, thoracic impedance (TI), respiratory rate (RR), rapid shallow breathing index (RSBI), night heart rate (nHR), and activity. All hospitalizations were adjudicated by an independent committee. Hospitalizations with HF as a primary cause (HFH) were identified. HFH with an admission outside of the customized data collection were excluded due to lack of sensor data. Each HFH was classified as unresolved if it was followed by all-cause hospitalization or death within 30 days of discharge; otherwise, it was classified as resolved. For each type of HFH, daily sensor values on the day before admission and the day before discharge were compared with a pairwise t-test. The changes in each sensor were compared between the resolved and the unresolved group via t-test. Significant difference in comparisons was defined as that with $p < 0.05$.
Results: Out of 149 HFHs, 109 were determined as resolved and 40 as unresolved. Additional HFHs were excluded if sensor data at admission or discharge was not available. Admission-to-discharge differences for resolved HFHs showed improvement in S3, S1, TI, and RR, and reduction in activity (see Figure). Admission-to-discharge differences for unresolved HFHs showed improvement in TI, worsening in RSBI, and reduction in activity. Changes in RSBI were significantly different between the two groups of HFHs.
Conclusions: Worsening in RSBI during hospitalization identified a group of patients with either early HF readmissions or death.



P1852

Echocardiographic predictors of early in-hospital heart failure during first ST segment elevation myocardial infarction

KM Elmaghraby[1]; H Shamseddin[1]; YT Kishk[1]; MM Reda Abdel Aziz[1]
[1]*Assiut University, Cardiology department, Assiut, Egypt*

Introduction: Acute heart failure complicates acute myocardial infarction as a result of complex interaction of structural, hemodynamic, neurohormonal, and genetic mal-adaptations. Left ventricular systolic function has been extensively studied in relation to development of HF, however left ventriuclar diastolic function contributes to symptoms and signs of clinical HF.

Purpose: To analyze the role of left atrial volume index (LAVI) compared to other conventional parameters of systolic and diastolic left ventricular function in patients with first time STEMI, in predicting in-hospital heart failure & mortality and development of HF and mortality over a follow up period of 6 months.

Methods: The present study is a prospective observational study done on 70 STEMI patients. Left ventricular EF, LV wall dimensions, left atrial volume (LAV), left atrial volume index (LAVI), Pulsed Doppler mitral flow velocity (E, A, E/A ratio, and deceleration time of early filling (DT), E/e' ratio and systolic parameters were measured within 24 hours after admission and then 6 months later. These variables were correlated with development of in hospital heart failure according to Killip classification and 6 months later by NYHA classification.

Results: 23 patients developed in hospital HF with Killip class>II, 20 of them being in class III (28.6%) and 3(4%) patients in class IV. A total of 4 patients died during admission (in-hospital mortality 5.7%). On follow up 6 months later, further seven patients died (10%) due to cardiac causes and twenty patients were readmitted either due to development of heart failure or new ischemic insult. Estimated LAV (mean ± SD) on admission was 47.7 ± 13.4, 60.8 ± 25.4, 77.9 ± 16.4 &78.2 ± 13.4 ml in patients with Killip class I, II, III & IV respectively (P.value0.000). LAVI (mean ± SD) on admission was 24.6 ± 7.3, 26.9 ± 10.3, 36.2 ± 3.9&38.9 ± 4.9 ml/m2 in patients with killip class I, II, III & IV respectively (P.value 0.000). Also DT decreased significantly from 209.3 ± 25.7 in Killip class I to 166.7 ± 23.1 in killip class IV patients (P.value0.000). E/e'increased significantly from 7.9 ± 2 in killip class I to 14.9 ± 4.5 in killip class IV patients (P.value0.000). LAVI (mean ± SD) in inhospital mortality cases was 37.9 ± 1.9 versus 28.4 ± 8.8 ml/m2 in survivors (P.value0.000) & it was 38 ± 3 in the follow up mortality cases versus 27.1 ± 8.4 ml/m2 in survivor follow up cases (P.value 0.000). On 6 months follow up measured LAVI was 24.44 ± 7.78, 28.61 ± 8.18 & 34.35 ± 6.49 ml/m2 in NYHA class I, II & III patients respectively (P.value0.001) .

Conclusions: LAVI and other determinants of systolic and diastolic functions have significant role in prediction of heart failure and mortality both in the in-hospital setting and after a follow up period of 6 months.LAVI, E/e'ratio & EF are the most significant predictors of in hospital heart failure. LAVI and E/e' were the most powerful predictors of mortality and heart failure during a follow up period of 6 months.

P1853

Value of natriuretic peptides and tissue doppler imaging in the estimation of intracardiac filling pressure in patients with cardiac amyloidosis

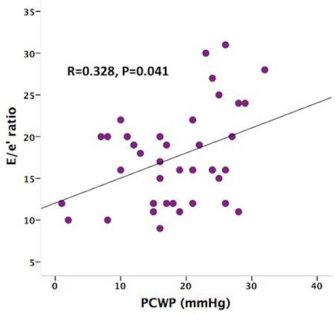
S Stephanie Brun[1]; E Cariou[1]; P Fournier[1]; D Ribes[1]; S Faguer[1]; D Carrie[1]; M Galinier[1]; O Lairez[1]
[1]*Toulouse Rangueil University Hospital (CHU), 31, Toulouse, France*

Background: - Estimation of ventricular filling pressures (VFP) is a determining factor in the follow-up of patients with cardiac amyloidosis (CA). Low VFP can lead to decreased cardiac output and symptoms of fatigue, with signs of hypotension and hypoperfusion. High VFP lead to shortness of breath and cardiac decompensation. Natriuretic peptides (NPs) and tissue Doppler imaging are daily used to monitor VFP in patients with CA. The aim of this study was to evaluate the value of NPs and Doppler parameters in estimating left VFP in patients with CA.

Methods: - Forty-six patients with biopsy verified light chain (29), AA (1), Apoliporotein A2 (1) or bone scintigraphy proven transthyretin (15) CA were retrospectively included. All patients underwent transthoracic echocardiography, BNP (20) or NT-proBNP (26) measurement and right heart catheterization (RHC).

Results - Median BNP and NT-proBNP levels were 786 [from 37 to 3798] and 3796 [from 1178 to 49402] ng/L, respectively. Echocardiography demonstrated left atrial enlargement with a mean volume of 44 ± 14 mL and low tissue Doppler lateral e' of 5 ± 1 cm.s-1. Median E/e' ratio was 18 ± 8 and pulmonary capillary wedge pressure (PCWP) by RHC was 18 ± 7 mmHg. There was no correlation between BNP (R = 0.308, P = 0187) or NT-proBNP (R=-0.095, P = 0.646) levels and PCWP. There was a slight correlation between E/e' ratio and PCWP (R = 0.341, P = 0.041; Figure).

Conclusion: In patients with CA, NPs do not accurately estimate PCWP. Tissue Doppler– derived mitral E/e' ratio is correlated with PCWP but the slight correlation requires to consider it carefully and to integrate others parameters to estimate intracardiac filling pressures.



P1854

Semi-automated detection of pulmonary congestion in patients with non-ST acute coronary syndrome by using of quantitative chest cardiac-CT analysis: analysis of methodological aspects

A Andreas Fabricius-Bjerre[1]; J Petersen[2]; M Heitmann[1]; H Elming[3]; H Ashraf[4]; KF Kofoed[5]; JT Kuhl[5]; L Kober[5]; OW Nielsen[1]
[1]*Bispebjerg University Hospital, Copenhagen, Denmark*; [2]*University of Copenhagen, Department of Computer Science , Copenhagen, Denmark*; [3]*University Hospital, Roskilde, Denmark*; [4]*Akershus University Hospital, Oslo, Norway*; [5]*Rigshospitalet - Copenhagen University Hospital, Copenhagen, Denmark*

Background: Quantitative assessment of pulmonary water content based on cardiac-CT could add objective information about pulmonary congestion to an already accurate method of diagnosing coronary artery disease. However, methodological problems related to semi-automated software, CT settings, and contrast enhancement remains to be examined.

Purpose: The objective was to identify the best imaging-biomarkers of pulmonary congestion, and to analyze the impact of various methodological effect modifiers.

Method: We identified patients with and without heart failure from a retrospective database with non-ST acute coronary syndrome patients who underwent cardiac-CT prior to invasive treatment. We defined HF cases as patients with Killip class > 1 and loop diuretic administered. Controls subjects had Killip class = 1, no loop diuretic administered, matched cases in regards to sex, age and smoking history.

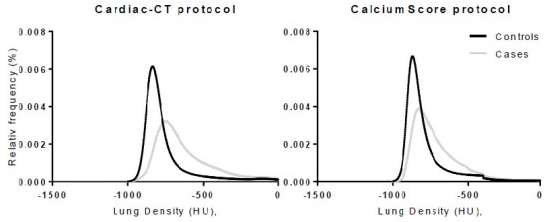
From the contrast based cardiac-CT protocol and the non-contrast calciumscore protocol the scans were reconstructed with full view in 0.5, 1 and 3 mm slice thickness using standard medium soft and hard kernel. We used in-house developed software to segment the lungs and extract the relative attenuation distribution histograms of from cases and control.

Results: 40 patients were included (10 cases, 30 controls). Manual and automated segmentation agreed perfectly (mean diff; 12ml, limits of agreement; -67ml to 89 ml). The attenuation distribution (in Hounsfield Units) for cases was skewed more to the right and flatter than for control subjects (see table). Slice thickness or softer reconstruction kernel did not significantly influence the segmented lung volume or the median lung density.

Conclusion: All the mathematical parameters of the histogram discriminated cases and control subjects, but the median was numerically best. The methods works in both cardiac-CT and calciumscore protocols and are robust to changes in voxel size and reconstruction kernel. Based on these result we propose this method is being further investigated in consecutive patients with all degrees of pulmonary congestion.

	Cardiac-CT Protocol	Calcium-score Protocol								
	Control	Cases	p	t-score	AUC	Control	Cases	p	t-score	AUC
Mean	-753 (20)	-647 (44)	<0.001	-11,50	1.00 (1.00 to 1.00)	-802 (31)	-705 (57)	<0.001	-7.76	0.95 (0.88 to 1.00)
Median	-807 (18)	-678 (43)	<0.001	-11,91	1.00 (1.00 to 1.00)	-837 (28)	-733 (56)	<0.001	-7.98	0.96 (0.89 to 1.00)
Kurtosis	8.8 (1.5)	4.4 (1.3)	<0.001	10,05	0.99 (0.96 to 1.00)	11.2 (3.0)	6.2 (1.9)	<0.001	6,46	0.89 (0.78 to 0.94)
Skew-ness	2.4 (0.3)	1.3 (0.4)	<0.001	8,17	0.98 (0.98 to 1.00)	2.6 (0.4)	1.2 (3.0)	<0.001	7.35	0.93 (0.85 to 0.96)

Mathematical parameters of the histogram in cases and control in the Cardaic-CT and Calciumscore protocol



Average lung density histogram from cases and controls in the Cardiac-CT and Calciumscore protocol

P1855

Department of Cardiology

K Kristina Miger[1]; A Fabricius-Bjerre[1]; C Maschmann[2]; J Wamberg[2]; MM Winkler Wille[3]; A Geilager Abild-Nielsen[3]; L Pedersen[4]; HH Lawaetz Schultz[4]; J Damm Nybing[3]; B Nybo[2]; O Wendelboe Nielsen[1]

[1]Bispebjerg University Hospital, Department of Cardiolgy, Copenhagen, Denmark; *[2]Bispebjerg University Hospital, Department of Emergency Medicine, Copenhagen, Denmark*; *[3]Bispebjerg University Hospital, Department of Radiology, Copenhagen, Denmark*; *[4]Bispebjerg University Hospital, Department of Respiratory Medicine, Copenhagen, Denmark*

Background/Introduction: Lung ultrasound (LUS) has been proposed as a point-of-care examination where B-lines are markers of pulmonary congestion. Most previous studies examined patients with existing signs of heart failure (HF), but there is lack of studies to examine its diagnostic value in unselected consecutive patients with dyspnoea and comorbidity.

Purpose: To examine the diagnostic value of B-Lines by LUS to a final diagnosis of acute HF (AHF) and the association to other signs of congestion by lung auscultation, and chest X-ray (CXR).

Methods: We included patients with acute dyspnoea admitted to Bispebjerg Hospital EDs over a 3 month-period. Inclusion criteria were all adults (<50 years) with acute dyspnoea (sudden onset or worsening of chronic dyspnoea within 14 days). We excluded patients who were respiratory unstable (a need for mechanic/non-mechanic ventilation), circulatory unstable (need inotropes), acute coronary syndrome, life expectancy < 3 months, not able to give consent. CT-examinations were only available daytime, why patients admitted 15 pm-02 am were excluded.

All patients were examined with physical examination, CXR, LUS, low-dose CT and echocardiography (Echo) within 12 hours of admittance. The maximum time between LUS, CT and Echo was 5 hours. A 14 zone LUS protocol with a cardiac probe and 18-20 cm of depth was used. Congestion on LUS was defined as at least one zone on each lung with 3 or more B-lines (vertical lines extending the whole field of view). AHF was defined as abnormal echocardiography (HfpEF, HfmrEF, HFrEF, tachyarythmia or severe valve disease) combined with increased left ventricular filling pressure on Echo-doppler and pulmonary congestion on CT.

Results: 40 consecutive patients were examined on January 2018, 22 females and 18 males, with a mean age of 74 years for females and 78 years for males. One third (37,5%) had chronic heart failure, 70% were active/past smokers, 25% had diabetes, 45% had copd, 5% had kidney disease, 20% had atrial fibrillation and 27,5% IHD.

Abnormal echo was found in 16 patients, while 10 patients had AHF (25%) and just 6 patients (15%) had a positive LUS for congestion (see Table). Congestion on LUS was significantly associated with AHF with a specificity of 93% and a sensitivity of 40 %, but it was not significantly associated to congestion on CXR or lung auscultation. Pleural effusion on LUS measured against CT was significant with a 98% specificity and a 77% sensitivity.

Conclusion: Our preliminary results suggest that bilateral B-Lines on LUS has a high specificity for pulmonary congestion and pleural effusion in consecutive breathless patients in the ED. But the sensitivity for cardiac abnormality and AHF seem low in these consecutive patents, meaning that absence of bilateral B-lines cannot rule out cardiac dysfunction or AHF. However, a firm conclusion must await larger studies, and updated data will be presented during the congress.

Comparisons of B-lines on lung ultrasound with other modalities in 40 patients										
		Acute HF		Congestion CXR		Rales on Ausc		Echo abnormal		
		No	Yes	No	Yes	No	Yes	No	Yes	
	Total	30	10	35	5	22	18	24	16	total
Congestion on LUS	No	28	6	31	3	20	14	22	12	34
	Yes	2	4	4	2	2	4	2	4	6
Chi2 p-value			0,011		0,094		0,247		0,148	
Sensitivity			40%		40%		22%		25%	
Specificity			93%		89%		91%		92%	

P1856

Association of impaired strain and development of in-hospital heart failure after acute myocardial infarction

S Torres[1]; PM Araujo[1]; A Nunes[1]; C Sousa[1]; PB Almeida[1]; V Ribeiro[1]; R Almeida[1]; J Rodrigues[1]; S Costa[1]; G Ferreira[1]; S Maia[1]; MB Campelo[1]; F Macedo[1]; MJ Maciel[1]

[1]Sao Joao Hospital, Porto, Portugal

Introduction: Strain imaging by speckle tracking echocardiography (STE) has been shown to provide important information on regional and global ventricular function and is therefore a helpful tool in risk assessment of patients with acute myocardial infarction (AMI).

Purpose: Since Killip classification is a powerful predictor of prognosis in AMI, we aimed to assess its relationship with myocardial strain imaging parameters.

Methods: We retrospectively evaluated patients (pts) who were admitted to our center due to AMI during a six-month period and who had strain evaluation done by two-dimensional (2D) speckle tracking echocardiography (STE). Global longitudinal strain and global circumferential strain of the left ventricle (LV) were assessed by 2D STE with layer-specific myocardial deformation quantitative analysis. Clinical, laboratorial and coronary anatomy data were also evaluated.

Results: A total of 76 pts, of whom 75% (n = 57) were male, with a mean age of 63.4 ± 12.0 years were included. The diagnosis was STEMI in 52.6% (n = 40) and NSTEMI in 47.4 % (n = 36). All pts were submitted to coronariography: 7.9% had left main significant disease, 40.8% had one-vessel disease, 27,6% had two-vessel disease, 17.1% had three-vessel disease and 6.6% had no significant coronary disease. In-hospital heart failure (HF) was defined by Killip class > I, thus dividing pts in two groups: group A [Killip I (KI); n = 50; 65.8%] vs group B [Killip >I (K>I); n = 26; 34.2%]. Pts in group B had significantly lower endocardial (-12.68 vs -15.53; p = 0.01), epicardial (-10.07 vs -12.52; p = 0.01) and mid-layer longitudinal strain (-11.33 vs -13.88; p = 0.01); lower LV ejection fraction (42.2 vs 49.8%; p = 0.03); higher left atrial volume (40.24 vs 28.66 ml/m2; p < 0.01) and higher BNP (856 vs 250 pg/ml; p < 0.01). There weren't significant differences concerning layer-specific circumferential strain, as well as other echocardiographic parameters (E, A, E', E/A, E/E', right ventricular function) and maximum troponin values.

Conclusion: In our study, pts with K>I had more impaired layer-specific longitudinal strain and therefore this parameter may also be a valuable tool for identification of pts with higher risk of in-hospital HF post-AMI, besides classic echocardiographic and laboratorial parameters.

Acute Heart Failure - Treatment

P1857

Clinical impact of temporal diuretic efficiency, in-hospital diuretic infusion and diuretic amount at discharge in acute heart failure

A Alberto Palazzuoli[1]; G Ruocco[2]; L Luschi[2]; I Evangelista[2]; R Nuti[2]

[1]Santa Maria Alle Scotte Polyclinic, Siena, Italy; *[2]University of Siena, Cardiovascular Diseases Unit, Department of Internal Medicine , Siena, Italy*

Background: Several studies showed the importance of adequate response to loop diuretics administration in acute heart failure (AHF) patients. Nevertheless, no data are currently available about the oral loop diuretic dose regimen after infusion and the risk assessment after discharge.
Purpose: To elucidate these aspects we sought to evaluate: 1-the most reliable diuretic efficiency (DE) formula over timing infusional period for outcome prediction; 2-the relationship among intravenous and oral loop diuretic administration and outcome.
Methods This is a single-center prospective randomized study in which we compared Low (LD) vs High (HD) dose of loop diuretic infusion and oral amount either during hospitalization and before discharge compared to outcome.DE formula was defined as weight loss/40 mg daily of furosemide and it was examined at day 1, day 3 and during the whole infusion period.
Results A total of 121 patients consecutively admitted for AHF were evaluated. A lower DE measured during the entire infusion period (AUC 0.69 [CI 0.60-0.79];$p < 0.001$) was able to predict outcome with greater significance than DE measured at day 3 and day 1 (AUC 0.64;$p = 0.007$ and AUC 0.56;$p = 0.229$ respectively). Both infusional and oral diuretic amount at discharge were able to predict poor prognosis (AUC 0.82;$p < 0.001$).HD group showed an higher rate of 180 days adverse events with respect to LD group (86% vs 22%; $p < 0.001$).
Conclusions: Low DE measured during the whole infusion period appears to be the best predictor for poor outcome.Therefore, the diuretic amount at discharge is much more related to an adverse outcome compared to low DE during hospitalization.

P1858

Prescription rate of beta-blockers and factors of its use or nonuse in patients hospitalized for acute heart failure (from the KCHF Registry)

Y Yoshikawa[1]; Y Tamaki[2]; H Yaku[1]; N Ozasa[1]; Y Inuzuka[3]; T Kato[1]; T Kimura[1]
[1]Kyoto University Graduate School of Medicine, Department of Cardiovascular Medicine, Kyoto, Japan; *[2]Tenri Hospital, Department of Cardiovascular Medicine, Tenri, Japan*; *[3]Shiga Medical Center for Adults, Department of Cardiology, Moriyama, Japan*

Background: The current guidelines recommend beta-blockers for reduction of morbidity and mortality in patients with heart failure with reduced ejection fraction (HFrEF).
Purpose: The current study sought to clarify the relationship between use or nonuse of beta-blockers in patients with acute heart failure and their clinical characteristics.
Methods: The Kyoto Congestive Heart Failure (KCHF) registry is a cohort without any exclusion criteria of patients hospitalized for acute heart failure in Japan. We classified patients with HFrEF into 2 groups by medication status at discharge: those on beta-blockers at discharge (Group A) and those not on beta-blockers at discharge (Group B). We compared the clinical characteristics between Group A and B.
Results: A total of 4056 patients were enrolled, including 1551 patients with HFrEF. After excluding those who died in hospital (N = 142), Group A included 1093 patients and Group B 316 patients. As shown in the table, there were significant differences not only in medical characteristics (such as age, history of hypertension and heart rate) but also in reduced physical and social function, including the presence of dementia and activities of daily living. A significantly higher proportion of patients in Group B suffered worsening heart failure during hospitalization than those in Group A. A multivariable logistic regression model assessed the odds for prescription of beta-blockers at discharge. As shown in the table, age = 80, dementia and ambulatory status remained as independent factors associated with prescription of beta-blockers at discharge.
Conclusion: Poorer social and physical functioning were independently associated with prescription of beta-blockers at discharge in patients with HFrEF. Further studies would be warranted to examine the effectiveness of beta-blockers for these frail patients.

Patient characteristics by beta-blockers

	Group A (N = 1093)	Group B (N = 316)	P value	Multi-variable Odds for prescription of beta-blockers	95% CI	P Value
Age≥80	387 (35%)	171 (54%)	<0.001	0.62	[0.45-0.86]	0.004
Male	755 (69%)	187 (59%)	0.001	1.26	[0.91-1.74]	0.16
Hypertension	699 (64%)	230 (73%)	0.004	0.73	[0.54-1.01]	0.057
Asthma	58 (5.3%)	22 (7.0%)	0.26	0.85	[0.47-1.53]	0.59
Dementia	128 (12%)	83 (26%)	<0.001	0.57	[0.38-0.85]	0.006
Heart rate <80/min	185 (17%)	78 (25%)	0.002	0.52	[0.36-0.75]	<0.001
Ambulatory status	940 (87%)	225 (72%)	<0.001	1.81	[1.23-2.68]	0.003
Worsening heart failure	228 (21%)	83 (26%)	0.041	NA	NA	NA

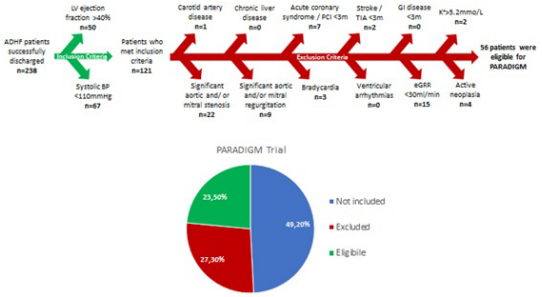
The multivariable model assessed 12 potential factors for prescription of beta-blockers at discharge, including the characteristics listed in the table.

P1859

Eligibility criteria for Sacubitril-Valsartan in patients admitted for heart failure: the real world ?

D David Cabrita Roque[1]; J Augusto[1]; M Santos[1]; D Candeias Faria[1]; J Baltazar Ferreira[1]; A Sacchetti[2]; L Melo[2]; A Oliveira Soares[1]; C Morais[1]
[1]Hospital Prof Fernando da Fonseca EPE, Cardiology, Amadora, Portugal; *[2]Hospital Prof Fernando da Fonseca EPE, Internal Medicine, Amadora, Portugal*

Background: Heart failure is the CV clinical condition with the biggest and most rapid growth in the world and the morbi-mortality associated with this disease is still in an epidemic scale.
Purpose: To evaluate the eligibility at hospital discharge for Sacubitril-Valsartan (SB) according to the inclusion and exclusion criteria of the Paradigm trial.



Methods: Paradigm main inclusion criteria was HFrEF NYHA II-IV, NT-proBNP = 600 pg/mL or = 400 pg/mL if hospitalized for ADHF in the previous 12 months and on a stable treatment for = 4 weeks with ACEI/ARB and BB. The main exclusion criteria were and eGFR <30 mL/min/1.73 m2, K+>5.2 mmol/L, symptomatic hypotension or SBP <100 mmHg, among others. ADHF was defined by the presence of = 2 signs or symptoms of HF.
Results: A total of 238 patients with ADHF were successfully discharged from our hospital in the período evaluated (8.4% of patients, n = 20, were excluded because of in-hospital death). Mean age of our population was 77.4 ± 0.7 years; 45.8% male). One hundred and twenty-one patients (56.7%) met the inclusion criterias of the Paradigm trial. Inclusion criteria were not met in 50 patients (21%) because of LVEF > 40% and in 67 patients (28.2%) because of low systolic blood pressure (SBP < 100mmHg at discharge). Among the patients who met the inclusion criteria, a total of 65 patients (53.7%) have been excluded according to the exclusion criteria in Paradigm protocol; the main exclusion criteria were the presence of a significant valvular stenosis (18.1%), followed by an eGFR <30ml/min/m2 (14%). Figure 1 summarizes our findings. Of the 238 patients, only 56 patients were eligible to initiate the treatment with Sacubitril-Valsartan.
Conclusions: Sacubitril-Valsartan is a new treatment for patients with HFrEF, who remain symptomatic after otimized treatment with ACEI and beta-blocker. However the study protocol excluded patients with severe comorbidities, often present in

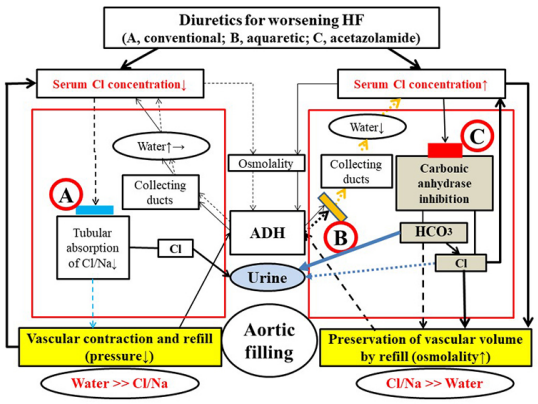
patients with HF. We concluded that in a "real world" population of HF patients, at hospital discharge, only one-quarter of the patients were eligible for this new drug.

P1860

Effects of acetazolamide (Diamox) on plasma volume, serum electrolytes and renal function in comparison with conventional diuretics

H Hajime Kataoka[1]
[1]*Nishida Hospital, Oita, Japan*

Background: According to the "chloride theory" for heart failure (HF) pathophysiology (AHA2015/ACC2016/ESC2016), changes in the serum chloride concentration are the primary determinant of changes in plasma volume, suggesting that manipulation of the serum chloride concentration could be a central therapeutic target for controlling body fluid in HF patients.
Purpose: The present study examined the effects of the chloride-regaining diuretic acetazolamide on plasma volume, serum electrolytes and renal function in comparison with conventional chloride-depletion diuretics.
Methods: I retrospectively analysed 13 data from treated with acetazolamide (Diamox treatment; group A, n = 13) or conventional diuretic treatment with a combination of loop diuretics, aldosterone blockade, and thiazide diuretics (group B, n = 13), which were matched based on diuresis-induced weight reduction (= 1kg) during resolution of worsening HF. Changes in plasma volume (Strauss method), renal function, and serum electrolytes under treatment were determined by peripheral blood tests.
Results: Treatment duration and body weight reduction by treatment did not differ between the A and B groups (27.6 ± 12.7 vs. 26.7 ± 15.8 days; -2.23 ± 1.11 vs -2.22 ± 1.06 kg). After each treatment, the serum chloride concentration markedly increased in group A, but decreased in group B (+5.31 ± 4.91 vs. -4.54 ± 4.68 mEq/L, $p < 0.0001$). Plasma volume (0.63 ± 13.1 vs. -12.1 ± 10.5%, $p < 0.01$) and renal function based on changes in the serum creatinine (0.048 ± 0.12 vs. 0.21 ± 0.24, $p < 0.047$) were better preserved in group A than in group B.
Conclusions: Under achievement of the same body weight reduction by diuresis, plasma volume and renal function were better preserved by diuretic treatment with acetazolamide than with conventional diuretic treatment. These differential effects are in accordance with my "chloride theory" for HF pathophysiology (Figure).



Figure

P1861

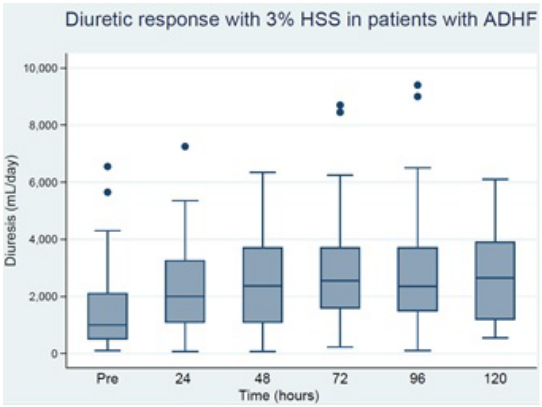
Hypertonic saline solution with furosemide for the treatment of congestive symptoms of acute heart failure

D Carrillo[1]; R Lopez-Vilella[1]; I Sanchez-Lazaro[1]; L Martinez-Dolz[1]; L Almenar[1]
[1]*Hospital Universitario y Politécnico La Fe, Heart Failure and Transplant Unit, Valencia, Spain*

Introduction: Hypertonic saline solution (HSS) favors the mobilization of extravascular fluid to the intravascular space and the excretion of this volume by the action of furosemide improving the congestive symptoms of acute heart failure (AHF).
Purpose: To describe the diuretic response after continuous infusion of 3% HSS with furosemide in patients with AHF.
Methods: A retrospective study of patients admitted to the hospital due to AHF, received a continuous infusion of 3% HSS 500ml with 200mg of furosemide for 24 hours each cycle. A box plot of the diuresis per day and a random-effects model of diuretic response over the time adjusted for glomerular filtrate rate, age and hours of HSS infusion.
Results: 38 patients were included. Only 6 patients didn't have more than 500 mL of diuresis compared to the previous 24 hours, these patients had lower baseline sodium and received more frequently thiazides (Table). After 24-hour HSS infusion, the diuresis increased 430mL, 1034mL after 48 hours (Figure). Elevation of creatinine in time affected de diuretic response to HSS with furosemide (-502.09mL 95% IC -979 to -25mL) (Table).
Conclusion: The infusion of SSH together with furosemide increased the diuretic response in patients with AHF. However, a combination of diuretics and several HSS infusion cycles in some patients were required to achieve the observed response.

Variable	>500mL after HSS	p	
No (n = 6)	Yes (n = 32)		
Age (years)*	69 (68-70)	66 (56-79)	0.85
Male gender	5 (83.33)	22 (68.75)	0.65
EFpHF	4 (66.67)	12 (37.50)	0.56
EFmrHF	0	2 (6.25)	
EFrHF	2 (33.33)	18 (56.25)	
Sodium**	130.4±4.97	137.45±4.62	0.01
Creatinina**	2.08±0.73	1.88±0.94	0.66
Previous furosemide dose (mg/d)*	130 (80-200)	60 (60-120)	0.08
Thiazides use	5 (83.33)	7 (21.88)	0.01
Antialdosterona	5 (83.33)	20 (62.50)	0.64
Hours of HSS	24 (24-48)	48 (24-96)	0.20
Hospital stay (days)	15.5 (10-16)	11.5 (7.5-28.5)	0.18
In-hospital mortality	2 (33.33)	8 (25.00)	0.29

Variables presented as absolute frequency and percentage. * median, interquartile range. ** media, standard deviation. HSS: 3% hypertonic saline solution



P1862

Correlation between degree of pulmonary congestion and rate of heart failure hospitalization in Heart Failure patients with reduced Left Ventricle Ejection Fraction. : Results from extended IMPEDANCE-

M Michael Kleiner Shochat[1]; A Shotan[1]; I Kleiner[2]; JM Weinstein[2]; I Dahan[1]; M Kazatsker[1]; A Asif[1]; S Meisel[1]
[1]*Hillel Yaffe Medical Center, Heart Institute, Hadera, Israel*; [2]*Saroka Medical Center, Cardiology, Beer Sheva, Israel*

Results of the IMPEDANCE-HF trial have shown that lung impedance (LI)-guided treatment reduces hospitalizations for heart failure (HF) and decreases HF-related mortality. The main trial was extended for an additional year to accrue more data on predictors of hospitalizations due to HF. The main aim of the study was to prove that HF patients with higher degree of long-standing pulmonary congestion are hospitalized more often.
Methods: Study population included 266 patients, with HF and LVEF = 35% in New York Heart Association class II-IV. Patients were randomized (1:1) to a control group treated by clinical assessment and a LI-guided group whose therapy was also assisted by LI. Patients were examined and LI measured monthly in our outpatient clinics. Noninvasive LI measurements were performed with the

high-sensitive device. Assessment of the degree of pulmonary congestion was by the new index ?LIR, measured at each visit and calculated as ?LIR = [currently measured LI/ normal baseline (calculated for each patient) -1] × 100 expressed as percentage. The annual average ?LIR for each patient was calculated as the mean of all ?LIR measurements at each consecutive year of follow-up (FU).
Results The cumulative FU period was 642 patient × years in the LI-guided group and 510 patient × years in the control group ($p = 0.001$). Groups were similar with respect to baseline characteristics. There were 249 HF hospitalizations in the LI-guided group (mean 0.38 per year) and 475 HF hospitalizations in the control group (0.93 per year, $p < 0.001$). Rate of HF hospitalization was divided into 4 categories as follows: Q1: 0.00-0.1; Q2: 0.11-0.32; Q3: 0.33-1.07, and Q4 >1.07 HF hospitalizations/ per year of FU. Number of patients in Q1:Q2:Q3:Q4 were 68 (51%), 39 (29%), 16 (12%) and 10 (8%) in the LI-guided group and 48 (36%), 29 (22%), 21 (16%) and 33 (25%) in the control group, respectively ($p < 0.01$). Results show that the level of congestion according to ?LIR during FU period increased progressively from Q1 to Q4 in both groups ($p < 0.001$).
Conclusions: LI-guided treatment of HF patients significantly reduces the incidence of HF hospitalizations.
Preemptive LI-guided treatment cases a shift of patients from Q3-4 to Q1-2 in the LI-guided group in comparison with the control group.
As a result of the above, the main predictor for HF hospitalizations is the degree of pulmonary congestion during the FU period.

P1863
Cardiogenic shock complicating peripartum cardiomyopathy: importance of early left ventricular unloading in combination with bromocriptine therapy

T J Pfeffer[1]; J-T Sieweke[1]; D Berliner[1]; T Koenig[1]; CN Napp[1]; J Tongers[1]; C Kuehn[2]; JD Schmitto[2]; D Hilfiker-Kleiner[1]; A Schaefer[1]; J Bauersachs[1]
[1]Hannover Medical School, Cardiology, Hannover, Germany; [2] Department of Cardiac, Thoracic, Transplantation and Vascular Surgery, Hannover, Germany

Background: Peripartum cardiomyopathy (PPCM), a rare heart disease with an onset during the last month of pregnancy or within the months postpartum, is characterized by heart failure with reduced ejection fraction in previously healthy women. A prolactin fragment is considered causal for the pathogenesis of PPCM. Treatment with the prolactin inhibitor bromocriptine in addition to heart failure therapy is associated with improved LV function and outcome. Nevertheless, in some cases PPCM is complicated by cardiogenic shock, representing a life-threatening situation. Catecholamine treatment in PPCM has been associated with adverse outcomes in animal models and patients. Mechanical circulatory support (MCS) with micro-axial flow-pumps and extracorporeal membrane oxygenation (ECMO) are increasingly used in the treatment of refractory cardiogenic shock. This study sought to investigate the role of early percutaneous MCS in combination with the prolactin inhibitor bromocriptine in cardiogenic shock complicating PPCM.
Methods and Results: Five PPCM patients with cardiogenic shock received MCS with either ImpellaCP microaxial pump only (n = 2) or in combination with veno-arterial ECMO (n = 3) in the setting of biventricular failure. In all cases MCS was combined with bromocriptine therapy and early administration of levosimendan. All patients survived the acute phase of cardiogenic shock, three patients were bridged to left ventricular assist device (LVAD). In our cohort MCS led to a significant reduction of catecholamine dosage while maintenance of blood pressure was achieved. In particular, early left ventricular unloading with ImpellaCP (= 24 hours) resulted in myocardial recovery, whereas a prolonged conservative management with catecholamines was associated with poor recovery. All three patients that could not be weaned from MCS and required permanent LVAD implantation had undergone prolonged conservative treatment with high dosages of dobutamine at secondary hospitals before transfer to our department (8 (IQR 7-8) days vs 1 (IQR 1-1) day, p = 0.2). Safety outcome was reasonable, as no major bleeding, no limb ischemia and no thromb-embolic event occurred during MCS.
Conclusion: MCS in PPCM patients with cardiogenic shock was associated with a 30-day survival of 100% and a favorable outcome. Remarkably, early left ventricular unloading combined with bromocriptine therapy was associated with left ventricular recovery. In contrast, patients treated with high catecholamine dosages for several days did not recover. Therefore, an immediate transfer to a tertiary hospital with experience in MCS for left ventricular unloading in combination with bromocriptine treatment seems to be crucial for treatment of cardiogenic shock complicating PPCM.

P1864
Non-invasive lung ventilation in patients with acute heart failure

K Akmal Koyirov[1]; S R Kenjaev[1]; U SH Ganiev[1]; S SH Khaitov[1]; Z A Kambarova[2]; M S Mirmaksudov[3]
[1]Republican Research Center of Emergency Medicine, Tashkent, Uzbekistan; [2]Tashkent Pediatric Medical Institute, Tashkent, Uzbekistan; [3]Tashkent Medical Academy, Tashkent, Uzbekistan

Background: It is known that unreasonable carrying out of artificial ventilation of lungs has undesirable consequences, the risk of development of infectious complications (primarily tracheobronchitis, sinusitis and ventilator-associated pneumonia) increases. In this regard, the use of noninvasive ventilation in patients with cardiogenic respiratory insufficiency is fully justified.
Aim: To study the effect of noninvasive ventilation on acid base balance, hemodynamics, external respiration in patients with acute heart failure.
Material and Methods: 31 patients with acute heart failure were treated, against standard treatment, noninvasive ventilation in BiPAP mode. The exclusion criteria included respiratory arrest and the need for immediate intubation, hypotension, upper airway obstruction, the inability to remove sputum or use of a facial mask.
Non-invasive ventilation with positive pressure was carried out with a face mask using IVL apparatus. In the non-invasive ventilation of the lungs in the BiPAP 10/5 cm H2O mode, a significant decrease in respiratory rate by 29.1% and a heart rate of 13.4% was observed through the face mask for 1 hour. Moreover, an improvement of ejection fraction of left ventricle (by 17,4%), the parameters of acid base balance and blood gases (PaO2 increased by 37.8%, PaCO2 decreased by 36.4%, SpO2 increased by 15.9%) also observed in our study.
Non-invasive ventilation can increase the vital capacity of the lungs, improve gas exchange and quickly restore the function of the respiratory system. Advantages of non-invasive ventilation are clinical efficacy, physiology of the method, comfort for the patient.
Conclusions: Non-invasive ventilation allowed to normalize the gas composition of blood, parameters of hemodynamics and external respiration in patients with cardiogenic respiratory failure avoiding intubation of the trachea. Control of the adequacy of ongoing respiratory support can be carried out on the basis of SpO2 monitoring and hemodynamic parameters, acid base balance and venous blood gasometry.

P1865
Trends in the performance measures of drug therapy for heart failure with reduced ejection fraction under the optimize heart failure care program

E Eugenio Reyes[1]; FER Punzalan[1]; PFM Reganit[1]; MJF Agbayani[1]
[1]Philippine General Hospital, Section of Cardiology, Department of Internal Medicine, Manila, Philippines

Trends in the performance measures of drug therapy for Heart Failure with reduced Ejection Fraction under the Optimize Heart Failure Care Program
In 2013, the Optimize Heart Failure Care Program was introduced in the Philippines. The major components of the program are education, the use of checklist, and monitoring of performance through a disease registry. We report here performance measures in the use of Class IA drugs for HFrEF on a yearly interval to establish trends. The utilization rates of Class IA drugs for HErEF before and after the introduction of the Optimize Heart Failure Care Program were measured through review of data in the Heart Failure Registry in the Philippines. Data from 2004 was used as the baseline parameter. The percentage of patients who were prescribed ACE-Inhibitors or ARB, Beta-blockers, Spironolactone, and Ivabradine before discharge were measured. The baseline Utilization rate of drugs were 72% for ACE-I/ARB, 34% for Beta-blockers, and 14% for MRA. When optimize was initiated, the utilization rates were 74.8% for ACE-I/ARB, 50% for Beta-blockers, 21% for MRA, and 15% for Ivabradine. When analysis was done on a yearly basis, the utilization rates for ACE-I/ARB were 73%, 75%, and 32%; for Beta-blockers 51%, 47%, and 23%; for MRA 2%, 24%, and 18%, and for Ivabradine 13%, 7%, and 16%. Utilization rates of Class IA drugs for heart failure with reduced ejection fraction improved with the introduction of the Optimize Heart Failure Care Program. However, it deteriorates overtime and it was associated with higher mortality. We recommend the continuous monitoring of performance measures on a yearly interval and establish trends, run the program continuously and repeatedly since new doctors get in and new patients come in, incorporate the program in the Heart failure pathways, and establish heart failure clinics so the unit can take over the continual improvement process.

Performance measures for HFrEF by year

Year	2004 n= 1078	2014 n = 86	2015 n = 319	2016 n = 125
ACE-I/ARB	776 (72%)	63 (73%)	240 (75%)	41 (32%)
Beta-blockers	366 (34%)	44 (51%)	151 (43%)	29 (23%)
MRA	150 (14%)	2 (2%)	77 (24%)	22 (18%)
Ivabradine	na	8/60 (13%)	16/239 (7%)	12/76 (16%)
Mortality Rate	10%	2.3%	3.2%	4.8%

The utilization rates of Class IA drugs and ivabradine for HFrEF by year of enrollment. There is sudden drop in the performance measures after 2 years.

P1866

Intra-aortic balloon counterpulsation pump in heart failure patients during MitraClip implantation

M Mirjam Kessler[1]; J Seeger[1]; J Woehrle[1]; W Rottbauer[1]; S Markovic[1]
[1]*University of Ulm, Department of Internal Medicine II, Ulm, Germany*

Background: MitraClip implantation emerged as a treatment option especially for patients with prohibitive surgical risk due to severe impairment of left ventricular function. The use of intra-aortic balloon counterpulsation pump extended the spectrum of percutaneous cardiac interventions, to complex high-risk procedures with acceptable outcome.
Purpose: To analyse immediate and 30-day results after percutaneous mitral valve repair using an IABP as circulatory support during MitraClip implantation
Methods: Since 2012 17 patients of 557 patients (3%) at our centre received an IABP during MitraClip implantation procedure. The indication for prophylactic IABP implantation was a severely reduced left ventricular function (22.8 ± 8.3%) and haemodynamic impairment (cardiac index 1.9 ± 0.4 l/min/m^2).
Results: The mean age of the predominantly male population was 66.8 ± 12.1 years, mean Logistic EuroSCORE was 6.8 ± 5.6 and mean ASA Score was 3.8 ± 0.4. The mean NT-pro BNP at baseline was 6616.1 ± 4748 pg/ml, and the mean New York Heart Association (NYHA) functional class was 3.5 ± 0.5. Grade of MR before Clip procedure was 3.4 ± 0.5. All procedures were carried out successfully, with 1.2 ± 0.4 implanted clips and achieving a sufficient MR reduction (grade of MR after Clip 1.5 ± 0.5). Length of in-hospital stay was 11.7 ± 14 (3-48) days. No peri- or postprocedural death and no periprocedural resuscitation were observed. All 17 patients had an event-free 30-day follow-up. One patient remained hospitalized due to refractory heart failure until the end of follow-up and died after 48 days.
Conclusion: Implantation of an IABP during MitraClip procedure may provide additional safety and improve procedural outcomes in the setting of high-risk percutaneous mitral valve repair in heart failure patients.

P1867

Is there changes in the diuretic response to hypertonic saline plus furosemide depending on the type of heart failure?

D Carrillo[1]; R Lopez-Vilella[1]; I Sanchez-Lazaro[1]; L Martinez-Dolz[1]; L Almenar[1]
[1]*Hospital Universitario y Politécnico La Fe, Heart Failure and Transplant Unit, Valencia, Spain*

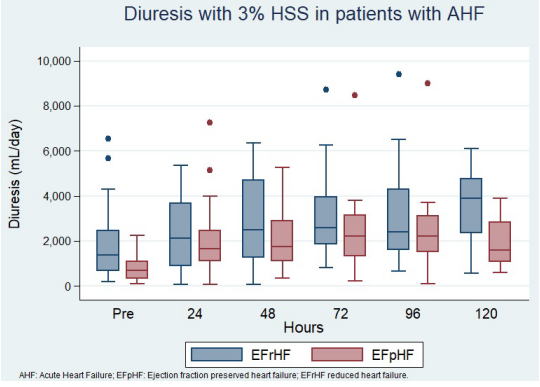
Background and Purpose: Hypertonic saline solution (HSS) in patients with heart failure (HF) may improve diuresis due to an increase in renal blood flow and may facilitate the action of diuretics. Our purpose was to describe the diuretic response to HSS in patients with acute HF according to the left ventricular ejection fraction (LVEF).

Characteristic of patients.

Variable	Left Ventricular Ejection Fraction				
	<45% (n = 24), n %	≥45% (n = 18), n %	p		
Age (y)*	65.83	13.8	68.55	12.09	0.46
Male gender	18	75.00	11	61.11	0.50
Ischemic aetiology of heart disease	6	25.00	1	5.56	0.10
Hospital admissions due to HF*	17	70.83	9	64.29	0.72
Previous furosemide dose (mg/d)**	60	60-150	80	60-120	0.91
Initial laboratory					
Sodium*	135.58	4.28	135.92	6.35	0.86
Creatinina*	2.08	0.82	1.71	0.95	0.26
Hours of 3%HSS**	60	24-120	48	24-48	0.32
In-hospital mortality	5	20.83	7	38.89	0.30

* Media, standar deviation, ** Median, interquartile range. HF: Heart failure, HSS: Hypertonic Saline Solution

Methods: Retrospective study of patients admitted because of acute HF, and received continuous infusion of 500mL of 3% HSS plus furosemide, as a treatment of congestive symptoms of HF. Variables was described and classified according to the presence of ejection fraction = 45% as preserved (EFpHF), otherwise as reduced (EFrHF). The diuresis in the 0, 24, 48, 72 and 120 hours after de initiation of HSS was graphed by LVEF categories. A regression model of random effects of diuresis conditioned by time between 0 and 120 hours of SSH infusion were made.
Results: Forty-two patients. Median age was 67 years (Table). After the infusion of HSS with furosemide, compared to the diuresis of the previous 24 hours, on average the diuresis increased 483mL in the first 24 hours (p = 0.22), 1080 in the 48 hours (p = 0.005), 1728 in the 72 hours (p = 0.00), EFpHF was not related to greater diuresis with respect to EFrHF (-436mL 95% CI -1268 to 394 p = 0.30) (Figure). However, the older age and the lower glomerular filtration rate were related to changes in the diuretic response (-49mL 95% CI -80 to -18 p = 0.002 and 16mL 95% 0.90 to 31 p = 0.038 respectively).
Conclusion: The infusion of HSS with furosemide increased the diuretic response without differences between EFpHF and EFrHF



P1868

Intravenous fluids in patients admitted with acute heart failure

D David Cabrita Roque[1]; D Candeias Faria[1]; J Augusto[1]; J Baltazar Ferreira[1]; J Simoes[1]; A Sacchetti[2]; L Melo[2]; A Oliveira Soares[1]; C Morais[1]
[1]*Hospital Prof Fernando da Fonseca EPE, Cardiology, Amadora, Portugal*;
[2]*Hospital Prof Fernando da Fonseca EPE, Internal Medicine, Amadora, Portugal*

Introduction: Acute Heart Failure (AHF) is a life-threatening disease requiring urgent treatment. Most of patients present with signs and symptoms of volume overload. However, in clinical practice, in addition to diuretic therapy many hospitalized patients receive intravenous fluids, which is counterintuitive.
Purpose: The aim of this study is to evaluate the association between the institution of fluid therapy and clinical outcomes in patients admitted in the Emergency Department for AHF.
Methods: Retrospective study of 258 consecutive patients admitted in the emergency department for ADHF, defined by the presence of = 2 signs or symptons of heart failure. Admission, maximum and discharge values of creatinine (Cr) were collected, along with other clinical, laboratory and therapeutic variables. The HF profile was assessed as according to the ESC guidelines. We focused on early treatment with fluids to avoid treatments performed in response to over-intensive diuretic treatment. We defined intravenous fluid therapy as any use of = 500ml of normal saline or half-saline in the first 24 hours of admission, and did not include administration of dextrose 5% solution because it would not enhance intravascular volume significantly.
Results: We evaluated 258 patients with ADHF (45.7% male, mean age of 74.6 ± 16.6 years). received intravenous fluid therapy: < 500ml (71.2%, n = 183) and = 500ml (28.8%, n = 74). The mean IV fluid volume was 195 ± 394ml. The median dose of Furosemide administered in the first 24 hours was 80 (60-100) mg. Mean baseline Cr was 1.29 (0.94-1.72) mg/dl, peak Cr was 1.49 (1.14-2.13) mg/dl and discharge Cr was 1.18 (0.95-1.60) mg/dl. The death rate during hospitalization was 8.1% (n = 21); 1-month readmission rate was 18.2%% (n = 47). The mean in-hospital length of stay was 12.5 ± 10.8 days, with no significant differences found between those who received (= 500ml) and those that didn't received fluids (< 500ml) (13.3 ± 10.3 vs. 12.1 ± 11.0 days, respectively, p = 0.118). We also found no association between in-hospital mortality and fluid therapy in this group of patients (10.8 vs 7.1%, respectively, p = 0.324)
Conclusions: Although some studies have suggested that fluid therapy in combination with diuretics provide hemodynamic and clinical improvements, in those studies

the volume used was very small. We demonstrated that the use of fluid therapy (= 500ml of normal saline or half-saline) in the first 24 hours of admission for acute heart failure as no impact on hospital outcomes or in-hospital mortality.

Acute Heart Failure - Clinical

P1869

Comparative analysis of short term outcomes of patients with heart failure with mid-range ejection fraction after acute decompensation

O Miro[1]; P Javaloyes[2]; V Gil[1]; FJ Martin-Sanchez[1]; J Jacob[1]; P Herrero-Puente[3]; J Marco-Hernandez[1]; V Rico[1]; G Martinez[1]; S Aguilo[1]; R Escoda[1]; VP Harjola[3]; J Parissis[4]; CE Muller[5]; P Llorens[2]
[1]Hospital Clinic de Barcelona, Emergency Department, Barcelona, Spain; [2]General University Hospital of Alicante, Emergency Department, Alicante, Spain; [3]Helsinki University Central Hospital, Emergency Department, Helsinki, Finland; [4]Attikon University Hospital, Cardiology Department, Athens, Greece; [5]University Hospital Basel, Cardiology Department, Basel, Switzerland

On behalf of: ICA-SEMES Research Group
Funding Acknowledgements: ISCIII (Spanish Ministry of Health) and FEDER (PI15/01019 and PI15/00773), Fundació La Marató de TV3 (2015/2510) and Calalan Govern (GRC 2014/0313)

Aims: To investigate short-term outcomes after an episode of acute heart failure (AHF) of patients with mid-range ejection fraction (between 40%-49%; HFmrEF) compared with patients with reduced (< 40%) and preserved (<49%) ejection fraction (HFrEF and HFpEF, respectively), and according to their final destination after emergency department (ED) health care.
Methods: This is an exploratory, secondary analysis of the EAHFE Registry, which includes consecutive AHF patients diagnosed in 41 Spanish EDs. Patients with echocardiography data were included and divided in HFrEF, HFmrEF and HFpEF. Primary outcome was 30-day all-cause mortality, and secondary outcomes were in-hospital all-cause mortality, hospital length of stay (LOS) longer than 10 days, and 30-day post-discharge ED revisit due to AHF and combined endpoint (ED revisit/death). Adjusted ratios were calculated for patients with HFmrEF compared with HFrEF and HFpEF; and for patients with HFmrEF admitted to internal medicine and not hospitalized compared with those admitted to cardiology.
Results: We included 6,856 patients (age 79 (10); 52.1% women): 21.6% had HFrEF, 14.3% HFmrEF, and 64.1% HFpEF. Main destinations after ED management for HFmrEF patients were internal medicine (293, 29.8%), cardiology (194, 19.9%) and not hospitalized (241, 24.5%). Outcomes for HFmrEF did not differ respect to either HFrEF or HFpEF (Figure 1). Compared with HFmrEF admitted to cardiology, internal medicine admission increased the 30-day post-discharge combined endpoint (HR = 1.598, 95%CI = 1.012-2.524, p = 0.044), and patients not hospitalized increased the 30-day post-discharge ED revisit (HR = 1.779, 95%CI = 1.114-2.829, p = 0.011) and combined endpoint (HR = 1.818, 95%CI = 1.165-2.836, p = 0.008).
Conclusion: Short-term outcomes of HFmrEF patients do not differ from those of the HFrEF and HFpEF patients, but patients admitted to internal medicine and not being hospitalized after the ED management of an AHF episode have increased risks after being discharged from hospital or ED in comparison with those admitted to cardiology.

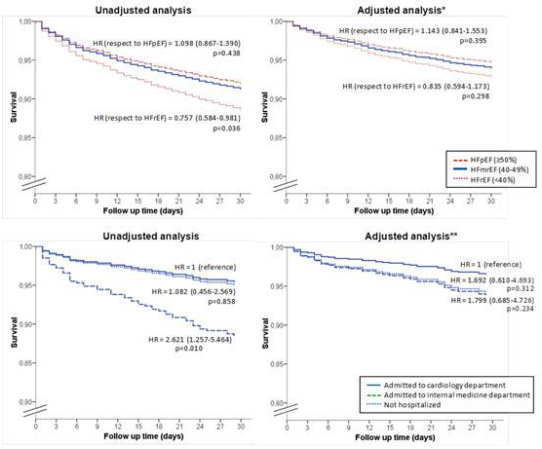


Figure 1

P1870

Non-alcoholic fatty liver disease and increased risk of all-cause mortality in elderly patients admitted for acute heart failure

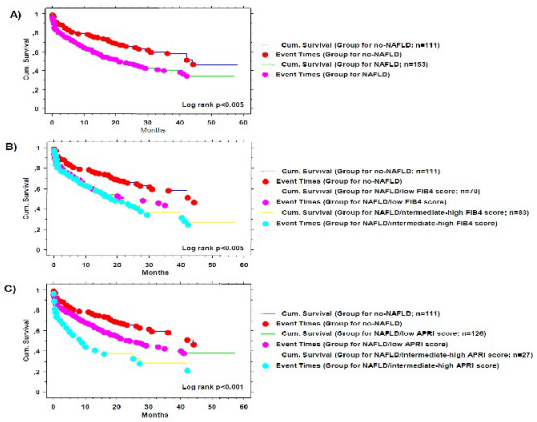
F Filippo Valbusa[1]; D Agnoletti[1]; G Scaturro[1]; L Scala[1]; S Calabria[1]; E Turcato[2]; P Arduini[2]; S Bonapace[3]; G Targher[4]; G Arcaro[1]
[1]Sacro Cuore - Don Calabria Hospital, Internal Medicine, Negrar-Verona, Italy; [2]Sacro Cuore - Don Calabria Hospital, Division of Geriatry, Negrar-Verona, Italy; [3]Sacro Cuore - Don Calabria Hospital, Division of Cardiology, Negrar-Verona, Italy; [4]University and Azienda Ospedaliera Universitaria Integrata of Verona, Section of Endocrinology, Diabetes and Metabolism, Verona, Italy

Introduction: Non-alcoholic fatty liver disease (NAFLD) is an emerging risk factor for incident heart failure (HF). It is currently unknown whether NAFLD predicts all-cause mortality in patients admitted for acute HF. We sought to determine whether NAFLD and its severity (diagnosed by ultrasonography and non-invasive fibrosis markers) were associated with the risk of in-hospital and post-discharge all-cause mortality in this particularly high-risk patient population.

Table 1

Cox Hazard Models	Hazard ratio(s)	95% CI	p value
Inadjusted model	1.70	1.20-2.39	<0.005
Adjusted model 1	1.86	1.30-2.66	<0.001
Adjusted model 2	1.61	1.11-2.35	<0.01
Adjusted model 3 (n = 223)	1.82	1.22-2.81	<0.005

Sample size, n = 264 unless noted otherwise. Other covariates included in the three multivariable regression models, together with NAFLD, were as follows: model 1: age and sex; model 2: age, sex, past history of HF, diabetes, CHD, CKD (i.e. eGFRMDRD < 60 ml/min/1.73 m2), COPD and pacemaker; model 3: adjustment for the same variables included in model 2 plus body weight, systolic blood pressure, LV-ejection fraction, use of ACE-I/ARBs, daily furosemide dosage, plasma albumin, NT-proBNP and GGT levels.



Methods: We studied 264 elderly patients, who were consecutively admitted for acute HF to our hospital between years 2013 and 2015, after excluding those with acute myocardial infarction, severe valvular heart diseases, kidney failure, cancer, cirrhosis of any etiology or known chronic liver diseases.
Results: Over a mean follow-up period of 23.2 months (range: 3 days-58 months), there were 140 (53%) total deaths. Of these, 24 deaths occurred during the first hospital admission (in-hospital death) and 116 deaths occurred after the hospital discharge over the follow-up period. Patients with NAFLD at hospital admission had significantly higher cumulative incidence rates of in-hospital and post-discharge all-cause mortality (singly or in combination) compared with those without NAFLD. This mortality risk was particularly increased among patients with advanced NAFLD fibrosis (Fig.1). In Cox regression analysis, NAFLD was associated with an increased risk of all-cause mortality (adjusted-hazard ratio 1.82, 95% confidence intervals 1.22-2.81, p < 0.005) even after adjustment for established risk factors and potential confounding variables (Table 1). Conclusion: NAFLD and its severity were independently associated with an increase risk of

in-hospital and post-discharge all-cause mortality in elderly patients admitted for acute HF.

P1871

Contemporary cardiovascular management in pre-hospital emergency medical services- comparison of acute heart failure, dyspnoea, chest pain, and ST-elevation myocardial infarction protocols

P Harjola[1]; VP Harjola[1]; M Kuisma[1]; M Christ[2]; X Escalada[3]; F Martin-Sanchez[4]; O Miro[5]

[1]Helsinki University Hospital, Emergency Care, Helsinki, Finland; *[2]Luzern Hospital, Emergency department, Luzern, Switzerland*; *[3]Hospital Clinic de Barcelona, Sistema d'Emergéncies Médiques, Catalunya, Barcelona, Spain*; *[4]Hospital Clinic San Carlos, Emergency department, Madrid, Spain*; *[5]Hospital Clinic de Barcelona, Emergency department, Barcelona, Spain*

Background: Acute heart failure (AHF) is one of the most important causes for hospital admission. Ca. 10 -20 % of AHF patients are first treated by pre-hospital emergency medical services (EMS). Whereas e.g. ST-elevation myocardial infarction (STEMI) protocols are well defined and adopted, there are no uniform protocols for AHF.
Purpose: Our aim was to find out the prevalence and contents of EMS protocols and compare those to other existing cardiovascular protocols in different European countries.
Methods: A survey was sent to 12 European countries. The study was designed to cover Finland, Denmark, Sweden, Norway, Germany, Poland, Czech Republic, France, Spain, Italy, Switzerland, and United Kingdom. The study cites reported data regarding different EMS units ranging from basic to advanced life support units as well as helicopter EMS. This analysis includes data from those EMS regions covering more than 20% of the countries' population.
Data on the prevalence of protocols for AHF, dyspnoea, chest pain STEMI as well as the diagnostic and therapeutic options of these protocols were collected. The prevalence of different protocols was compared by Fisher exact test.
Results: We received 34 surveys from 3 countries fulfilling the inclusion criteria: 19 from Spain (covering 40.0 million citizens, 86.0% of the Spanish population), 9 from Switzerland (covering 2.3 million, 27.1% of the population) and 6 from Finland (covering 3.5 million, 63.3% of the population). Twenty-seven (79.4%) of these EMS regions had a specific protocol for AHF, 29 (85.3%) for dyspnoea, 30 (88.2%) for chest pain and STEMI (p = NS for all comparisons). Spanish EMS had less frequently AHF protocols (73.7% compared to 100% in Switzerland and Finland, p = 0.1). The following diagnostic and therapeutic options were included in the EMS protocols (% of EMS by permanent standing order/ % of EMS after EMS physician's consultation): i.v. line (72.4/17.2), ECG (65.5/17.2), troponin point-of-care test (POCT) (3.6/0) or BNP POCT (3.6/0), ultrasound assessment (3.6/0), oxygen supplementation (72.2/20.7), non-invasive ventilation (51.7/24.1), invasive mechanical ventilation (37.9/27.6), i.v. diuretic (55.6/25.9), i.v. nitrates (34.6/30.8), and i.v./s.c. opiates (70.4/18.5)
Conclusions: Current data suggests that pre-hospital EMS protocols for suspected AHF are common. I.v. line, ECG and ventilatory support are fairly common interventions whereas the use of troponin and BNP POCT and ultrasound are very rarely available.

P1872

Digoxin and its impact on acutely decompensated chronic heart failure

M Al Jarallah[1]; R Rajesh[1]; A R Al-Saber[2]; R Dashti[1]; B Bulbanat[1]; M Ridha[3]; I Al Zakwani[4]; K Sulaiman[5]; P Panduranga[5]; J Al Suwaidi[6]; K Alhabib[7]; W Almahmeed[8]; N Bazargani[9]; A Al-Motarreb[10]; H Amin[11]

[1]Sabah Al Ahmad Cardiac Center, Al Amiri Hospital, Cardiology , Kuwait, Kuwait; *[2]Kuwait Technical College, Statistics , Kuwait, Kuwait*; *[3]Adan Hospital, Cardiology, Kuwait, Kuwait*; *[4]Sultan Qaboos University , Department of Pharmacology & Clinical Pharmacy, College of Medicine & Health Sciences, Muscat, Oman*; *[5]Royal Hospital, Cardiology, Muscat, Oman*; *[6]Hamad General Hospital, Cardiology, Doha, Qatar*; *[7]King Fahad Cardiac Center, Cardiology, Riyadh, Saudi Arabia*; *[8]Sheikh Khalifa Medical City, Cardiology, Abu Dhabi, United Arab Emirates*; *[9]Dubai Hospital and Rashid Hospital, Cardiology, Dubai, United Arab Emirates*; *[10]Sana'a University, Internal Medicine, Sana'a, Yemen*; *[11]Mohammed Bin Khalifa Cardiac Centre, Cardiology, Bahrain, Bahrain*

On behalf of: Gulf CARE
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Aim: To study the impact of digoxin in acutely decompensated chronic heart failure (ADCHF).
Subjects & Methods: Data was analyzed from 5005 consecutive patients admitted to 47 hospitals in 7 Middle Eastern countries with AHF from February to November, 2012. Patients were categorized into ADCHF patients off digoxin therapy (A1) and ADCHF patients on digoxin therapy (A2). Chi-square test of independence was utilized for A1 and A2.
Results: In Gulf-CARE registry 45.56 % (2280/5005) were identified as ADCHF patients where 28.6% (652/2280) patients were already on digoxin therapy. Patients on NYHA IV were seen more with digoxin group 35.6% (232/652) while non-digoxin group had 29.5% (480/2280) p = 0.001. CAD, hypertension and dyslipidemia were seen more with non-digoxin group and was statistically significant p = 0.001. In hospital major bleeding, cardiogenic shock, intubation, stroke and mortality were reported almost same in both groups with no statistical significance.
Conclusions: In ADCHF patients digoxin has no impact on in-hospital major bleeding, cardiogenic shock, intubation, stroke and mortality.

Role of digoxin in ADCHF

Characteristics	Acute Decompensated Chronic Heart Failure		
Without Digoxin n = 1628 A1	With Digoxin n = 652 A2	P-Value	
Gender (Male)	1628 (63.2%)	652 (63.7%)	0.453
Age, Years	63.53 ± 13.18	58.50 ± 14.95	0.001*
Hypertension	1120 (68.8%)	400 (61.3%)	0.001*
Type 2 DM	853 (52.4%)	321 (49.2%)	0.390
CAD	889 (54.6%)	299 (45.9%)	0.001*
Dyslipidemia	702 (43.1%)	229 (35.1%)	0.001*
Smoking	242 (14.8%)	129 (19.7%)	0.004*
Intubation ventilation	140 (8.6%)	61 (9.4%)	0.565
Cardiogenic Shock	126 (7.7%)	60 (9.2%)	0.249
Stroke	23 (1.4%)	5 (0.8%)	0.206
Major Bleeding	46 (2.8%)	23 (3.5%)	0.659
AF	100 (6.1%)	32 (4.9%)	0.254
NYHA IV	480 (29.5%)	232 (35.6%)	0.001*
Beta Blocker before admission	834 (51.2%)	300 (46.0%)	0.024*
On discharge Digoxin	299 (18.4%)	204 (31.3%)	0.001*
Mortality	100 (6.1%)	38 (5.8%)	0.656

CAD = Coronary Artery Disease, NYHA = New York Heart Association

P1873

Role of cardio renal anemia syndrome in acute heart failure

M Al Jarallah[1]; R Rajesh[1]; I Al Zakwani[2]; R Dashti[1]; B Bulbanat[1]; M Ridha[3]; K Sulaiman[4]; P Panduranga[4]; J Al Suwaidi[5]; W Almahmeed[6]; K Alhabib[7]; H Amin[8]; N Bazargani[9]; A Al-Motarreb[10]; A Alsheik Ali[6]

[1]Sabah Al Ahmad Cardiac Center, Al Amiri Hospital, Cardiology , Kuwait, Kuwait; *[2]Sultan Qaboos University , Department of Pharmacology & Clinical Pharmacy, College of Medicine & Health Sciences, Muscat, Oman*; *[3]Adan Hospital, Cardiology, Kuwait, Kuwait*; *[4]Royal Hospital, Cardiology, Muscat, Oman*; *[5]Hamad General Hospital, Cardiology, Doha, Qatar*; *[6]Sheikh Khalifa Medical City, Cardiology, Abu Dhabi, United Arab Emirates*; *[7]King Fahad Cardiac Center, Cardiology, Riyadh, Saudi Arabia*; *[8]Mohammed Bin Khalifa Cardiac Centre, Cardiology, Bahrain, Bahrain*; *[9]Dubai Hospital and Rashid Hospital, Cardiology, Dubai, United Arab Emirates*; *[10]Sana'a University, Cardiac Sciences, Sana'a, Yemen*

On behalf of: Gulf CARE
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Background: Cardio renal anemia syndrome (CRAS) in acute heart failure (AHF) is considered to be a high risk condition.
Subjects and **Methods:** Patients were categorized into group of AHF patients without CRAS and group of AHF patients with CRAS. Chi-square test of independence was utilized for A1 and A2.
Results: In Gulf-CARE registry 26.8% (1343/5005) patients were identified as CRAS patients, where anemia was observed in 54.5% (2728/5005) and

chronic kidney disease (CKD) in 45.1% (2257/5005) patients. In-hospital cardiogenic shock, intubation, stroke was reported almost similar in both groups. In-hospital major bleeding was seen more with A2 1.4% (19/1343) when compared to A1 0.6% (21/3662) with a statistical significance p = 0.003. The mortality rate was almost similar in both groups 6.2% (228/3662) in A1 and 6.3% (85/1343) in A2.

Conclusion: In the setting of acute heart failure, CRAS is not considered to be an independent predictor of in-hospital cardiogenic shock, stroke and mortality.

Comparison between CRAS & Non CRAS

Characteristics	Non-CRAS(n = 3662) A1	CRAS(n = 1343) A2	p-Value
Age, mean (SD), years	5714.7	65 13.9	0.001
Female , no %	32.2% (1180)	51.7% (694)	0.001
Smoking	25.8% (954)	11.8% (158)	0.001
Obstructive Sleep Apnea	1.6% (58)	3.1% (41)	0.001
Coronary Artery Disease	42.8% (1569)	57.2% (768)	0.001
Type II Diabetes	40.9% (1496)	60.4% (811)	0.001
Hypertension	55.2% (2023)	77.1% (1036)	0.001
Dyslipidemia	6.9% (253)	36.6% (491)	0.001
Atrial Fibrillation	11.2% (409)	14.7% (198)	0.001
Peripheral Vascular Diseases	3.5% (129)	7% (94)	0.001
Hemoglobin g/dL, mean (SD)	13.32.3	10.61.5	0.001
Creatinine mg/dL, mean (SD)	1.10.8	2.21.7	0.001
Chronic Kidney Disease / Dialysis	6.9% (253)	36.6% (491)	0.001
Intubation/Ventilation	8.5% (312)	8.3% (112)	0.84
Cardiogenic Shock	8.2% (300)	7.9% (102)	0.49
Major Bleeding	0.6% (21)	1.4% (19)	0.003
Stroke	1.4% (51)	1.3% (17)	0.73
Death	6.2% (228)	6.3% (85)	0.89

P1874

Relationship between on-treament blood pressure and outcomes in patients with heart failure

D David Cabrita Roque[1]; M Santos[1]; J Augusto[1]; J Baltazar Ferreira[1]; D Candeias Faria[1]; J Simoes[1]; P Magno[1]; A Oliveira Soares[1]; C Morais[1]
[1]*Hospital Prof Fernando da Fonseca EPE, Cardiology, Amadora, Portugal*

Background: Blood pressure (BP) is a well known and studied CV risk factor. However, when CV disease is established, the optimal level of BP is not well defined, and some studies had shown that lower BP is related to increased mortality.

Purpose: We aim to evaluate the relationship between BP at admission, during hospitalization and at hospital discharge, with clinical outcomes.

Methods: Retrospective study of 258 consecutive patients admitted in the ER for HF, defined by the presence of = 2 signs or symptoms of HF. Admission and discharge values of systolic blood pressure (SBP) were recorded. We further divided our population according to the first SBP registered at hospital admission and at discharge: group 1 <130mmHg (31.8 and 64.3%, respectively); group 2 130-160mmHg (37.2 and 28.7%, respectively) and group 3 >160mmHg (31 and 3.9%, respectively). The HF profile was assessed according to the ESC guidelines. We also evaluated patients' medication before admission, during hospitalization and at discharge.

Results: We included 258 patients with ADHF (45.7% male, mean age of 74.6 ± 16.6 years). Emergent hospital admission was more frequent in admission group 3 (61.3% vs 28.1% in group 2 and 28.1% in group 1, p <0.001). Admission group 3 also presented more frequently with acute pulmonary oedema (66.3% vs 17.7% in group 2 and 13.4% in group 1, p <0.001). Chronic renal disease was less frequent in admission group 3 (20% vs 37.5% in group 2 and 31.7% in group 1, p = 0.040); previous acute coronary syndrome was more frequent in admission group 1 (45.1% vs 29.2% in group 2 and 25% in group 3, p = 0.015). Ejection fraction was significantly lower for patients in both admission and discharge group 3 (admission: mean 42% group 3 vs 58.8% group 1 vs 74.4% for group 2), p = 0.019; discharge: mean 26% group 3 vs 65.7% group 1 vs 47.2% group 2, p = 0.004). There were no significant differences in hospital mortality between admission SBP groups (7.3% group 1, 9.4% group 2, 7.5% group 3, p = 0.855). Interestingly, patients in admission group 3 had shorter lengths of stay (mean 9.4 vs 13.5 for group 2 and 14.2 days for group 3, p <0.001). Of note, prior prescription of ACEIs/ARB and beta blockers was unrelated to admission SBP categories. There were no differences in readmission rates for ADHF at 1, 3, 6, 9 and 12 months after discharge, according to SBP categories. There was a trend for patients in groups 1 and 3 to have higher mortality rates after discharge (14.5% for group 1 and 10% for group 3 vs 5.4% for group 2, p = 0.128), suggesting a J-shaped curve for mortality according to SBP.

Conclusions: During hospitalization, SBP does not seem to have an association with mortality; however, according to the SBP values at discharge, those patients with the highest and the lowest values are those with higher risk of mortality at 1 year FUP, suggesting that in HF SBP has a J-shaped curve, and that the least possible BP may not be an adequate treatment target.

P1875

Heart and mind interaction in heart failure

I Aguiar Ricardo[1]; J Ribeiro Agostinho[1]; ISS Goncalves[1]; J Rigueira[1]; A Ferreira-Nunes[1]; R Santos[1]; N Andre[1]; T Guimaraes[1]; N Cunha[1]; R Pires[2]; FJ Pinto[1]; D Brito[1]
[1]*Cardiology Department, Santa Maria Hospital, CHLN, CCUL, Lisbon University, Cardiology, Lisbon, Portugal*; [2]*Faculty of Psichology and Educational Sciences, CINEICC, University of Coimbra, Lisbon, Portugal*

On behalf of: RICA-HFTeam

Introduction and aim: Anxiety and depression appear to contribute to morbidity in heart failure (HF). However they are rarely evaluated. Our aim was to characterize these aspects in HF patients (pts), and to evaluate their potential impact on prognosis.

Methods: Single center prospective study including pts admitted for acute or chronic decompensate HF (index admission) who gave written informed consent for inclusion in a post-discharge follow-up program (by protocol).

The Hospital Anxiety and Depression Scale (HADS) - validated Portuguese version - was used for anxiety and depression screening. We defined for each condition: abnormal value - HADS>11; normal - HADS < 7; and borderline - HADS= 8-10. The test was performed the first time at discharge, and repeated at 9+3 months during follow-up (Fup). Cox regression, Kaplan-Meier survival analysis, Spearman, Mann-Whitney and Wilcoxon correlation analysis were used.

Results: 40 pts (66.5 ± 11.4 years, 75% men, 67.5% with hypertension, and 32.5% with diabetes) were included. At the time of first HADS application, 85% had left ventricle ejection fraction < 40%, and 95% were in NYHA functional class I-II; for 40% of patients, it was the first hospitalization due to HF.

At the first evaluation:

1)Depression - 15% of pts were classified with abnormal HADS, and 27.5% with borderline HADS; the value of HADS was associated with weight (p = 0,026, r= -0,352), blood pressure (p = 0,038, r= -0,329) and anxiety (p < 0,001, r= 0,625); 2) Anxiety - 20% had abnormal HADS, and 25% had a borderline value.

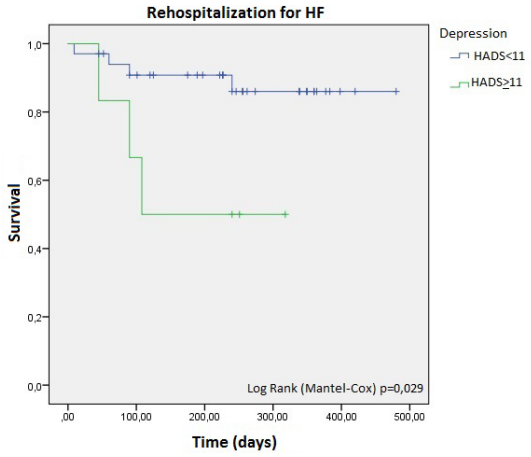
The presence of altered HADS correlated with female gender (p = 0,028; Z= 2,196), first HF hospitalization (p = 0,035, Z= -2,107) and depression.

Anxiety and/or depression were associated with a negative impact on general symptoms (p = 0,023, r= -0,377 and p = 0,002, r= -0,494, respectively) and overall quality of life (p = 0,005, r= -0,459 and p= 0,0001, r= -0,591, respectively), evaluated by the Kansas City Cardiomyopathy Questionnaire.

During Fup, all cause and HF rehospitalization rates were 25%, and 17.5%, respectively.

There was no improvement in anxiety or depression scores during Fup. HADS >11 for depression was a predictor of HF rehospitalization (p= 0,048); anxiety did not predict events.

Conclusion: Anxiety and/or depression have impact on the quality of life of HF pts. The presence of depression predicts rehospitalization for HF, which can be attributed, at least in part, to the difficulty in self-management of the syndrome, contributing to a vicious cycle deserving attention and preventive management in the follow-up of these patients.



Rehospitalization and depression in HF

Coronary Artery Disease - Pathophysiology and Mechanisms

P1876

Diagnostic value of ZNF606 expression from monocytes in coronary artery disease

L Lu Lu[1]; ZY Huang[1]; JB Guo[2]; AH Chen[2]
[1]The First Affiliated Hospital, Guangzhou University of Chinese Medicine, Department of Cardiology, Guangzhou, China People's Republic of; *[2]Southern Medical University,, Department of Cardiology, Heart Center, , Guangdong, China People's Republic of*

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Background: Although coronary artery angiography (CAG) shows high degree of specificity in coronary artery disease (CAD) diagnosis, it is an invasive procedure that causes discomfort to patients and may lead to various complications. Early atherogenesis is characterized by the adherence of blood circulating monocytes. hence, this study hypothesized monocyte gene expression changes in patients with CAD may have diagnostic value.
Purpose: We aimed to evaluate the increase in related mRNAs from monocytes may become a new non-invasive means for diagnosing CAD in the early stage,
Methods : Chip data (GSE9820) retrieved from Gene Expression Omnibus (GEO) was reanalyzed, and the selected candidate genes meeting specific conditions were upregulated and verified for diagnostic values for CAD in the prospective cohort study that recruited 194 individuals: group Non-CAD (GN), n = 68; group CAD (GC), n = 126. The GC patients of 53, 50, and 23 were categorized as having 1 (GC1), 2 (GC2) or = 3 (GC3) coronary arterial stenosis, respectively. All candidate mRNA expressions were analyzed from patients' monocytes with quantitative PCR (q-PCR). Receiver-operating characteristic (ROC) curves and the area under the ROC curves (AUCs) were used to evaluate the mRNAs' feasibility for CAD diagnosis. AUCs = 0.8 were accounted as high diagnostic efficiency for CAD.
Results: GBA2, CSTF3, ZNF606 and MPP5 were selected as candidate mRNAs from chip data reanalysis. GBA2 ($P = 0.002$) and ZNF606 ($P < 0.001$) expressions were significantly increased in GC. ZNF606 showed significant increase by adjusting the risk factors with logistic regression analysis (OR = 3.624, 95% CI: 1.815, 7.491, $P < 0.001$), and its expression level was positively correlated with age ($\beta = 0.04 \times 10\text{-}3$, $P < 0.001$). The AUCs (and 95% CI) of ZNF606 expression in GC2 and GC3 are = 0.8 showing high diagnostic efficiency in CAD.
Conclusions: These findings suggest that ZNF606 expression from monocytes may be a novel and specific diagnostic means of CAD, especially in multiple coronary artery stenosis.

P1877

Single nuclear polymorphism a1166c of agtiir1 gene and cardiac remodeling after st segment elevation myocardial infarction

OV Petyunina[1]; MP Kopytsya[1]; IR Vyshnevska[1]
[1]Government institution"L.T. Malaya Therapy National institute of the National academy of medical sci, Kharkiv, Ukraine

Purpose: To perform medical-genetic analysis of dynamic of structural and functional myocardial parameters, heart rate variability data depending on polymorphism ?1166? of R1 receptor of angiotensin II (AGTIIR1) gene in patients with myocardial infarction with ST segment elevation - STEMI.
Matherials and methods: 87 patients with STEMI, 70 (80%) male and 17 (20%) female at average age ($58{,}94 \pm 10{,}16$) years were examined. Patients were hospitalized during first three days after selective coronary angiography and infarct-related artery stenting were performed. After 6-month observation period patients were reexamined. Allele polymorphism A1166C of AGTIIR1 gene was determined by polymerase chain reaction in real time, heart rate variability (HRV) - Cholter 24-hour monitoring, morpho-functional data - ultrasound research.
Results and discussion. In patients with ??+??-genotypes compared with ?? on 1-3 day of STEMI higher level of left ventricular (LV) end diastolic diameter (EDD) (? = 0,004), LV end systolic diameter (ESD) (? = 0,043), LV myocardial mass (MM) (? = 0,041), frequency of mitral regurgitation (? = 0,028), the tendency to higher LV end diastolic volume (EDV) (? = 0,089) were revealed. These means unfavorable structure of early after infarction myocardial remodeling (RM). After 6 month patients with ??+??- genotypes compared with ?? demonstrated higher LVEDD (? = 0,083), left atrium (? = 0,091), LVMM (? = 0,081). When analysed echocardiographic data in acute period of STEMI and after 6-month observation, groups with ?? and ??+??-genotypes demonstrated significant or tendency to higher level of LVEDV (? = 0,06, ? = 0,034), LVEDD (? = 0,057, ? = 0,01), LV ejection fraction (EF) (? = 0,037, ? = 0,07) respectevly. In patients with AC+CC-genotypes compared with AA were lower level of SDNN ($P = 0{,}049$), HF (? = 0,053), higher level of LF ($P = 0{,}069$) and LF/HF-index ($P = 0{,}046$).
Conclusions: Polymorphic ??+??-genotype cariers compared with ??-genotype of AGTIIR1 gene demonstrated more relevant increase of left ventricular diameters and volume, left atrium and LV myocardial mass in acute period of STEMI. After 6-month period in both groups LV dilatation and LVEF were observed. These data refer to the similar with Frank-Starling law dynamic of compensation. Patients with ??+??-genotypes compared with A? demonstrated unfavorable structure of LV CR and associates with more expressed sympathic-vagous dysbalance.

P1878

Artificial neural network for prediction of coronary artery disease in patients with abnormal myocardial perfusion

VA Kuznetsov[1]; EI Yaroslavskaya[1]; DV Krinochkin[1]; DV Teffenberg[1]; SM Dyachkov[1]
[1]Tyumen Cardiology Research Center, Tomsk National Research Medical Center, Tyumen, Russian Federation

Introduction: It is challenging often to detect coronary artery disease (CAD) without coronary angiography (CAG) in atypical patients with myocardial perfusion abnormalities by single photon emission computed tomography (SPECT) data. The purpose of the study was to reveal predictors of significant coronary lesions in patients with myocardial perfusion abnormalities by SPECT using artificial neural network.
Methods: From 13,283 consecutive patients with suspected CAD we selected patients after (99)Tc(m)-methoxyisobutylisonitrile (MIBI) gated SPECT and CAG who had no more than 3 months between the tests. There were 47 patients among them who had abnormal SPECT. We divided these patients in two groups: with significant coronary lesions (= 50% of lumen) by CAG and without.
Results: In 15 patients with abnormal SPECT and CAD compared to patients without CAD (n = 32) we observed more often acute myocardial infarction (37.1 vs 6.5%, $p = 0.005$) and higher level of serum glucose (6.9 ± 2.5 vs 5.3 ± 0.8 mmol/l, $p = 0.007$). Reduced left ventricular (LV) systolic function (LV ejection fraction < 50%) was more frequent in these patients (17.4 vs 7.4%, $p < 0.001$), as well as mild, moderate or severe mitral regurgitation (81.3 vs 59.4%, $p = 0.026$). They had higher index of LV wall motion abnormalities (1.4 ± 0.3 vs 1.0 ± 0.1), and only patients of this group had signs of myocardial scars detected by echocardiography (31.3%, all $p < 0.001$). According to the results of discriminant analysis, CAD was associated with index of LV wall motion abnormalities and mitral regurgitation. The obtained sensitivity, specificity and positive predictivity were 81%, 82%, and 81%, respectively. Then, artificial neural network was used to improve the diagnostic accuracy of the method. Application of multilayer perceptron allowed obtaining sensitivity, specificity and positive predictivity as 69%, 94%, and 85%, respectively.
Conclusion: Application of artificial neural network allowed to improve diagnostic accuracy of CAD detection in patients with abnormal SPECT.

P1879

Dynamics of the left ventricle remodeling in patients with Q- wave myocardial infarction

G U Guzal Mullabayeva[1]; RD Kurbanov[1]
[1]*The Republican Specialized Center of Cardiology, Tashkent, Uzbekistan*

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Purpose of the study: a comparative study of the dynamics of postinfarction remodeling of the left ventricle (LV), in patients with Q- wave myocardial infarction (MI) in a high-risk group.
Materials and Methods: The study included 294 male patients (mean age 52.6 ± 9.1 years) with primary Q- wave IM. Patients were included on the 10-14th day of the disease. Patients were referred to clinical and instrumental examinations for 6 months, 1st and 2 years of follow-up. All patients echocardioscopy (ECHO) were carried out. The following parameters were measured and calculated: end diastolic LV size (EDS), end systolic size of the LV (ESS), LV ejection fraction (LV EF). To quantify the geometric shape of the LV, the sphericity index (SI) = d 1/ d 2 was determined , where d1 is the longitudinal end-diastolic dimension of the LV, d2 is the transverse end-diastolic LV dimension. Results of the study: In two years of follow-up, the total mortality was 11.9% (35 patients). From non-cardiac causes 3 patients (1%) died, total cardiac mortality occurred in 32 (10.8%) patients, including sudden coronary death - in 24 (8.1%) patients. For the comparative analysis, the patients were divided into 2 groups: 1 group of surviving patients (n = 259), 2 group of the poor prognosis (n = 32). On 6 months Group 2 patients treated more often for progressive angina, the cases of hospitalization for the destabilization of the state and reinfarction. Thus, at the end of the follow-up period, reinfarction cases were registered in 40 patients (13.6%), 15 (46.8%) of them were observed in patients with group 2. On the 10-14th day, the SI index (normally tending to 2) in both compared groups was comparatively the same. Later in the group with an unfavorable prognosis there was a decrease in SI from 1.64 to 1.45($p < 0.05$), whereas in the group 1 the negative dynamics is not traced. Moreover, by the end of the second year of observation, the index of SI in the first group is close to 2. A summary of linear LV indices showed that already on the 14th day of the disease the group 2 had higher rates of EDS and ESS. By the 6th month in the 2 group there ESS was an increase of 8,2% ($p < 0,05$) and end EDS by 14% , while in the group 2 this trend is unreliable. By the end of the 1-year follow-up, the increase in EDS in 2 group relative to the initial values were already 14% and 19% ($p < 0.05$).In the same period, in the 1 st group, there was a significant reduction in the EDS by 5.2% ($p = 0.004$). It should be noted that by the end of the second year of follow-up, the first group showed a favorable dynamics in relation to these indicators. Conclusion: The progression of remodeling after MI is determined not only due early pathological remodeling. An important contribution is made by repeated MI, persistent angina pectoris.

Coronary Artery Disease - Treatment

P1880

Effect of intra-coronary (IC) Tirofiban following aspiration thrombectomy on infarct size, in patients with large anterior ST-segment elevation myocardial infarction (STEMI) undergoing primary PCI

A Basuoni[1]; WAEL El-Naggar[1]; M Mahdy[1]; S Al-Kaffas[1]
[1]*Cairo University Hospitals, Cardiology , Cairo, Egypt*

Background: Thrombus embolization during percutaneous coronary intervention (PCI) in ST-segment elevation myocardial infarction (STEMI) is common and results in sub-optimal myocardial perfusion and increased infarct size. Two strategies were proposed to reduce distal embolization and improve outcomes after primary PCI are bolus intra-coronary (IC) Tirofiban and manual Aspiration Thrombectomy.
Objective: To evaluate effect of Intra-coronary delivery of bolus Tirofiban following Aspiration Thrombectomy on reduction of infarct size using cardiac magnetic resonance imaging (cMRI) in patients with large anterior STEMI undergoing primary PCI.
Methods: A Prospective single-blind randomized controlled trial was conducted between August, 2014 and November, 2015. 50 patients with large anterior STEMI were screened at 2 sites in one country (Egypt). Aspiration Thrombectomy was performed in all patients using a 6 F aspiration catheter. Patients were randomized to IC Tirofiban (Study group) and no IC Tirofiban (control group). To ensure high intra-thrombus drug concentrations, a 25 mcg/kg bolus of Tirofiban was administered locally at the site of the infarct lesion via the aspiration catheter after flushing of the aspiration catheter well.
Primary end point was infarct Size at 30 Days measured by cMRI. Secondary end point was myocardial blush grade at the end of the PCI procedure. Major Adverse Cardiac and Cerebrovascular events (MACCE) at 30 days defined as re-infarction, stroke, severe heart failure and death.
Results: Evaluable MRI results at 30 days were present in only 40 of 50 patients (80%), with the most common reasons for missing data being patient re-infarction prior to 30 days and inability to tolerate the procedure. Patients randomized to IC Tirofiban compared with no IC Tirofiban had a significant reduction at 30 days infarct size (median, 15451 mm3 - IQR, 17404 mm3 - n = 20) vs (median, 43828 mm3 - IQR, 49599 mm3 - n = 20) P value= 0.002. myocardial blush grade results at the end of the PCI where present in 50 patients, randomized to IC Tirofiban compared with no IC Tirofiban had no significant difference (P value= 0.67). There is no significant difference in MACCE at 30 days between patients received bolus IC Tirofiban and patients who did not receive (P value= 0.723).
Conclusions: In patients with large anterior STEMI presenting early after symptom onset and undergoing primary PCI, infarct size at 30 days was significantly reduced by bolus IC Tirofiban delivered to the infarct lesion site following manual Aspiration Thrombectomy. There is no significant difference in MACCE at 30 days between patients received bolus IC Tirofiban and patients who did not receive.

P1881

Single centre experience with Impella CP in different clinical settings

I Sousa Casasnovas[1]; J Jorge Garcia Carreno[1]; M Juarez Fernandez[1]; C Devesa Cordero[1]; V Bruna Fernandez[1]; F Diez Delhoyo[1]; R Sanz Ruiz[1]; F Fernandez Aviles[1]; M Martinez Selles[1]
[1]*University Hospital Gregorio Maranon, Madrid, Spain*

Introduction: Impella CP is an intravascular microaxial blood pump that can support the circulatory system during a maximum of 5-7 days. The use of this short duration mechanical assist device in cardiogenic shock has significantly increased in the last few years.
Purpose: Our aim is to summarize our first experience using the Impella CP system in patients with refractory cardiogenic shock or undergoing high risk percutaneous coronary interventions.
Methods: We present a retrospective registry, conducted in a tertiary center, which shows our initial experience using Impella CP in different clinical situations. The device was cannulated percutaneously, by the interventional cardiologist at the hemodynamic lab, using the Seldinger technique under fluoroscopy guidance. The usual approach consisted in advancing the Impella Catheter to the ascending aorta and placing the pigtail at the left ventricle, 3 cm beyond the aortic annulus.
Results: From August 2017 to January 2018, Impella CP was initiated in ten cases, six were male (60%) and the mean age was 64.8 ± 17.9 years. Every patient had severe left ventricle dysfunction at admission (26.5 ± 9.14%) and the overall survival rate at hospitalization discharge was 70%.
Eight patients were assisted with the Impella System due to refractory cardiogenic shock despite high dose of inotrope drugs. Mean left ventricle function at admission was 26.9 ± 9.9%. Mean serum lactate before placing the device was 6.4 ± 4.5 mmol/L and two patients had cardiac arrest. The most frequent etiology was acute myocardial infarction that occured in five patients, followed by fulminant myocarditis in two cases and advanced heart failure due to restrictive cardiomyopathy in the remaining patient. The only major complication referred in these patients was the perforation of the left ventricle wall which was solved by cardiac surgery.
In three patients, Impella CP was successfully placed together with a veno-arterial extracorporeal membrane oxygenation, in order to unload the left ventricle.
On the other hand, the Impella device was used to support percutaneous coronary intervention in two patients with multivessel coronary disease and left ventricle dysfunction. It was placed before the procedure and removed after achieving revascularization without complications.
Conclusion: In our experience, the Impella CP System seems to be an effective and safe hemodynamic support therapy, with a low complications rate. Interestingly, it allows unloading the left ventricle in those patients being assisted with veno-arterial extracorporeal membrane oxygenation who develop ventricle distension.

P1882

Role of coronary collateral circulation in late presenter myocardial infarction

C Carmen Collado Moreno[1]; A Gutierrez-Barrios[2]; D Canadas-Pruano[3]; A Giraldez-Valpuesta[3]; M Alba-Sanchez[3]; S Gamaza-Chulian[3]; E Diaz-Retamino[3]; D Ruiz-Fernandez[3]; J Oneto-Otero[3]; G Calle-Perez[2]; R Zayas-Rueda[2]; E Marante-Fuertes[2]; R Vazquez-Garcia[2]
[1]*Puerto Real Hospital, Department of Cardiology, Puerto Real, Spain*; [2]*University Hospital Puerta del Mar, Cardiology, Cadiz, Spain*; [3]*General Hospital of Jerez, Cardiology, Cadiz, Spain*

Aim: Demonstrate if good coronary collateral circulation(CCC) may be related to myocardial viability and left ventricular ejection fraction (LVEF) in late presenter myocardial infarction (MI) patients (>24h).

Methods: Ambispective multicenter study on 164 patients with a late presentation MI and angiographic evidence of a thrombotic occlusion (TIMI 0) of a major coronary artery from 2009 to 2016.
The Rentrop and Werner score were used for the angiographic categorization of CCC. Two experienced cardiologists retrospectively evaluated the angiographies in a blinded manner to classify the CCC into grades.
12 patients were prospectively followed up and left ventricular(LV) wall motion score(WMS) was assessed for each of the 17 segments of the LV with a visual scoring system in which 1 = normal, 2 = hypokinetic, 3 = akinetic, and 4 = dyskinetic.
Results: The median follow up was 3.4 years(IR 1.1-5.5 years). Culprit vessel revascularization was attempted in 83% of the patient (129/155) and successfully recanalized in 84% of them (108/129). Successful PCI of culprit vessel was not associated neither with LVEF at baseline (46 ± 13vs50 ± 10 p = 0.06) nor with increase in LVEF, WMS at baseline and at follow up (p>0.1 for all).
LVEF was significantly higher in patients with good CCC at baseline (53 ± 8 vs 45 ± 12, p <0.001) and at follow-up (56.7 ± 11vs 44 ± 11,p = 0.01). Qualitative assessment of culprit vessel territory motion showed significant differences between patients with poor and good CCC(p = 0.019): dyskinesia (15%vs3%); akynesia (41%vs12%), Hipokynesia (22%vs59%) and normokynesia (22%vs25%) respectively.
Myocardial viability in the culprit vessel territory was confirmed in 56.6% of patients (90/159), 4.5% of them had akinesia and viability was assessed by a stress echocardiogram. Viability was significantly higher in good compare to poor CCC patients (76.5%vs33.8%, p <0.001).
Rentrop and Werner classification were respectively correlated to: LVEF (r = 0.38, p = 0.001 and r = 0.32, p = 0.005);WMS at baseline (r=-0.605, p0.049 and r=-0.55, p = 0.07) and WMS at follow-up (r=-0.66 p = 0.01 and r=-0.47, p = 0.11) and both classifications were significantly higher in patients with myocardial viability: 1.77 ± 0.9vs0.9 ± 0.9 p <0.001 for Rentrop and 1 ± 0.6vs0.49 ± 0.5, p <0.001 for Werner.
Rentrop and Werner were also correlated with follow-up EKG: Number of leads with persistent ST segment elevation (r=-0.78, p = 0.004 and r=-0.63, p = 0.03) and number of leads with Q waves (r=-0.72, p = 0.01 and r=-0.57, p = 0.06) respectively
Conclusions: Good CCC was related to myocardial viability and LVEF in late presenter MI patients. These patients could benefit from revascularization even late in the course of a MI. A randomized trial should be encouraged to confirm these findings.

P1883

Intraoperative inflammatory response and heart metabolism in patients with severe ischemic heart failure

N Maroz-Vadalazhskaya[1]; I Russkikh[2]
[1]Belarusian State Medical University, Minsk, Belarus; *[2]Scientific and Practical Center of Cardiology , Minsk, Belarus*

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Surgical treatment of severe ischemic heart failure (IHF) remains under discussions due to multiple impact factors and relatively low rate of survival.
Aim the study was to test the hypothesis of the inflammatory impact on the heart metabolism during open heart surgery in patients with severe IFH as well as to identify the blood biomarkers as a risk factors of adverse cardiac events.
Cohort: 32 male patients with a mean age of 55,2 years, LVEF <35% and SIHF were included. Patients of gr.1 with stable IHF (n 24 pts, mean age 54.8 ± 11.6 yrs, LVEF 31.7 ± 3.3) underwent CABG along, while 8 patients of gr.2 with IHF and ambulatory NYHA class IV (mean age 56.9 ± 7.6 yrs, LVEF 25.3 ± 2.1, PAPrsyst 56.2 ± 7.4 mm Hg) had CABG+LVAD. All patients were operated in similar conditions. H-FABP, IL-6, IL-6 receptors, glucose, lactate and free fatty acids (FFA) were assessed before surgery, during ischemia and after coronary reperfusion in simultaneously taken arterial and coronary sinus blood.
Results: Patients of both groups basally had significantly increased levels of FFA (p = 0,0001) and lactate (p = 0,0004), and patients of group 2 had lower utilization of FFA after surgery than preoperatively (p <0,0001). Before surgery a 6-fold increased IL-6 level was found in group 2 (p = 0.03 vs normal range), but normal level in gr.1 (between groups p = 0,01). During operation at the end of total ischemia period the increasing of IL-6 was found in both groups, but more significant in coronary sinus in gr.2 (p = 0.03). Simultaneously the increasing of IL-6 receptors level was revealed in coronary sinus blood in gr.2 (OR 1,2-5.1, p = 0.004). Patients of gr.1 had the falling of IL-6 receptors in both arterial and coronary sinus samples (p = 0.06 and p = 0.029 resp.) before repefusion. After reperfusion a 7-fold rocketing of H-FABP (p <0.000), glucose and FFA coronary sinus levels (p <0,001 for both; FFA between arterial and coronary sinus p = NS) was found in patients of gr.2. Preoperatively IL-6 strongly correlated with PAPr sys (r = 0,62 p = 0,001), during ischemia IL-6 as well as IL-6 receptors correlated negatively with postoperative LVEF (p = 0,01), ESVI (p = 0,01). Coronary sinus blood H-FABP level after reperfusion correlated with preoperative right ventricle systolic function (FAC r=-0.54, p = 0.003), systolic pulmonary pressure (r = 0.38, p = 0.037), and early postoperative cardiac death (r = 0.47, p = 0.01) in whole cohort. In patients of gr.2 the level of IL-6 receptors, coronary sinus H-FABP and FFA correlated with the duration of inotrope and artificial circulation support (p = 0,0001), early cardiac death (p = 0,001).
Conclusion: the rocketing of IL-6 receptors is linked to the myocardial washing out of glucose and FFA in IHF patients. The inflammative response could be a cause of myocardial death as well as metabolic depletion in patients with severe IHF, especially in group with end-stage HF. IL-6 receptors and H-FABP could be taken as markers of adverse cardiac events after open-heart surgery.

P1884

Promising 12-months clinical results for anaortic multivessel all-arterial minimally invasive direct coronary bypass surgery via distal mini-sternotomy

I Martinovic[1]; S Lindemann[2]; M Irqsusi[1]; J Mirat[3]; A Vcev[3]; T Wittlinger[4]; M Noutsias[5]
[1]University Hospital Giessen and Marburg, Cardiovascular Surgery, Marburg, Germany; *[2]Helios Hospital Warburg, Cardiology, Warburg, Germany*; *[3]University J.J. Strossmayer, Internal Medicine, Osijek, Croatia*; *[4]Asklepios Clinic Goslar, Cardiology, Goslar, Germany*; *[5]University Clinic Halle (Saale), Mid-German Heart Center, Department of Internal Medicine III (KIM-III), Division of Cardiology, Halle, Germany*

Background: Minimally-invasive direct coronary artery bypass grafting (MIDCAB) was developed to decrease perioperative morbidity, some of which may be related to the use of cardiopulmonary bypass and to cross-clamping of the aorta. We report our initial experience with multivessel MIDCAB through the distal mini-sternotomy (DIMS). DIMS is performed to achieve access to the left and right internal thoracic arteries and to reach the left anterior descending coronary artery, diagonal branches and right coronary artery.
Methods: Between January 2016 and January 2017, n = 12 patients with significant coronary artery disease of the LAD and the RCA underwent multivessel, all-arterial MIDCAB through a distal midline skin incision from the fourth intercostal space to the xyphoid process, with L-or T-shaped division of the sternum. The mean-age was 61.5 +/- 5.2 years (range: 52-71 years).
Results: Patients underwent all-arterial revascularization: LIMA in 12 patients, radial artery (RA) in 10, RIMA in 2 patients. The mean number of grafts per patient was 2.08+/-0.4 (range: 2-3). The mean length of the skin incision was 8.5 +/- 1.3 cm (range: 7 to 11 cm). There was no perioperative ischemia, postoperative bleeding or arrhythmia events. No postoperative cognitive dysfunction occured. The mean hospital stay was 5.6 days. None major adverse cardial event (MACCE) ocured at the 12-month follow-up. All patients were in New York Heart Association class I, and no wound complication occurred during follow-up.
Conclusions: Although MIDCAB-DIMS is technically more demanding than conventional procedures and our experience is limited, we conclude that this technique can be used safely in selected patients promising 12-months follow up results.

P1885

Manual thromboaspiration in patients with myocardial infarction: in-hospital assessment of class of heart failure and systolic function

I A Leonova[1]; S Boldueva[1]; D Maznev[1]; E Shloido[2]; I Kochanov[1]
[1]North-Western Sate Medical University named I.I. Mechnikov, St-Petersburg, Russian Federation; *[2]City hospital ? 2, Saint-Petersburg, Russian Federation*

Since the publications on manual thromboaspiration (MT) in ST-elevation myocardial infarction (STEMI) are controversial, it is of interest to assess the severity of heart failure (HF) in such patients during hospitalization.
Materials and Methods: It was performed a retrospective analysis of 146 cases of STEMI treated by percutaneous coronary intervention (PCI). The average age of patients was 60.8 ± 1.3 years, 97 men (66%) and 49 women (34%). In 78% of patients, STEMI was a debut of coronary artery disease. All patients were discharged alive.
Results: Patients were divided into 2 groups: 80 patients treated by PCI only and 66 patients treated by PCI plus MT. Patients of both group were similar by gender, age, localization of MI (anterior MI (55% without MT and 53% with MT p>0.05). The majority of patients in both group (95,9%) had TIMI 3 coronary blood flow. While the degree of myocardial perfusion less than 3 on the MBG scale was 8.2% in the group without MT and 4.1% in patients with MT (p < 0.05). The debris was obtained in 88.4% of cases of thromboaspiration. The majority of patients, both in the group without MT and with MT had a preserved systolic function at the time of discharge (73,3% vs 85,7% p < 0.05). The mild systolic dysfunction of the left ventricle (ejection fraction up to 40%) was observed in 23.3% of patients in the group without MT and 10.9% with MT (p < 0.05); moderate systolic dysfunction (ejection fraction 40-30%) - 3.4% vs. 1.4%, respectively (p < 0.05). Severe systolic dysfunction (ejection fraction less than 30%) was not observed in both group. Mild mitral regurgitation was present

in 39% of patients without MT and 33% after thrombaspiration (p < 0,05); moderate and severe mitral regurgitation - 14.4% and 9.6% (p < 0,05), tricuspid regurgitation of 2-3 degrees-4.8% versus 0.68%, respectively (p < 0,05). 20% of examined patients had pulmonary hypertension. Pulmonary hypertension was observed in 11.6% of patients without thrombospiration and in 2.7% of patients after thromboaspiration (p < 0,05). At discharge 46% patients without MT and 56.32% with MT had no symptoms of HF. The I functional class of HF by NYHA was almost the same in both groups - 21.2% versus 18.5% (p>0.05). However, II and III functional classes HF were more often observed in the group without thromboaspiration - II functional class - 30.1% without MT and 24.5% with MT (p < 0,05); III functional class - 2.7% against 0.68% respectively (p < 0,05).
Conclusions: Performing of manual thromboaspiration could prevent the formation of systolic dysfunction in patients with severe thrombotic lesion of the coronary artery, which provides a lower functional class of heart failure at discharge and improves short-term prognosis in patients with myocardial infarction.

P1886
Mid-range systolic dysfunction outcomes in ST elevated acute coronary syndrome

M Moz[1]; F Cordeiro[1]; J Guimaraes[1]; F Goncalves[1]; R Margato[1]; P Mateus[1]; JI Moreira[1]
[1]*Hospital Center of Tras-os-Montes and Alto Douro, Cardiology, Vila Real, Portugal*

Introduction: mid range systolic dysfunction (MidR) represents a new group of patients in whom the prognosis and therapeutic options are not well established post ST elevated acute myocardial infarction (STEMI). These patients were excluded from most randomized trials so there is limited data on their management.
In this study we compare the prognosis of these patients versus patients with normal systolic function (N) and depressed systolic function (Dep)
Methods: Retrospective study of consecutive patients admitted with non-fatal STEMI diagnosis submitted to primary coronary intervention between January 2011 and December 2016. Systolic function was evaluated using ejection (EF) fraction and we compared 3 groups of patients: N with EF = 50%; MidR With EF = 40% and <50% and Dep with EF <40%.
Medical records were used to collect sociodemographic, clinical, previous medical history (heart failure, renal failure, cardiovascular risk factors) and coronary angiography data.
The endpoints studied were heat failure, death and a composite of major adverse events (MACE): revascularization, re-infarction, heart failure and death.
Results: 442 patients were included in the analysis with 65 ± 13.4 years. There were differences in age (N = 63.0; MidR = 65.6 and Dep = 68.4 years p <0.05), prior myocardial infarction (N = 25%; MidR = 25% and Dep = 50% p <0.05) prior coronary intervention (N = 27.6%; MidR = 31.0% and Dep = 41.4% p <0.05) and anterior descending artery as culprit vessel (N = 28.4%; MidR = 33.8% and Dep = 37.8% p <0.05) between groups.
Median follow up was 24 months (14-42 IQR). In multivariate analysis MidR was associated with worse outcome then N patients as they had more heart failure (HR = 4.2 CI:1.6-10.9), heart failure and death (HR = 2.6 IC:1.3-5.45) and MACE (HR = 1.9; CI:1.16-3.13) during follow-up. There were also a trend to higher mortality but did not reach statistical significance (OR = 1.8 p = 0.08).
Conclusion: MidR patients despite the lack of evidence guideline based effective therapies are a group of patients with a clearly worse outcome than patents with N. It is essential to develop new strategies to improve these patients outcomes.

P1887
Effect of intracoronary adenosine administration during primary PCI

A Metwaly[1]; M Altahhan[1]; M Mokarrab[1]; T Bssiony[1]; M Alshorbagy[2]
[1]*Al-Azhar University, cardiovascular department, Cairo, Egypt*; [2]*Al-Azhar University, Clinical Pathology, Cairo, Egypt*

Background: Aim of the present study was to evaluate effect of intracoronary (IC) adenosine versus placebo in STEMI patients undergoing primary PCI (pPCI).
Methods: for eligible STEMI patients this study includes 55 patients divided into two groups, study group who received IC adenosine (30 patients) and control group (25 patients) who received standard therapy , all were subjected to immediate pre and post pPCI 12 leads ECG, pPCI within 90 minutes from first medical contact, TIMI flow grade,TIMI myocardial perfusion grade (TMP), and full study of trans thoracic echocardiography (TTE) within 24 hrs and follow up TTE 40 days post MI. Patients who were randomized to the adenosine group were given 6 mg of adenosine (diluted into 5 ml normal saline) through the guiding catheter into the culprit coronary artery after aspiration of the present thrombi (if applicable) and just prior to stent deployment.
Results: Incidence of ST resolution , TIMI flow grade , TMP grade was significantly higher in the IC adenosine group than in the placebo group ,Furthermore, we found a larger increase in LVEF with a parallel reduction in the incidence of heart failure in the IC adenosine group. Finally, IC adenosine administration was associated with a significantly lower incidence of major adverse cardiac events
(MACE) both at short and long term follow up
Conclusions: This study is demonstrating a clinical benefit for IC adenosine in hard endpoints, such as adverse cardiovascular events and Heart failure in STEMI patients undergoing primary PCI.

P1888
Management of patients diagnosed with tako-tsubo syndrome

C Carmen Collado Moreno[1]; RF Garcia-Gonzalez[1]; I Valiente-Aleman[2]; D Castro-Sanchez[3]; S Blasco-Turrion[1]; I Lobo-Torres[1]; A Gomez-Juanatey[1]; PJ Gonzalez-Perez[1]; FJ Morales-Ponce[1]
[1]*Puerto Real Hospital, Department of Cardiology, Puerto Real, Spain*; [2]*Puerto Real Hospital, Critical Medical Medicine, Puerto Real, Spain*; [3]*University of Cadiz, Cadiz, Spain*

Background and Purpose: Takotsubo syndrome (TTS) was first described in Japan in 1990 by Sato and Mayo Clinic criteria were proposed in 2004 and modified in 2008 facilitating the diagnosis of TTS. The aim of this study is to describe prevalence, clinical features, treatment and short-term prognosis of patients diagnosed with TTS.
Methods: A restrospective observational study of patients admitted to Intensive Care Unit (ICU) of our hospital meeting the criteria for TTS was performed between March 1st 2007 and February 28 th 2017.
Results: A total of 1602 patients with diagnosis of acute MI were registered but only 30 patients fulfilled inclussion criteria for TTS.
The prevalence of TTS was 1.87% with a mean age of 59.73 ± 10.9 years. TTS was more frequent in women (83.3%). Cardiovascular risk factors were hypertension (56.6%), dyslipidemia (30%), diabetes (20%) and smoking (13.3%). Anxiety or depressive disorders were only found in 2 patients (6.6%). Preferred treatments at discharge were aspirin (96%), beta blockers (90%), ACEI/ARBs (83.3%), statins (70%) and DAPT (53.3%). One month follow-up of these patients revealed one death (3.3%) due to cardiovascular disease. This patient suffered a second episode of TTS after an elective major surgical intervention.
Conclusions:
We found a limited number of patients, nevertheless TTS showed an important short-term mortality and prevalence between Acute Coronary Syndromes admitted to our ICU. Clinical features were similar to the International Registry except anxiety or depressive disorders. Beta blockers were preferred to ACEI/ARBs.

P1889
Therapeutic particularities and evolution of acute coronary syndrome in patients with chronic kidney disease

S Antit[1]; B Ben Kaab[2]; C Gharbi[2]; I Slama[1]; S Belakhel[2]; I Boussabeh[1]; M Thameur[1]; L Zakhama[1]; S Benyoussef[1]
[1]*Interior Security Forces Hospital, Department of Cardiology, Marsa, Tunisia*; [2]*Interior Security Forces Hospital, Department of medicine interne, Marsa, Tunisia*

Background: Although the improvement of the diagnostic and therapeutic means, the impact of chronic kidney disease (CKD) on mortality and morbidity in patients acute coronary syndrome (ACS) is still under estimated. The aim of our study is to determine the therapeutic and follow up particularities of ACS in patients with CKD.
Methods: We conducted a retrospective descriptive study on 100 patients hospitalized in interior security forces hospital in Marsa between 2010 and 2016 for an ACS. Our study population was divided into two groups : group 1 patients with creatinine clearance superior or equal to 60ml per minute (50 patients) and group 2 patients with creatinine clearance under 60 ml per minute (50 patients). For every patient included, we assessed demographic, clinic, therapeutic and follow up data.
Results: The mean age of our study population was 61.88 years, 87 males and 13 females. Group 2 patients were older and have more comorbidities than group 1 patients : diabetes p = 0.005, arterial hypertension p = 0.008 and stoke p = 0.001. While diagnosed with ACS, group 2 patients had more acute pulmonary edema (p < 0.001), more left ventricular hypertrophy (p = 0.001) and left ventricular dysfunction (p = 0.001) in echocardiography. Group 2 patients had less thrombolysis (p = 0.001), less low-molecular-weight heparin, beta blockers and angiotensin-converting enzym inhibitors. In percutaneous coronary intervention they had more two and three vessel disease than group 1 patients (p = 0.01). During follow up (48 months), group 2 patients had more major acute cardiovascular and cerebral events (MACCE) than group 2 patients (coronary restenosis p = 0.05, heart failure p < 0.001, death p = 0.001).

Conclusion: ACS represents an event of poor prognosis in patients with CKD. Guidelines require ACS to be managed similarily in patients with CKD as patients with normal renal function.

P1890

Radial artery accesses is associated with lower mortality in patients undergoing primary PCI : a report from scaar

E Elmir Omerovic[1]
[1]*Sahlgrenska University Hospital, Gothenburg, Sweden*

Background: The purpose of this observational study was to evaluate effects of radial artery access (RA) versus femoral artery access (FA) on risk of 30-days mortality (primary endpoint), in-hospital bleeding, stroke and cardiogenic shock (secondary endpoints) in patients with STEMI undergoing primary PCI.
Methods: We used data from SCAAR registry (Swedish Coronary Angiography and Angioplasty Registry) for procedures performed in Sweden between 2005-2016. We evaluated the primary and secondary endpoints in 44,125 patients with STEMI, n = 24,119 in RA and n = 20,006 in FA. The two groups were compared using multilevel logistic regression to account for hierarchical database. Adjustments for differences in baseline characteristics were made with propensity score. The following variables were included in the calculation of the propensity score: age, gender, smoking habits, hypertension, diabetes, hyperlipidaemia, severity of coronary artery disease, previous infarction, previous PCI, previous CABG, anticoagulation therapy with glycoprotein IIb/IIIa receptor antagonists (GP IIb/IIIa), bivalirudin, P2Y12 antagonist, unfractionated heparin/low-molecular weight heparins (UH/LMWH), DES, completeness of revascularization, number of stents, type of lesion, reperfusion time, pretreatment with P2Y12 antagonist, regular vs. off-hours, calendar year, hospital and pharmacological treatment after discharge. We used instrumental variable (IV) method (for adjustment of hidden bias) for sensitivity analysis with calendar year as the treatment-preference instrument. Regression modelling was performed before and after exclusion of patients with cardiogenic shock.
Results: The two groups were different in baseline characteristics with RA patients having generally less traditional risk factors. There were 2,308 (5.2%) deaths, 889 (3.7%) in RA and 1,419 (7.1%) in FA. After adjustment, RA was associated with lower risk of death (OR 0.50, 95% CI 0.45 - 0.57, P <0.001), lower risk of in hospital bleeding (OR 0.46, 95% CI 0.39 - 0.54, P <0.001) and lower risk of cardiogenic shock after PCI (OR 0.50, 95% CI 0.42 - 0.59, P <0.001). We found no interaction between access site and age, gender and cardiogenic shock regarding 30-days mortality and bleeding. Access site did not modify risk of stroke. IV analysis have shown similar risk estimates for death at 30-days and cardiogenic shock. Exclusion of patients with cardiogenic shock did not substantially change the estimated risk of death at 30 days.
Conclusions: In patients with STEMI, primary PCI through radial artery access is associated with reduced risk of 30-days mortality, in-hospital bleeding and cardiogenic shock. Our study supports current ESC guidelines which recommend RA as the first choice for primary PCI.

Valvular Heart Disease - Epidemiology, Prognosis, Outcome

P1891

Anemia is an independent risk factor of adverse outcome in patients with prosthetic valve endocarditis and heart failure

MM Monica Mariana Baluta[1]; E Panaitescu[2]; MM Vintila[3]
[1]*Carol Davila University of Medicine-St Pantelimon Clinical Emergency Hospital-Cardiology Department, bucharest, Romania*; [2]*Carol Davila University of Medicine and Pharmacy , Medical Informatics and Biostatistics, Marketing, Medical Technology , Bucharest, Romania*; [3]*St. Pantelimon Emergency Hospital, Cardiology, Bucharest, Romania*

Introduction: Anemia from prosthetic valve endocarditis (PVE) has a multifactorial origin and represents a disease marker. Nevertheless, current work does not analyzed anemia as prognostic element in patients with an initial antibiotic only intention to treat in a potentially "surgical" disorder.
Purpose: The objective of our study is to evaluate how the hemoglobin (Hb) levels would affect the clinical course, short and long-term prognosis in prosthetic valve endocarditis patients with initial medical intention to treat.
Methods: We analyzed retrospectively 126 cases of infective endocarditis admitted over 5 years (2000-2004) in two centers with reciprocal and surgical backup. From those cases we selected 56 patients with PVE (n = 29 early, n = 27 late) with prior heart failure syndrome. Initial follow up was done at the end of full course of antibiotic (AB) therapy. Long-term follow-up was done after 12.87 ± 0.97 years with the help of national insurance database. Analyzed variable: clinical; hemoglobin at admission: HbA, at the end hospitalization in the medical depatament: HbFin. Patients lost to follow up were excluded from our analysis.
Results: Short term outcome with initial antibiotics only intention to treat and irrespective of antibiotics type with overall AB cure duration 33.55 ± 12.8 day was: 90.4% survival rate, 2% in-hospital death, 71% responders to antibiotics, 21.4% of patients referred for early valve surgery with 66.6% surgical survival rate. Deceased patients presents with a significant (p = 0.07) lower initial hemoglobin (8.58 ± 1.38 g/dl) than survivors (9.76 ± 1.40 g/dl) while final hemoglobin remains persistent low 8.46 ± 0.87 g/dl in first category compared with 10.64 ± 1.4 g/dl in the latest (p = 0.001). Long-term follow up survival rate was 44%, very low compared with other contemporary analysis. After exclusion of those lost to follow up at final follow up (12.87 ± 0.97 years), the same findings were observed regarding hemoglobin levels: HbIn in survivors was10.01 ± 1.55 g/dl versus 9.21 ± 1.22 g/dl in those deceased (p = 0.06), HbFin being 10.81 ± 1.53 g/dl in survivors versus 9.98 ± 1.54 g/dl in deceased ones (p = 0.08). Anemia was not statistically related to hemodynamic instability irrespective of baseline ejection fraction or NYHA class.
Conclusions: Hemoglobin levels were significantly lower in deceased patients than in survivors and this fact correlates significantly with short-term and long-term mortality making it an important independent risk factor of death. In this old series of patients with prosthetic valve endocarditis the initial conservative intention to treat fail at long-term follow. Whether early surgery approaches in this category provide a relevant benefit could not be established due to small sample size.

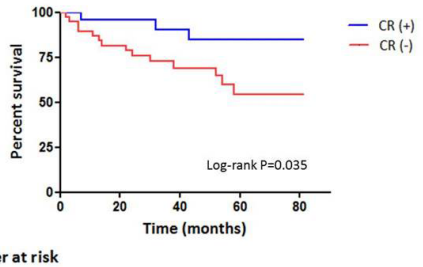
P1892

Predictive value of exercise stress echocardiography in asymptomatic patients with severe aortic regurgitation and preserved ejection fraction

S-J Sung-Ji Park[1]; SY Lee[1]; EY Kim[1]; SA Chang[1]; JO Choi[1]; SC Lee[1]; SW Park[1]
[1]*Samsung Medical Center, Seoul, Korea Republic of*

Background: The management of asymptomatic patients with severe aortic regurgitation (AR) and preserved left ventricular (LV) systolic function has remained controversial. We aimed to evaluate the value of exercise stress echocardiography (ESE) in asymptomatic severe AR with preserved LV systolic function as predicting high risk patients who might benefit from early referral for surgery.
Methods: Symptom-limited treadmill ESE was performed in 67 asymptomatic with severe AR (effective regurgitant orifice area >20 mm2, regurgitant volume >30ml), LV end-systolic diameter < 50 mm and preserved LV function (ejection fraction (EF) >50%). Post-exercise EF increase of >4% was defined as contractile reserve (CR). The primary outcome was defined as the composite of development of symptoms, deterioration in LV function (EF < 50%) and aortic valve replacement (AVR) at follow-up. The operation performed within 60 days from ESE was excluded.
Results: CR (+) was noted in 28 and CR (-) in 39 patients. Compared with CR (+), the CR (-) group was older (52.0 ± 14.0 years vs CR 43.8 ± 10.6 years, p = 0.011) and had higher Ln N-terminal natriuretic peptide (NT-proBNP) [CR 5.2 (4.5-5.7) vs CR 4.1 (3.7-5.1), p = 0.001]. Also CR (-) group showed lower exercise time than CR (+) group (576 ± 159 seconds vs 671 ± 108 seconds, p = 0.008). Otherwise, there were no differences in demographics and imaging data between 2 groups according to CR. During follow-up duration of 46 ± 23 months, the primary outcome occurred in 17 (25%) including development of symptoms (n = 9), new onset LV systolic dysfunction (n = 1) and AVR (n = 7). 14 of 17 were CR (-) group. And the survival rate during follow-up was significantly lower in the CR (–) group than in the CR (+) group of asymptomatic severe AR patients (log-rank P = 0.035).
Conclusion: In asymptomatic patients with severe AR and preserved LVEF, the absence of CR in ESE was an independent predictor for deterioration of symptoms or LV systolic function, and suggesting that ESE may be able to further stratify the current guideline for AVR.

Figure. Kaplan-Meier survival curves in asymptomatic severe aortic regurgitation (AR) patients according to the presence of contractile reserve (CR).



Number at risk

CR (-)	39	30	22	11	0
CR (+)	28	22	13	7	0

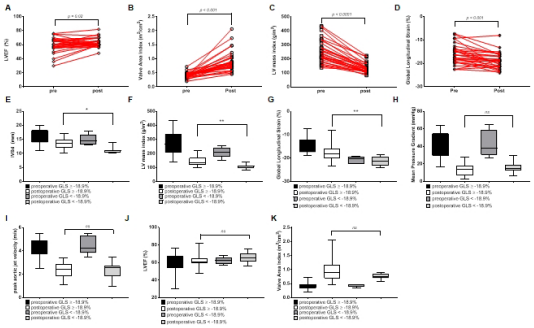
P1893

Left ventricular global longitudinal strain as a predictor of left ventricular reverse remodelling after surgical aortic valve replacement

P Zafirovska[1]; I Milev[1]; L Georgievska Ismail[2]; N Hristov[1]; RA Rosalia[3]; Z Mitrev[1]
[1]*Zan Mitrev Clinic, Cardiosurgery, Skopje, Macedonia The Former Yugoslav Republic of*; [2]*University Clinic of Cardiology, Skopje, Macedonia The Former Yugoslav Republic of*; [3]*Zan Mitrev Clinic, Clinical Research, Skopje, Macedonia The Former Yugoslav Republic of*

Introduction: In aortic stenosis (AS) the left ventricular ejection fraction (LVEF) is commonly used as an indicator of disease severity and the necessity for surgical aortic valve replacement (SAVR). However, impaired LVEF (< 50%) only identifies advanced disease. Thus, more sensitive, cardiac parameters that could identify severe AS at an earlier stage would improve clinical decision making and prognosis.
Purpose: To evaluate left ventricular (LV) global longitudinal strain (GLS) as an independent parameter to assess SAVR procedural success and to determine its pre-operative prognostic significance regarding LV reverse remodelling after surgery.
Methods: We performed detailed pre- and postoperative 2D echocardiography using Philips EPIQ 7, in 30 patients (65.47 ± 10.55 years; 56.7 % males) that underwent SAVR, including evaluation of GLS with speckle tracking. The mean follow-up period was 4.9 ± 0.73 months.
Results: All patients were symptomatic with an LVEF of 59.33 ± 10.74%. The mean pre-operative aortic valve area index (AVAi), LVmass index (LVMi) and GLS were 0.41 ± 0.10 cm^2/m^2, 256.2 ± 81.7 g/m^2 and -16.05 ± 4.23%, respectively. The mean GLS improved to -18.82 ± 3.46% ($p < 0.01$) after surgery which coincided with an increased mean AVAi, 1.72 ± 0.68 cm^2/m^2 ($p < 0.01$) and decreased mean LVMi of 135.1 ± 36.4 g/m^2 ($p < 0.01$). In contrast, mean post-operative LVEF only slightly increased to 63.30 ± 6.61% ($p = 0.022$). Pre-operative GLS showed a positive correlation with the post-operative LVMi ($r^2 = 0.35$, $p < 0.01$), diastolic septal thickness (IVSd) ($r^2 = 0.33$, $p < 0.01$) and GLS ($r^2 = 0.35$, $p < 0.01$).
Applying a cut-off value of -18.9%, in the patients with better pre-operative GLS (>-18.9%) we observed a significant improvement of postoperative LVMi, IVSd and GLS values (Fig. 1) suggesting better LV reverse remodelling compared to patients with a pre-operative GLS of >-18.9.
Conclusion: The GLS of the LV is abnormal in severe AS patients and precedes LVEF deterioration. SAVR improves the LV GLS implicating an improvement of the subclinical systolic dysfunction. Better preoperative GLS values are associated with more successful LV reverse remodelling after surgery.

Figure 1. Pre- and postoperative hemodynamic parameters



P1894

Prediction of mortality after Transcatheter Aortic Valve Implantation: A comparison of Logistic EuroSCORE, EuroSCORE-II and STS score

E Munoz-Garcia[1]; M Munoz-Garcia[1]; A J Antonio Jesus Munoz Garcia[1]; JM Garcia-Pinilla[1]; AJ Dominguez-Franco[1]; F Carrasco-Chinchilla[1]; JH Alonso-Briales[1]; JM Hernandez-Garcia[1]; MF Jimenez-Navarro[1]; E De Teresa-Galvan[1]
[1]*University Hospital Virgen de la Victoria, Department of Cardiology, Malaga, Spain*

Transcatheter aortic valve implantation (TAVI) is an established treatment alternative to surgical aortic valve replacement in high-risk and inoperable in patients with severe and symptomatic aortic stenosis. In addition, in recent years, it has been proposed in patients with intermediate or low risk, whose results are unknown yet. The aim of this study was to analyze the surgical risk of patients treated with TAVI and to evaluate clinical outcomes in according to risk scores.
Methods: Between April-2008 and December-2016, 582 patients with severe and symptomatic aortic stenosis were treated with TAVI. The surgical risk estimation was analyzed through Logistic EuroSCORE, EuroSCORE-II and STS score, and were categorized into low, intermediate and high risk.
Results: In according to logistic EuroSCORE and STS score, 29.5% and 21.3% were high surgical risk, intermediate 40.1% and 61.4% and low 30.4 and 21.3, respectively.
In-hospital and late mortality higher for patients at high surgical risk according into logistic EuroSCORE (2.3% in low risk vs. 1.7% intermediate vs. 7% in high, p = 0.017 and 22.15 vs. 33.3% vs. 45.3%, p = 0.001, respectively. However, there were no significant differences for in-hospital mortality among the different groups according to STS score (5% vs. 2.2% vs. 5.6%, p = 0.667) and for late mortality (25.3% vs. 29.5% vs. 51.3%, p = 0.001). The logistic EuroSCORE and EuroSCORE-II presented an acceptable capacity for in-hospital mortality, the area under the curve was 0.652 (95% CI 0.510-0.795), p = 0.02 and 0.646 (95% CI 0.518-0.774), p = 0.026, respectively. However, STS score did not presented discriminant ability, the area under the curve was 0.560 (95% CI 0.410-0.710), p = 0.365.
Conclusions: In our series, patients categorized into high surgical risk were associated with increase mortality at 30 days. Logistic EurtoSCORE and EuroSCORE-II presented discriminatory power

Valvular Heart Disease - Treatment

P1895

Long-term outcomes after transcatheter aortic valve replacement in high-risk patients with severe aortic stenosis.

E Munoz-Garcia[1]; M Munoz-Garcia[1]; A J Antonio Jesus Munoz Garcia[1]; F Carrasco-Chinchilla[1]; JM Garcia-Pinilla[1]; AJ Dominguez-Franco[1]; JH Alonso-Briales[1]; JM Hernandez-Garcia[1]; MF Jimenez-Navarro[1]; E De Teresa-Galvan[1]
[1]*University Hospital Virgen de la Victoria, Department of Cardiology, Malaga, Spain*

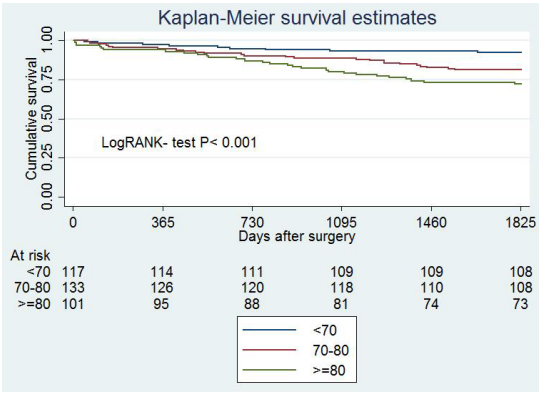
Transcatheter Aortic valve Replacement (TAVR) has emerged as an alternative to surgical aortic valve replacement for patients considered at high or prohibitive operative risk. It is widely known the short and mid-term outcomes, however, is limited about long-term outcomes. The aim of this study was to determine the survival and the factors predicting mortality after TAVR with the CoreValve prosthesis.
Methods: From April 2008 to December 2017, the CoreValve prosthesis was implanted in 620 patients with symptomatic severe aortic stenosis with deemed high risk.
Results: The mean age was 79.5 ± 6.8 years. The logistic EuroSCORE and STS score were 17.4 ± 11% and 6.01 ± 4%, respectively. The implantation success rate was 98.87%. In-hospital mortality was 3.7%, and the combined endpoint of death, vascular complications, myocardial infarction or stroke had a rate of 15.5%. The late mortality (beyond 30 days) was 33.9%. Survival at 1, 2, 3, 4, 5, 6 and 7 years were 89.2%, 82.3%, 70.8%, 62.1%, 54%, 47% and 41.9% respectively, after a mean follow-up of 41.4 ± 27 months. The NYHA functional class improved from 3.1 ± 0.6 to 1.77 ± 0.7 in the follow-up. The predictors of cumulative mortality were: Charlson index [HR 1.18 (95% CI 1.09-1.28), p = 0.001], Acute Kidney Injury [HR 1.83 (95% CI 1.29-2.57), p = 0.001], Frailty [HR 1.67 (95% CI 1.17-2.14), p = 0.001], Left ventricular ejection fraction [HR 1.011 (95% CI 1.051-01.874), p= 0,027], COPD [HR 1.4 (95% CI 1.05-1.87), p= 0,022] and protective factor was a higher Karnosfky index [HR 0.992 (95% CI 0.983-0.998) p= 0.048].
Conclusions: TAVR is associated with significant survival benefit throughout 2.99 years of follow-up. Survival during follow-up depends particularly among patients with associated comorbidities and left ventricular ejection fraction

P1896

Age-dependent morbidity and mortality outcomes after surgical aortic valve replacement

Al Amjad Hussain[1]; AA Auensen[1]; CB Brunborg[1]; LG Gullestad[1]; KIP Pettersen[1]
[1]*Oslo University Hospital, Cardiology, Oslo, Norway*

Objectives: Surgical aortic valve replacement is commonly avoided in patients over 80 years old based on assumptions of increased morbidity and strenuous rehabilitation. To examine the validity of these assumptions, we analyzed predefined outcomes in age-based cohorts of patients who underwent open heart surgery.



Age-dependent survival after SAVR

Methods: This study prospectively enrolled 351 consecutive patients referred for aortic valve replacement. Patients were assessed preoperatively and one year after surgery for symptoms, physical function (6 min. walk test; 6MWT), mental status (mini mental status examination; MMSE), quality of life (QoL; SF36), and adverse events (AEs). Five-year all-cause mortality data was recorded.
Results: One-, three-, and five-year survival rates were 94%, 80%, and 72% in the oldest group, and did not significantly differ from the middle age group (logRANK, P = .10) but were slightly lower than patients < 70y. Symptom score, NYHA class and QoL improved in all groups, while 6MWT and MMSE score declined in patients >80 y. After surgery, length of index stay and readmission rate were similar among the three groups The incidence of delirium and infections was higher in the oldest group, whereas the risks of new pacemaker, TIA/Stroke, myocardial infarction and heart failure were the same across age groups.
Conclusions: Surgical AVR shows comparable prognostic importance in patients of >80 years old versus 70-79 years old. The oldest age group had a significant improvement in symptoms and QoL after surgery, but experienced slightly more delirium and infections post operatively. Active respiratory mobilization and IUC removal might prevent adverse events, and measures to prevent delirium and confusion after surgery should be considered in elderly patients.

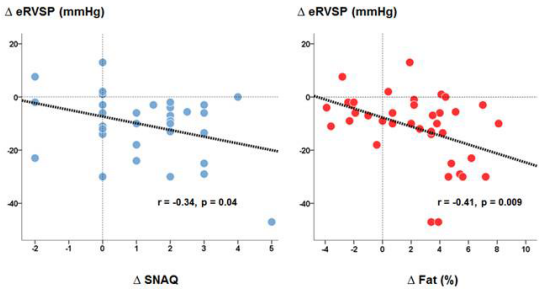
P1897

Changes of body composition after valve surgery in patients with mitral valve disease

KSA Kim[1]; HJW Ha[2]
[1]Hallym University Sacred Heart Hospital, Anyang-Si, Gyeonggi-Do, Korea Republic of; *[2]Yonsei University College of Medicine, Cardiology Division, Seoul, Korea Republic of*

Funding Acknowledgements: a Korea Science and EngineeringFoundation (KOSEF) grant

Background: Patients with chronic heart failure have alteration in body composition as a reduction in fat mass, lean body mass and bone mass. However, body wasting in valvular heart disease and the impact of corrective valvular surgery on body composition has not been investigated.
Purpose: We hypothesized that body wasting in severe mitral valve (MV) diseases is reversible through MV surgery.
Methods: Forty eight patients who were scheduled to undergo MV surgery were consecutively enrolled after excluding patients with combined valvular heart disease, ischemic heart disease, cardiomyopathies, and diseases or who were taking medications that could affect metabolism. All patients were subjected to simplified nutritional assessment questionnaire (SNAQ) for appetite, laboratory tests, echocardiography, and dual-energy X-ray absorptiometrybefore and one year after MV surgery.
Results: One year after MV surgery, the patients showed increased appetite and improved laboratory data as well as hemodynamic improvement. Bone mineral density and body fat percentage were significantly increased, and lean body mass was decreased, despite no changes were observed in body weight. Patients with ?fat = 2% showed significantly higher pre-operative estimated right ventricular systolic pressure (eRVSP) level and greater decrease in eRVSP after surgery than patients with ?fat < 2%. Also, both ?SNAQ and ?fat showed significant negative relationship with ?eRVSP.
Conclusion: In patients with severe MV disease, corrective MV surgery led to favorable outcomes in wasting process as well as hemodynamic improvement. Particularly, right ventricular pressure overload showed a close association with the changes in appetite and body fat percentage



Relationship of ?SNAQ and ?fat with RVSP

P1898

Prognostic impact of pulmonary diseases in the results of transcatheter aortic valve implantation

PM Paulo Maia Araujo[1]; M Braga[1]; S Torres[1]; A Nunes[1]; R Pinto[1]; J Rodrigues[1]; RA Rodrigues[1]; PB Almeida[1]; MB Campelo[1]; JC Silva[1]; MJ Maciel[1]
[1]Sao Joao Hospital, Cardiology, Porto, Portugal

Introduction: Transcatheter aortic valve implantation (TAVI) is an effective treatment for patients (pts) with symptomatic severe aortic stenosis, considered at high surgical risk. Pulmonary disease (PD) is frequent in these pts and can have a post procedural impact on morbi/mortality.
Purpose: To evaluate the impact of PD in complications, mortality, functional capacity and improvement of symptoms after TAVI.
Methods: Retrospective analysis of pts submitted to TAVI in a tertiary care center (October 2014 to December 2016). Clinical, laboratorial and spirometric data were evaluated. All pts had symptomatic severe aortic stenosis prior to the procedure and the decision for referral for TAVI was made by a multidisciplinary Heart Team. PD was defined as the presence of a previous diagnosis of obstructive (COPD, asthma) and/or restrictive pulmonary disease or a significant airway obstruction/restriction in spirometry.
Results: A total of 89 pts were submitted to TAVI during the referred time period. The mean age was 80.2 ± 7.1 years and 51.7% (n = 46) were female. Seventeen pts (19.1%) had PD and in 35.3% of these, PD was the main reason for referral to TAVI, instead of surgery. PD was classified (according to the Chronic Lung Disease classification in the STS score) as: mild in 64.7%, moderate in 23.5% and severe in 11.8%. Baseline NYHA class was similar between patients with/without PD: II - 52.9% vs 59.7% ; III - 47.1% vs 37.5%; IV - 0% vs 2.8% (p = 0.64). The mean EuroSCORE II was significantly higher in pts without PD (6.2% vs 3.5%; p = 0.05), but the mean age was similar (PD - 77.3 y; no PD - 80.9 y; p = 0.48).
During hospitalization, the median stay was similar (PD - 15.2 vs no PD - 14.4 days; p= 0.94). The incidence of complications was tendentially higher in pts without PD (70.8% vs 47.1%), although not significant (p = 0.06). Only one patient had in-hospital mortality (no PD).
At 6-month after discharge, mean BNP was similar between groups (PD: 351 vs no PD: 395 pg/ml; p = 0.67), but LVEF was significantly higher in pts with PD (64% vs 51%; p = 0.05).
At the end of a mean follow-up time of 386 ± 93 days after discharge, PD pts referred significantly lower rates of functional capacity improvement (50.0% vs 87.5%; p < 0.01) and higher rates of NYHA class = 2 (85.7% vs 29.7%; p < 0.01).
Hospitalizations were tendentially higher in PD pts (47.1% vs 24.3%), although not significant (p = 0.06). Cardiovascular mortality and all-causes mortality were similar (PD: 0% vs no PD: 4.3%, p = 0.39; PD: 11.8% vs no PD: 5.7%, p = 0.38).
Conclusion: Pts with PD have similar results in morbi-mortality during hospitalization and in mortality during follow-up. However, one year after the procedure, the PD group has a higher proportion of pts remaining symptomatic and with less improvement in functional capacity. Therefore, in this population, PD has a negative prognostic impact on morbidity after TAVI.

P1899

Clinical characteristics and intermediate term outcomes post mitral valve Clip for high-risk patients with more than moderate mitral regurgitation: single center experience in Saudi Arabia

AA Elasfar[1]; HA Naeim[1]; OA Amoudi[1]; L Khedr[2]; I Alharbi[1]; R Abuelatta[1]
[1]Madina Cardiac Center, Madina, Saudi Arabia; *[2]Tanta University Hospital, Adult Cardiology, Tanta, Egypt*

Background: The current evidence suggests that the primary role for Mitral Valve Clip is to treat symptomatic moderately severe and severe mitral regurgitation (MR) in patients who are either unsuitable or at high risk for MV surgery.
Objectives: We sought to report the clinical characteristics and the one year outcome of high risk patients undergoing percutaneous mitral valve clip.
Methods: This study is a retrospective cohort study for all patients who underwent percutaneous mitral valve clip in our center between June 2013 and October 2016 and who have completed at least one year of follow-up. Symptomatic patients with grades 3 to 4 MR and a high surgical mortality risk, based on the consensus opinion of heart team meeting involving cardiac surgeons, expert interventional cardiologists and echocardiographers were enrolled for percutaneous mitral valve clip.
Results: 62 patients had percutaneous mitral valve clip and completed at least 12 months of follow-up. The average age was 60.56 years, 24.19 were females, 50% were diabetic, 46.77 were hypertensive, 12.90 had ESRD and 11.29 % had anemia. Coronary artery disease (CAD) was present in 59.41 %, prior CABG in 11.67 and prior PCI in 35.48. Technically, the procedure was successful in 96.77 % of cases, 24.19 % had 2 clips and 11.29 had 3 clips. The average EF fraction of the left ventricle was 25% and all patients had at least 3/4 MR. regarding the outcome after 1 year of follow-up; the readmission rate was 25.8% and the mortality rate was 14.5%.
Conclusion: The readmission and mortality rates post mitral valve clip insertion for symptomatic high risk patients with at least moderate severe MR were lower than the internationally published data but the average age of our patients was 10 years younger. Further studies on larger number of patients are needed to confirm the long term outcome after mitral valve clip.

P1900

Impact of paravalvular regurgitation in morbimortality of patients undergoing transcatheter aortic valve implantation

A Alzira Nunes[1]; S Torres[1]; M Braga[1]; P Maia Araujo[1]; J Rodrigues[1]; R Pinto[1]; R Andre Rodrigues[1]; P Bernardo Almeida[1]; D Magalhaes[1]; M Belchior Campelo[1]; J Carlos Silva[1]; M Julia Maciel[1]
[1]Sao Joao Hospital, Cardiology Service, Porto, Portugal

Introduction: Transcatheter aortic valve implantation (TAVI) has emerged as an alternative therapeutic intervention with superior hemodynamic performance for patients with severe, symptomatic aortic stenosis who are at high risk for surgical aortic valve replacement (SAVR). Nevertheless, there are some concerns regarding safety aspects of the procedure such as paravalvular regurgitation (PVR). Although the incidence of significant PVR has declined dramatically with the advent of newer-generation prosthetic valves, mild PVR remains common and its clinical impact has been inconsistent.
Purpose: To assess the impact of PVR after TAVI on morbimortality during hospitalization and follow-up.
Methods: We retrospectively evaluated patients (pts) who were submitted to TAVI in a tertiary care center between October 2014 and December 2016. PVR was assessed at the end of the procedure with aortography. Clinical and laboratorial data were evaluated.
Results: A total of 89 pts, of whom 51.7% (n = 46) were female, with a mean age of 80.2 ± 7.1 years, were included. All pts had symptomatic severe aortic stenosis prior to TAVI. The median EuroSCORE II was 4,5% (0.8-25.9). The implanted valves were: CoreValve Evolut – 67 pts (75.3%), CoreValve - 16 pts (18%), CoreValve Portico - 3 pts (3.4%) and LOTUS Edge Valve System - 3 pts (3.4%). The vascular access was: femoral - 84 pts (94.4%); transaortic - 2 pts (2.2%) and subclavian - 3pts (3.4%). Postprocedural PVR was present in 46 pts (51.7%), mostly of mild degree (44 pts), moderate degree in 2 pts and severe in none. There was a tendency for higher incidence of PVR in the CoreValve Portico valves (100%) comparing to the remaining: CoreValve - 62.5%; CoreValve Evolute - 47.8%; Lotus Valve - 33.3% (p = 0.22). The incidence of PVR was not significantly different between the vascular accesses: femoral - 51.2%; transaortic - 50%; subclavian - 66.7% (p = 0.87). Comparing pts with and without PVR, the mean of length of stay (13 vs 15 days; p = 0.56) and the incidence of complications (65.2% vs 67.5%; p = 0.82) were similar. Only one patient had in-hospital mortality (no PVR). One year after discharge, pts with or without PVR had similar: rates of NYHA class = II (36.6% vs 43.2%; p = 0.5), hospitalizations for cardiovascular (CV) causes (15.2% vs 12.2%; p = 0.68) and CV mortality (4.3% vs 2.4%; p = 0.63). Conclusion: Our study did not show an increase in morbimortality associated with PVR after TAVI. However, we believe that every effort should be made in order to reduce the incidence of this clinical problem.

Myocardial Disease - Clinical

P1901

Contribution of iron status to malfunctioning of human cardiomyocytes and cardiofibroblasts in the course of myocarditis

K A Kamil Aleksander Kobak[1]; M Dziegala[1]; P Franczuk[1]; M Kasztura[1]; M Tkaczyszyn[1]; M Drozd[1]; K Josiak[2]; N Sidorowicz[3]; P Gac[4]; L Kiczak[5]; J Bania[6]; W Banasiak[3]; P Ponikowski[2]; EA Jankowska[1]
[1]Wroclaw Medical University, Laboratory for Applied Research on Cardiovascular System, Department of Heart Diseases, Wroclaw, Poland; *[2]Wroclaw Medical University, Department of Heart Diseases, Wroclaw, Poland*; *[3]Military Hospital of Wroclaw, Centre for Heart Diseases, Wroclaw, Poland*; *[4]Military Hospital of Wroclaw, Radiology Department, Wroclaw, Poland*; *[5]Wroclaw University of Environmental and Life Sciences, Department of Biochemistry, Pharmacology and Toxicology, Wroclaw, Poland*; *[6]Wroclaw University of Environmental and Life Sciences, Department of Food Hygiene and Consumer Health, Wroclaw, Poland*

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Background: Iron is indispensable for the maintenance of optimal cellular functioning and stands at the crossroads of the cellular processes such as energy metabolism and inflammation. This issue could be of a particular importance in the context of myocarditis, where the main cells involved in the pathophysiology are cardiomyocytes and cardiofibroblasts, and their functioning is particularly sensitive to changes in iron status.
Purpose: We assessed the expression of genes responsible for intracellular iron metabolism and malfunctioning of cultured human cardiomyocytes (HCMs) and cardiofibroblasts (HCFs) exposed to sera from patients with acute phase of myocarditis and after 6 weeks, compared with healthy controls. We also related their expression with the clinical profile of patients.
Methods: In HCMs and HCFs cultured with sera from patients for 48 hours, we analyzed expression of genes involved in iron metabolism (ferritin heavy chain [FTH], ferritin light chain [FTL] and transferrin receptor 1 [TfR1]) and myocardium malfunctioning (matrix metalloprotease 1 [MMP1], transforming growth factor beta-1 [TGFB1], galectin-3 [LGALS3]) at the mRNA level using qPCR. Iron status of patients was defined by serum iron and serum ferritin.
Results: HCFs exposed to sera from patients in an acute phase of myocarditis compared to those treated with sera from healthy controls, displayed an increased expression of TfR1 ($p < 0.01$), indicating intracellular iron depletion. HCFs exhibited augmented expression of FTH ($p < 0.01$), FTL ($p < 0.05$) as well as upregulated expression of MMP1 ($p < 0.05$), suggesting increased proremodeling potential. Higher expression of TfR1 was associated with increased expression of MMP1 ($R = 0.74$, $p < 0.01$).
HCMs cultured with acute phase sera also exhibited increased expression of TfR1 ($p < 0.05$) , as compared with cells treated with sera from healthy controls. HCMs displayed upregulated expression of TGFB1 ($p < 0.05$) and LGALS3 ($p < 0.05$), also suggesting cardiomyocyte hypertrophy and cell malfunctioning. Further, an upregulation of LGALS3 in HCMs was also strongly associated with TfR1 upregulation ($R= 0,89$; $p < 0.0001$).
When compared with iron profile of patients, increased expressions of TfR1 and LGALS3 in HCMs were associated with serum ferritin level ($R = 0.96$ and $R = 0.89$, respectively; $p < 0.05$). In HCFs, serum iron level was associated with augmented expression of TfR1 ($R= -0.86$; $p < 0,05$) and FTL ($R=-0.83$; $p < 0,05$).
When exposed to sera collected after 6 weeks, both cell lines exhibited a decrease of TfR1 expression ($p < 0.01$ for HCFs, $p < 0.001$ for HCMs), as compared with those cultured with acute-phase sera. Expression of MMP1 ($p < 0.05$), FTH ($p < 0.01$) and FTL ($p < 0.01$) in HCFs also decreased after 6 weeks showing a similar pattern, that their increase was characteristic for acute phase of myocarditis.
Conclusions: The results suggest that iron homeostasis may be associated with malfunctioning of cardiomyocytes and cardiofibroblasts in acute myocarditis.

P1902

The significance of computed tomography with late contrast enhancement in diagnosis of myocarditis and prognosis in dilated cardiomyopathy syndrome

I Indira Alieva[1]; O Blagova[1]; N Gagarina[1]; A Nedostup[1]; E Kogan[1]; V Sulimov[1]; S Ternovoy[1]
[1]*I.M.Sechenov First Moscow State Medical University, Moscow, Russian Federation*

Background: A generally accepted method of noninvasive diagnosis of myocarditis is an MRI, but it is contraindicated in patients with implanted devices and does not assess the coronary arteries. In the same time the possibilities multidetector computed tomography (MDCT) in diagnosis myocarditis in comparison with myocardial biopsy never previously studied.
Purpose: to study the significance of cardiac MDCT in diagnosis of the myocarditis in patients with dilated cardiomyopathy (DCM) syndrome in comparison with myocardial biopsy and its prognostic value.
Methods: 127 patients (92 male, 46.9 ± 11.8 years) with DCM syndrome (LVEDD 6.6 ± 0.8 cm, LVEF 29.7 ± 9.5%) were included. All of them were undergone 320-slices MDCT with an assessment of the late contrast enhancement (LCE), measurement of viral genome, anti-heart antibodies, Echo-CG and MRI (n = 21). MDCT data were compared with the results of coronary angiography in 48 patients. Fifty myocardial biopsies were performed (30 endomyocardial biopsies, 7 intraoperative biopsies, 9 autopsies, 4 examination of explanted hearts). Comparison group included 18 patients with coronary heart disease without DCM (LVEDD 4.7 ± 0.5 cm, LVEF 59.3 ± 4.9%). The mean follow-up was 12 [2; 32] months.
Results: the myocarditis was diagnosed using complex investigation in 81 (63.8%) patients, its combination with genetic DCM in 19 (15.0%) patients, using the morphological study - in 70.0% and 14.0% of patients. Low contrast enhancement was found in 4 patients (type 1). LCE was detected in 72 patients: 12 - subendocardial (type 2), 4 - intramyocardial (type 3), 44 - subepicardial (type 4), 12 - transmural (type 5); 51 patients had no LCE (type 0). There was no LCE in comparison group. Sensitivity and specificity of all types of LCE for diagnosis of the myocarditis were 64.0% and 82.2%, positive and negative predictive value 88.9% and 50.7%, in comparison with biopsy results - 68.2%, 91.7%, 93.8% and 61.1% respectively. MDCT identified also noncompact myocardium (n = 29, 22.8%), coronary atherosclerosis (n = 33, 26.0%), which was confirmed by coronary angiography in 16 patients. LCE correlated with: 1) diagnostic signs: disease duration, acute onset, its association with infection (r=-0.185, 0.196 and 0.332), morphologic signs of myocarditis (r = 0,320, type 3-5); 2) functional signs: NYHA class (r = 0.183), VTI (r=-0.304), 3) mortality (r = 0.176), $p < 0.05$. The mortality in LCE-positive patients was significantly higher than in LCE-negative (19.4% vs 9.1%, $p < 0.05$; RR 1.37 95% CI 0.99-1.89).
Conclusions: MDCT with an assessment of LCE can be used in diagnosis of myocarditis in patients with DCM syndrome, including those with contraindications to MRI. The diagnostic value of MDCT in diagnosis of myocarditis versus the morphological study of the myocardium quite high and comparable to MRI possibilities. The LCE in the myocardium correlated with the presence of myocarditis, the degree of functional disorders and prognosis.

P1903

Mechanical unloading as a novel treatment option for chronic inflammatory cardiomyopathy

C Tschoepe[1]; S Sophie Van Linthout[2]; O Klein[2]; T Mairinger[3]; E Potapov[4]; B Pieske[1]; F Spillmann[1]
[1]*Charité - Universitätsmedizin Berlin, Campus Virchow-Klinikum (CVK) Kardiologie, Berlin, Germany*; [2]*Berlin-Brandenburg Center for Regenerative Therapies, Berlin, Germany*; [3]*Helios Klinikum, Pathologie, Berlin, Germany*; [4]*Deutsches Herzzentrum Berlin, Berlin, Germany*

Background: Short-term mechanical circulatory support is an appropriate method to stabilize patients in shock including those with acute fulminant myocarditis (M) by unloading. Mechanical cues, involving integrins, are major drivers of cardiac fibroblast activation leading to increased production of extracellular matrix.
Aim: We aimed to investigate whether unloading via a percutaneously implanted left ventricle (LV) assist device (Impella-pump system) over 4 weeks is a strategy to improve heart failure due to chronic inflammatory cardiomyopathy.
Methods and Results: An Impella was implanted in a patient with severe M and pre-cardiogenic shock despite immunosuppression. Endomyocardial biopsies (EMB) were taken over time. Impella implantation led to an improvement in LV-EF (from 15 to 53%) and a reduction in NT-pro-BNP levels (from 8700 to 690 pg/ml). During unloading, cardiac immune cell presence decreased, paralleled by a 2.0-fold, 2.0-fold, 3.9-fold, and 6.6-fold drop in a1, a5, a6, and a10 integrin EMB mRNA expression, respectively, an effect, which was abrogated after removal of the pump. Imaging mass spectrometry further revealed a change in total protein muster including the modulation in extracellular matrix production as shown by a decrease in collagen a-2VI and vimentin expression during unloading.
Conclusion: Prolonged unloading with an Impella device offers a circulatory support with additional disease modifying effects important for bridge to recovery in patients with fulminant M.

P1904

Plasma exchange for patients with inflammatory dilated cardiomyopathy

V Viktoriia Kulikova[1]; AV Nedostup[1]; OV Blagova[1]; VA Zajdenov[2]; AG Kupriyanova[3]; IA Nechaev[1]; AA Ragimov[1]
[1]*I.M. Sechenov First Moscow State Medical University, Department of Internal medicine, Moscow, Russian Federation*; [2]*Institute of Transplantology and Artificial Organs, Moscow, Russian Federation*; [3]*Research Clinical Institute of pediatrics, Moscow, Russian Federation*

Purpose: We report the clinical efficiency of plasma exchange (PE) in patients with inflammatory dilated cardiomyopathy (iDCM). It was used either with immunosuppression drugs or without them.
Methods: fourteen patients with iDCM (13 male, mean age 44.8 ± 11.5 years, left ventricular end-diastolic diameter (LVEDD) 6.3 ± 0.6 cm, left ventricular end-diastolic volume (LVEDV) 182.7 ± 33.5 ml, left ventricular ejection fraction (LVEF) 33.5 ± 8.1%, NYHA functional class 2 [1;3]) underwent a single volume PE filled with 0.9% sodium chloride. All the patients had a high level of at least two auto-antibodies (AABs) directed against cardiac nuclear antigens, endothelial, cardiomyocytes, conduction and smooth muscle cells. Patients underwent evaluation including heart CT scan (n = 11), MRI (n = 3), endomyocardial biopsy (EMB) (n = 5), myocardial perfusion scan (n = 4), and coronary angiography (n = 3) to diagnose myocarditis. Clinical and echocardiographic parameters were assessed at baseline a 4.9 ± 2.1 and 13.2 ± 1.9 month follow-up. We also evaluated a 6-minute walk test (6MWT) distance at baseline just after PE and a 6.6 ± 1.5 and 14.3 ± 2.6 month follow-up. AABs level was assessed at baseline a 5.1 ± 1.9 and 12.5 ± 1.0 month follow-up. All patients were required to be under stable oral medication with maximal tolerated dose of ß-blockers/ angiotensin-converting enzyme inhibitor/ aldosterone antagonists at least 3 month before PE. Four iDCM patients were treated by immunosuppressive drugs (hydroxychloroquine, azathioprine or methylprednisolone) before PE. Seven patients got it after PE. The mean dose of methylprednisolone was 8 [8; 17.25] mg per day.
Results: AABs level significantly decreased just after PE and during the follow-up ($p < 0.05$). Patients had significant improvement in LVEF (33.5 ± 8.1% vs. 41.4 ± 8.2% at first follow up, $p < 0.05$, and 46.3 ± 12.7% at second one, $p>0.05$), LVEDD (6.3 ± 0.6 vs. 6.1 ± 0.6 cm and 6.1 ± 0.7 cm, $p < 0.05$), left atrial volume (102.8 ± 40.6 vs. 84.3 ± 25.1 ml, $p < 0.05$, and 98.0 ± 30.8 ml, $p>0.05$), and 6MWT distance (434.2 ± 55.9 vs. 458.0 ± 44.3 m just after PE, 526.0 ± 69.6 m and 502.0 ± 61.8 at first and second follow-up respectively, $p < 0.05$). Seven patients with absolute LVEF improvement >10% were classified as responders. iDCM non-responder patients were characterized by lower systolic pulmonary artery pressure (correlation ratio 0.68, $p < 0.05$). One of them underwent heart transplantation.
Conclusions: PE improves both cardiac function and daily activities in patients with iDCM due to myocarditis. A positive response is observed in 50% of iDCM patients. PE helps avoid using high doses of immunosuppressive medications.

P1905

Prognostic value of global longitudinal deformation in determining the risk of progression of heart failure in the cohort of belarusian patients with hypertrophic cardiomyopathy

S Komissarova[1]; E Zakharava[1]; T Sevruk[1]; I Ustinova[1]
[1]*Republican Scientific and Practical Centre of Cardiology, Minsk, Belarus*

Background: An algorithm for assessing the risk of sudden cardiac death (SCD) was developed in the latest ESC Guidelines -2014, but there are no recommendations for assessing the risk of other severe complications for hypertrophic cardiomyopathy(HCM), such as the progression of chronic heart failure(CHF). The purpose of our study is to assess the prognostic value of global longitudinal contractility, as a predictor of adverse outcomes associated with the progression of CHF in a cohort of patients with HCM.
Methods: 124 patients with HCM (82 male and 42 female) aged 16 to 79 years (median 48 years) were examined. In addition to the traditional echocardiographic study, all patients underwent 2 D speckle-tracking echocardiography, according to which the global longitudinal strain (GLS) was determined. The main clinical endpoints in this study included mortality associated with CHF and hospitalization for progression of CHF.
Results: Among 124 patients, 17 (12.9%) had symptoms of CHF NYHA class III-IV at initial examination. Progression of CHF symptoms to NYHA FC III-IV in 24 (19.4%) patients with HCM occurred with a preserved systolic function (LVEF> 50%) and only 7 (5.6%) patients had systolic dysfunction (LVEF <50%). During the follow-up period (median follow-up of 3 years), the following adverse outcomes were recorded

in 23(18.5%) of 124 patients with HCMC: SCD developed in 4 patients, SCD with successful resuscitation and ICD implantation in 3 patients, lethal outcome due to progression of CHF up to the "end stage" - in 2 patients, hospitalization due to the progression of CHF symptoms to III-IV NYHA class- 14. Regression analysis was performed to determine the predictors of adverse outcomes associated with CHF mortality and hospitalization due to the progression of CHF. Due to the small number of SCD-related events, the risk of adverse outcomes associated with SCD was not analyzed. Multifactor analysis showed that the following characteristics were independent risk factors for the lethal outcome and hospitalization from the progression of CHF: decrease in global longitudinal deformation <10.5% (RR 0.75, 95% CI 0.62-0.89, p = 0.0015), an increase in the left atrial volume index> 35.1 ml /m2 (RR 1.03, 95% CI 1.00 - 1.06, p = 0.019). The cumulative 3-year probability of developing an adverse event is 7.6 (7.5-7.7)%.
Conclusion: The global longitudinal strain is associated with the development of adverse events associated with the progression of CHF in HCM and can be used to identify patients with a high risk of developing CHF progression and an unfavorable outcome.

P1906
Clinical-pathological profiles responsible for advanced heart failure, heart transplantation, left ventricular assist device implantation and death for heart failure in Hypertrophic cardiomyopathy

G Galati[1]; A Di Lenarda[2]; A Margonato[1]
[1]*San Raffaele Hospital and Scientific Institute (IRCCS), Heart Failure Unit and Division of Cardiology, Cardiothoracic and vascular Department, Milan, Italy*; [2]*Cardiovascular Center A.S.S. 1 of Trieste, Cardiovascular Department, Trieste, Italy*

Background: Over the last 50 years, advanced heart failure (AdvHF) in hypertrophic cardiomyopathy (HCM) was overlooked. Neither large case series nor clinical trials on this topic have been reported. The main clinical-pathological profiles responsible for AdvHF in HCM are: 1) End-stage HCM (ES-HCM) defined by an ejection fraction (EF) = 50%; 2) Left-Ventricular outflow obstruction despite optimal pharmacological and not pharmacological therapy (Refractory HOCM); 3) Nonobstructive HCM with preserved EF (HNOCMpEF).
Purpose: Based on a systematic revision of all published manuscripts on this topic, this study describes the prevalence of the three main HCM phenotypes responsible for AdvHF, heart transplantation (HTx), left-ventricular assist device (LVAD) implantation and death for heart failure (HF) despite the contemporary management of HCM.

Table 1

	Adv HF (= 205)	HTx/LVAD implantation/ HF-Death (= 119)	HTx/LVAD implantation (= 68)	HF-Death (= 51)
ES-HCM	133 (64.9%)	89 (74.8%)	49 (72.1%)	40 (78.5%)
Refractory HOCM	11 (5.4%)	1 (0.8%)	0 (0%)	1 (1.9%)
HNOCMpEF	61 (29.7%)	29 (24.4%)	19 (27.9%)	10 (19.6%)

Methods: The study screened 120 manuscripts in MEDLINE and EMBASE on HCM cases of AdvHF and HTx published since 2000 until December 2017, in adult patients (= 18 years old). The authors identified 8 manuscripts eligible for the analysis, 4 of whom where excluded for incomplete information before HTx. 205 patients with AdvHF due to HCM, despite optimal therapy, were included in the main analysis. AdvHF was defined by severe NYHA symptoms (class III and IV), because in all the manuscripts this definition was used. Minimum reported follow-up was 6.1 years.
Results: Table 1 shows the prevalence of phenotypes responsible for AdvHF/HTx/LVAD implantation/HF-Death. Of 205 HCM patients, 119 (58%) underwent HTx, LVAD implantation or died for HF.
Conclusion: AdvHF in HCM has a poor prognosis. With the current management of HOCM only a very little percentage of these patient experiences AdvHF. Less than 1/3 of HNOCMpEF patients had AdvHF due to restrictive physiology and less than 1/4 of these patients had a poor prognosis. Nowadays, ES-HCM represents the main cause of AdvHF in HCM and the major determinant for poor outcome. Although it has been managed with HTx or LVAD implantation, a significant percentage (78.5%) died for HF. This reflect poor attention and portrays an unmet need for ES-HCM patients. These findings reinforce the emphasis on long-term surveillance of HCM patient in order to timely identify patients at risk of ES evolution and early start the standard HF therapeutic (pharmacological and non-pharmacological) armamentarium

P1907
Does hypertension influence prognosis of hypertrophic cardiomyopathy?

D-G Dae-Gyun Park[1]; W-W Seo[1]; S-E Kim[1]; J-H Lee[1]; K-R Han[1]; D-J Oh[1]
[1]*Hallym University Kangdong Sacred Heart Hospital, Seoul, Korea Republic of*

Backgrounds: Any cardiac or systemic condition increasing left ventricular pressure, for instance, hypertension or aortic stenosis, was excluded from diagnosis of hypertrophic cardiomyopathy by strict definition in the past. However, patients with hypertrophic cardiomyopathy might be accompanied by hypertension over the course because hypertension is so prevalent disease or risk factor in real world.
Purpose: We investigated whether hypertension would give an additional effect on the prognosis of hypertrophic cardiomyopathy. Method: We enrolled 102 patients with hypertrophic cardiomyopathy based on the definition of 2014 ESC guideline except for apical hypertrophy from 1997 to 2015. Patients were divided into hypertensive (H) group and normotensive (N) group. We compared the echocardiographic findings and mortality rates between two groups.
Result: Among 102 patients, there were 53 hypertensive patients (52%) and 49 normotensive patients. Median follow up period was 5.8 years. The mean age of each group was 67.1 ± 12.5 (H) vs. 55.3 ± 15.1 (N) years (P < 0.01). The mean systolic blood pressure of was 129.7 ± 27.0 (H) vs. 126.0 ± 22.6 (N) mmHg (P = 0.51). The mean septal wall thickness of left ventricle was 19.2 ± 3.6 (H) vs. 18.9 ± 3.6 (N) mm (P = 0.66). And the mean posterior wall thickness of left ventricle in each group was 12.1 ± 1.9 (H) vs. 11.2 ± 2.3 (N) mm (P = 0.04). Mortality rate in each group was 41.5% (H) vs. 18.3% (N) (P = 0.01). Hypertensive group showed higher mortality rate and thicker posterior wall thickness than normotensive group, but there was no statistical significance on multivariate analysis. On univariate analysis, old age, female, hypertension, posterior wall thickness and left ventricular mass index were associated with all-causes mortality. Logistic regression analysis revealed that only old age was independently associated with all-causes mortality.
Conclusion: In our study, hypertension did not show statistical influence on all-causes mortality in patients with hypertrophic cardiomyopathy. But, there are some trends in thickening of left ventricular wall and all-causes mortality associated with hypertension.

P1908
Comparison of echocardiographic parameters in patients with obstructive and non-obstructive hypertrophic cardiomyopathy

T-H Tomas Honek[1]; J-K Jan Krejci[1]; J-M Jan Machal[2]; L-G Ladislav Groch[1]; J-S Jan Sitar[1]; J-M Jaroslav Meluzin[1]; L-S Lenka Spinarova[1]
[1]*St. Anne's University Hospital, Department of cardiovascular diseases, Brno, Czech Republic*; [2]*Masaryk University, Department of pathophysiology, Brno, Czech Republic*

Introduction: Hypertrophic cardiomyopathy (HCM) is characterized by thickening of left ventricular walls in the absence of provoking hemodynamic causes. Based on the presence of intraventricular obstruction, we can distinguish obstructive and non-obstructive type of HCM. According to presence and seriousness of symptomatology we can choose one of therapeutic approaches, conservative (lifestyle changes and pharmacological therapy) or invasive, especially alcohol septal ablation (ASA).
Objectives and methodology: The study objective was to compare the development of echocardioagraphic parameters and functional status in one-year, three-years and five-years period in patients with HCM. The set of patients was divided into three groups; the first group consisted of patients with non-obstructive type of HCM (n = 38), the second group with presence of significant obstruction treated conservatively (n = 45) and the third group with obstructive type of HCM treated with ASA (n = 38).
Results: In the non-obstructive HCM group, a significant change in left ventricular outflow tract gradient (LVOTG) or New York Heart Association (NYHA) class did not occur during the follow-up (p = NS). In the obstructive group of patients treated conservatively, LVOTG decreased from 64.4 ± 54.7 mmHg to 51.4 ± 47.5 mmHg in the first year (p = NS), to 45.1 ± 40.1 mmHg in the third year (p < 0.05), and to 60.5 ± 67.4 mmHg in the fifth year (p = NS), respectively. NYHA class remained stationary for all periods (p = NS). In the obstructive group of patients treated with ASA, LVOTG decreased from 76.5 ± 51.2 mmHg to 24.6 ± 18.4 mmHg in the first year, to 23.1 ± 21.3 mmHg in the third year, and to 37.4 ± 48.3 mmHg in the fifth year (all p < 0.001), respectively. Similarly, the improvement in NYHA class was observed (all p < 0.01).
Conclusion: The presence of intraventricular obstruction is one of the most important indicators determining progress and development of this disease. The LVOTG decline after ASA defined the difference in the development of other echocardiographic parameters between both conservatively treated groups (non-obstructive

and obstructive) with the ASA group, and led to the improvement or stabilisation of left ventricular morphology. Likewise, it was observed the improvement in functional status after ASA.

P1909

Predictors of survival in recent-onset idiopathic dilated cardiomyopathy: effect of dose of discharge beta blocker on left ventricular ejection fraction

D-G Park[1]; W-W Seo[1]; S-E Kim[1]; J-H Lee[1]; K-R Han[1]; D-J Oh[1]
[1]*Hallym University Kangdong Sacred Heart Hospital, Seoul, Korea Republic of*

Background: Left ventricular systolic function in more than one-third of patients with recent-onset dilated cardiomyopathy (DCM) recovered in short-term follow-up.
Purpose: We sought to determine clinical or echocardiographic predictors for recovery of left ventricular ejection fraction (LVEF) and all-cause mortality in recent-onset idiopathic DCM. And, we evaluate whether dose of therapeutic drugs such as beta blocker (BB) or angiotensin-converting enzyme inhibitor (ACEI) might affect clinical outcomes.
Methods: We enrolled consecutively 114 patients with firstly diagnosed idiopathic DCM. Exclusion criteria were, as follows, valvular heart disease, acute coronary syndrome, known ischemic heart disease, stress cardiomyopathy or tachycardia-induced cardiomyopathy. We evaluated clinical factors, including comorbidity; laboratory findings, including cardiac enzymes, B-type natriuretic peptide and C-reactive protein; serial electrocardiographic data; echocardiographic parameters at admission and follow-up. At discharge, BB, ACEI or angiotensin receptor blocker (ARB) was recorded, and standardized with carvedilol (25 mg /day) or ramipril equivalents (5 mg/day), and analyzed for predictor of outcomes such as change of LVEF and all-cause mortality.
Results: 51% of all patients demonstrated at least an increase of 8 ejection fraction units with median follow-up of 2.6 years, and 39% of all patients showed an LVEF of = 0.45. At discharge, 67% of all patients were receiving a BB and 95% were receiving ACEI or ARB. In multivariate analysis, absence of complete left bundle branch block (p = 0.022) and high dose of BB (p = 0.007; = 25-mg carvedilol equivalent) were significantly associated with an improvement of LVEF (10% increase of baseline LVEF) during follow-up examinations. On Kaplan-Meir survival curve, with median follow-up of 5 years, cumulative survival rate of improvement group is 96% and 86% at 1 and 3 years, respectively; compared with non-improvement group, 86%, 75% (p = 0.028). In multivariate analyses, lower follow-up LVEF (p = 0.032, hazards ratio = 0.95) and lower body mass index (p= 0.034, hazards ratio = 0.85) were independently related to all-cause mortality.
Conclusions: In our study, half of patients with recent-onset idiopathic DCM showed significant improvement of LVEF during follow-up. Recommended high-dose of BB at discharge was independently associated with an improvement of LVEF which was related to better survival rate. Thus, early recommended high-dose of BB might have a favorable effect on better survival for patients with recent-onset dilated DCM through inducing improvement of LVEF.

P1910

Early changes in echocardiographic parameters predict prognosis in patients with recent onset dilated cardiomyopathy

J Krejci[1]; P Hude[1]; E Ozabalova[1]; H Poloczkova[1]; D Mlejnek[1]; V Zampachova[1]; I Svobodova[1]; K Benesova[2]; J Jarkovsky[2]; L Spinarova[1]
[1]*St. Anne's University Hospital, Masaryk University, Brno, Czech Republic*;
[2]*Institute of Biostatistics and Analyses of Masaryk University, Brno, Czech Republic*

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Introduction: Prognostic stratification in patients with recent onset dilated cardiomyopathy (RODC) is essential for the timing of additional therapeutic steps, including the implantation of ICD (with or without cardiac resynchronization function), mechanical circulatory support or heart transplantation.
Purpose: To evaluate the significance of the early changes in echocardiographic parameters on the presence of combined mortality-morbidity endpoint in 5-year follow-up.
Patients and Methods: We assessed 212 RODCM patients with left ventricular ejection fraction (LVEF) 24.1 ± 7.1% at the time of diagnosis, mean age 46.9 ± 11.6 years, NYHA class 2.3 ± 0.6 and symptoms duration at baseline control 2.6 ± 2.5 months. An early changes in echocardiographic parameters were defined as the difference between baseline and 3-month examinations. Combined mortality-morbidity endpoint was defined as the presence of death, resuscitation for cardiac arrest, appropriate ICD discharge, heart transplantation or implantation of mechanical circulatory support and unscheduled hospitalization or outpatient visit for cardiovascular reason.
Results: A 10% percent increase in LVEF was associated with reduced incidence of defined endpoint (HR 0.579; p < 0.001), increase in left ventricular enddiastolic diameter by 10mm nearly doubled the incidence of the endpoint (HR 1.923; p = 0.022), similarly 10mm higher left atrial diameter worsened the prognosis (HR 1.926; p = 0.014). On the contrary, the increase in systolic and diastolic mitral annular velocities decreased the incidence of the endpoint (HR 0.811; p = 0.023 and HR 0.859; p = 0.028). Changes in right ventricular diameter and function or E/e'ratio did not change the prognosis.
Conclusion: Early changes in some echocardiographic parameters may help in the risk stratification of patients with RODCM.

P1911

Effect of Ivabradine on left ventricular functional recovery in patients with dilated cardiomyopathy

J Y Jae Yeong Cho[1]; K H Kim[1]; H Park[1]; H J Yoon[1]; K H Lee[1]; D S Sim[1]; N S Yoon[1]; Y J Hong[1]; H W Park[1]; J H Kim[1]; Y Ahn[1]; M H Jeong[1]; J G Cho[1]; J C Park[1]
[1]*Chonnam National University Hospital, Cardiology, Gwangju, Korea Republic of*

Background: Previous studies have shown that ivabradine has a favorable impact on LV reverse remodeling in heart failure with reduced ejection fraction (HFrEF). Left ventricular functional recovery (LVFR) is not uncommon in dilated cardiomyopathy (DCM), but there is lack of data regarding the effect of ivabradine on LVFR of DCM in real clinical practice.
Purpose: Therefore, the aim of this study was to investigate the impact of ivabradine added to conventional HF management on LVFR in patients with DCM.
Methods: Among 335 hospitalized patients with DCM and acute decompensated HF (ADHF), a total of 268 patients who had echocardiography studies at admission and 6 months of follow up were enrolled and divided into two groups; ivabradine group (n = 64, 57.7 ± 16.3 years, 54 males) vs. non-ivabradine group (n = 204, 65.8 ± 14.6 years, 161 males). LVFR was defined as LVEF = 50% at follow-up echocardiography. Baseline characteristics, echocardiographic findings and laboratory findings were compared between two groups.
Results: Baseline clinical characteristics, laboratory, and echocardiographic findings were not different between the groups except for age (ivabradine group vs. non-ivabradine group; 57.7 ± 16.3 vs. 65.8 ± 14.6 years, p < 0.0001). Prescribed medications for HF also were not different. On follow up echocardiography at 6 months, LV function was recovered in 83 patients (31.0%). Diabetes, level of N-terminal pro-B type natriuretic peptide at 3-month follow-up, and LV end-systolic dimension were independent predictors of LVFR in patients with DCM, but the use of ivabradine was not a predictor of LVFR [19 LVFR (29.7%) in ivabradine group vs. 64 LVFR (31.4%) in non-ivabradine group, p = 0.799].
Conclusion: LVFR was not uncommon in DCM (31.0%) and Diabetes, level of N-terminal pro-B type natriuretic peptide at 3-month follow-up, and LV end-systolic dimension were independent predictors of LVFR. However, the use of ivabradine fails to demonstrate additional favorable effects on LVFR in Korean patients with DCM.

P1912

Mutation spectrum of 10 sarcomeric genes in Russian patients with dilated cardiomyopathy

A Bukaeva[1]; M Polyak[1]; N Kotlukova[2]; Y Frolova[1]; S Dzemeshkevich[1]; E Zaklyazminskaya[1]
[1]*Russian Research Center of Surgery, Moscow, Russian Federation*; [2]*Pirogov Russian National Research Medical University , Moscow, Russian Federation*

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Background: Dilated cardiomyopathy (DCM) is the leading cause of heart failure, with prevalence up to 1:2500. DCM is characterized by high mortality rate and clinical and genetic heterogeneity. To date, more than 50 genes are reported to be responsible for DCM, and sarcomere genes are reported to have the highest rate of mutations found in this cohort of patients.
Purpose: to estimate the prevalence of mutations in sarcomeric genes in Russian DCM patients.
Methods. The cohort of patients included a total of 53 probands with diagnosed DCM, 20 of them were children before age of 18 y.o. (15 boys and 5 girls) and 33 were adult patients (M:F ratio is 20:13). All patients underwent high-throughput semiconductor sequencing using targeted oligoprimer panel flanking the coding area of MYBPC3, TAZ, TPM1, LDB3, MYL2, ACTC1, MYL3, MYH7, TNNI3, and TNNT2 genes. All potentially significant findings and undercovered areas were re-analyzed by direct Sanger sequencing.
Results: We have revealed 13 pathogenic and/or likely pathogenic genetic variants in 12 probands (22% of whole DCM cohort). Eleven patients were heterozygous carriers, and 1 patient had a combination of two heterozygous variants.
In pediatric group we have revealed 6 clinically significant findings in 6 probands (30%), 3 of them were in the MYH7 gene, 1 in the MYBPC3 gene, 1 in the TPM1 and 1 in the TNNT2 gene. Three of these variants were predicted to be deleterious by in

silico analysis: c.5655+5G>C and p.Q1029P in the MYH7 gene, and p.T721I in the MYBPC3 gene. Three other findings (p.E1799K in the MYH7 gene, p.R173Q in the TNNT2 gene, and p.D230N in the TPM1 gene) were previously published mutations associated with dilated cardiomyopathy.
In adult cohort we have detected 7 mutations in 6 (18%) probands. Five of them were found in the MYH7 gene: four are missense changes, and one is non-frameshift deletion (c.5754_5756delCAA in MYH7). One adult male patient carried two changes in the MYH7 gene: an undescribed, in silico predicted damaging, substitution p.V1360D in addition to the known mutation p.P151L. MYH7 gene in our cohort also harbors p.G181R and p.Q419K rare mutations. We have discovered two new variants in the MYBPC3 gene (p.V563A and p.A1632T).
Conclusion. We note that the rate of mutations in 10 sarcomeric proteins were about 20%, what is lower than expected. Further study is needed to prove this mutations rate in Russian DCM patients.

P1913

Frequency and predictors of thromboembolic events in patients with left ventricular noncompaction

NV Varionchik[1]; OV Blagova[1]; EV Pavlenko[1]; AV Nedostup[1]; VP Sedov[1]; NV Gagarina[1]; EA Mershina[2]; VE Sinitsyn[2]
[1]I.M. Sechenov First Moscow State Medical University, Moscow, Russian Federation; *[2]Roszdrav Medical Rehabilitation Center, Moscow, Russian Federation*

Background: Left ventricular noncompaction (LVNC) is associated with high risk for heart failure, arrhythmias, thromboembolism, and sudden cardiac death.
Purpose: This study is sought to investigate the frequency and the predictors of thromboembolic events in patients with LVNC.
Methods: A total of 107 patients with LVNC were included (male, 59%); mean age, 45.4 ± 14.9 years, (18-78 years old). In 25 cases 3 visualizing methods were used to diagnose LVNC, in 76 cases - 2 different methods. The mean LV ejection fraction was 38.5 ± 14.4%, LV end-diastolic diameter was 6.0 ± 0.8cm, left atrium (LA) volume was 94.3 ± 37.8ml. Echocardiography (n = 107), computed tomography (n = 84), MRI (n = 41), coronary angiography (n = 28) were performed. The median follow-up was 13 months [3.5; 36.0], from 1 month up to 10 years. The data were analyzed in SPSS21. P values of <0.05 were considered statistically significant.
Results: 14 patients (13.1%) were diagnosed with intracardiac thrombosis; 4 other patients had a previous history of it. Thrombi location involved LA, including auricle, both left and right ventricle. Embolic events occurred in 8.4% patients (n = 9): 6 suffered ischemic stroke, 3 - peripheral embolism (renal artery - 1, ophthalmic artery - 1, embolic myocardial infarction verified at the autopsy together with ischemic stroke - 1). Several other cases of myocardial infarction are also likely to be of embolic etiology. Altogether intracardiac thrombosis and/or embolic events occurred in 20.6% patients (n = 22). LV dilation, systolic and diastolic dysfunction were significantly more frequent in patients with thromboembolic events. They had significantly higher NYHA functional class (class 3 [1.75; 3.0] v class 2 [1.0; 3.0], p <0,05; AUC 0.717), greater LV end-diastolic volume (174.2 ± 55.7ml v 144.1 ± 65.0, p <0.05 AUC 0.663), greater LA volume (116.7 ± 32.5ml v 88.1 ± 37.0ml, p <0.01; AUC 0.834), ?/? ratio (2.4 [2.25; 3.05] v 1.3 [0.9; 1.7], p <0.001; AUC 0.827), lower LV EF (31.4 ± 11.3% v 40.3 ± 14.6%, p <0.05) compared with patients without thromboembolic events. Moreover, they more frequent suffered with microvascular ischemia in the absence of coronary atherosclorosis (36.3% v 15.3%, p <0.05). There was no significant difference in atrial fibrillation (AF) between groups. This was due to early anticoagulant treatment in the presence of AF. Twenty patients were administered antithrombotic therapy: 17 received anticoagulants (warfarin - 13, rivaroxaban - 3 dabigatran - 1); 3 patients received aspirin. In 95% of cases (n = 21) thromboembolic events occurred before anticoagulant prescription.
Conclusion: Thromboembolic events are typical for LVNC. In our group of 107 patients their frequency is 20.6%. Our data demonstrate that LA volume = 90 ml, ?/? = 2.0, LV end-diastolic volume = 130.0 ml, NYHA functional class = 3, and microvascular ischemia should be considered additional indications for anticoagulant treatment in patients with LVNC, besides atrial fibrillation and low LV EF.

P1914

Intramyocardial inflammation correlates with poor prognosis in patients with cardiac AL amyloidosis

F Felicitas Escher[1]; CS Siegismund[2]; DL Lassner[2]; MG Gross[2]; RL Linke[3]; HPS Schultheiss[2]
[1]Charite - Campus Virchow-Klinikum (CVK), Berlin, Germany; *[2]Institute of Cardiac Diagnostics and Therapy (IKDT), Berlin, Germany*; *[3]amYmed, Reference Center of Amyloid Diseases, Martinsried, Germany*

Aims: To evaluate the influence of endomyocardial biopsy (EMB)-proven intramyocardial inflammation on mortality in patients with cardiac transthyretin amyloid (ATTR) or amyloid light-chain (AL) amyloidosis.

Methods and Results: We included 54 consecutive patients (age mean ± SD, 68.83 ± 9.59 years; 45 men) with biopsy-proven cardiac amyloidosis. We followed up patients from first diagnostic biopsy to as long as 36 months (mean ± SD, 11.5 ± 12) and compared their outcome with information on the all-cause mortality with or without proof of inflammation in EMB. Intramyocardial inflammation was assessed by quantitative immunohistology.
Patients suffering from amyloidosis revealed a significant poor prognosis with proof of intramyocardial inflammation in contrast to those without inflammation (log-rank p = 0.036). A patient's regrouping indicated AL amyloidosis to have a significant impact on the all-cause mortality (log-rank p = 0.012). A multivariate analysis confirmed intramyocardial inflammation and AL amyloidosis as causative parameters of increased mortality. The detailed subgroup analysis showed that patients suffering from AL amyloidosis with intramyocardial inflammation have a significantly worse prognosis in comparison to AL amyloidosis without inflammation and ATTR with or without inflammation, respectively (log-rank p = 0.014, contingency Fisher's exact p = 0.008).
Conclusion: Our study reports for the first time a high incidence (48.1%) of intramyocardial inflammation in a series of patients with cardiac amyloidosis underlying EMB and could show that in patients with AL cardiac amyloidosis, intramyocardial inflammation correlated significantly with increased mortality. Our data have a direct clinical impact because one can hypothesize that additional immunomodulating / anti-inflammatory treatment regimens in patients with biopsy-proven inflammation of heart muscle tissue could be beneficial for patients suffering from cardiac AL amyloidosis.

P1915

Clinical characterization of Takotsubo-syndrome in 84 consecutive patients over 6 years

M Noutsias[1]; F Muehleck[2]; N El-Danasouri[2]
[1]University Clinic Halle (Saale), Mid-German Heart Center, Department of Internal Medicine III (KIM-III), Division of Cardiology, Halle, Germany; *[2]University Hospital of Jena, Jena, Germany*

Background: The pathogenesis of Takotsubo-syndrome (TTS), as well as its diverse clinical presentations, are incompletely understood.
Purpose: Clinical characterization of TTS patients, and of a possible association between the different wall motion abnormality types (TTS-WMAT) with clinical parameters.
Results: We evaluated n = 84 consecutive TTS patients (age: 71.5+12.0 years; females: 79%), as confirmed by left ventricular (LV) angiography (LVEF: 46.9+14.1%) and exclusion of relevant coronary artery disease by acute coronary angiography, being admitted to our tertiary center from 04/2009 until 01/2017 (26% prospective patient evaluation). The majority of patients (69%) presented an apical TTS-WMAT, followed by the midventricular (MV) TTS-WMAT (24%), while the remaining focal (5%) and the basal (2%) TTS-WMAT were infrequent. An acute infection was diagnosed in 24% of the TTS-patients as possible physical stress situation, while an acute emotional stress situation was present in 44% of the patients. The LV enddiastolic pressure (LVEDP) was 26.5+11.9 mmHg. N = 2 patients had been admitted after cardiopulmonary resuscitation, and 14% of the patients had a cardiogenic shock being treated with catecholamines on admission. 52% of the patients had coronary artery disease with stenosis grade >50% at least in one coronary artery, however, no indication for percutaneous coronary intervention was confirmed in any of these patients. The mean Troponin I levels on admission were elevated (1.3+2.0 µg/l), as well as the mean BNP (769.2+1,388.9 pg/l), and the mean CRP (48.6+71.9 mg/l). The statistical analysis of apical or MV TTS-WMAT with various clinical parameters revealed significant associations with age (apical: 74.0+10.5 versus MV: 66.9+10.7 years) and LVEDP (apical: 29.0+11.4 versus MV: 21.4+10.1 mmHg). No significant associations were confirmed among others with type of ECG alterations (i.e. ST-elevations, ST-depression, T-wave inversions), physical or emotional stress, LVEF, cardiogenic shock, Troponin I, BNP and CRP. The 6-months-mortality was 6%, and 1 female patient had a fatal outcome after her third recurrence of TTS (apical TTS-WMAT).
Conclusions: Our data on consecutive 84 TTS patients in our tertiary center confirm that the majority are females (79%) at advanced age, and 93% present with the leading apical, followed by the MV-TTS-WMAT, while the basal and focal TTS-WMAT are infrequent (< 10%). The percentage of cardiogenic shock on admission is considerable in TTS patients (ca. 14%), as well as its short-term mortality (6%). The significant association of lower age and lower LVEDP with the MV- compared with the apical TTS-WMAT might provide clues for a better understanding of the diverse clinical phenotypes of TTS.

P1916

Persistent subclinical myocardial dysfunction after aortic coarctation correction

H Helena Nascimento[1]; M Braga[1]; V Ribeiro[1]; C Sousa[1]; F Macedo[1]; C Cruz[1]; MJ Maciel[1]
[1]*Sao Joao Hospital, Porto, Portugal*

Background: Aortic coarctation (CoA) adult population is growing, because of major improvements in both diagnostic and therapeutic approaches. However, even after a successful repair, hypertension and left ventricular (LV) myocardial dysfunction may still occur. The aim of our study was to assess the role of 2-D speckle tracking echocardiography (STE) in the early detection of subclinical myocardial dysfunction in patients with CoA repaired.
Material and Methods: This study was based on a retrospective analysis of adult patients (pts) with the diagnosis of repaired CoA, followed-up in a Grown-up Congenital Heart Disease Centre. Patients with significant concomitant lesions (except for bicuspid aortic valve without stenosis) and clinical LV systolic dysfunction were ruled out. Epidemiologic and clinical data were collected and inserted in a registry base. Transthoracic echocardiograms were reviewed in order to assess global longitudinal strain (GLS) using 2-DSTE (Echopac Software, GE). The data were compared with those obtained from14 healthy subjects (7 male;median age 31 years-old, interquartile range: 25-50).
Results: From the twenty-one pts with repaired CoA studied, 12 were women and median age was 35 years-old (interquartile range: 31-40). Bicuspid aortic valve was present in 5 patients (23.8%). Surgical repair was performed in 16 pts (76.2%): resection with subclavian artery flap aortoplasty (7); head-to-head anastomosis (1) and woven Dacron patch (1). Median age at correction was 6 years-old (interquartile range: 3-21). The remaining 5 pts (23.8%) were submitted to percutaneous intervention. Twelve of these patients were controlled hypertensive (57.1%). All pts were in sinus rhythm and LV hypertrophy was observed in 2 (9.5%). Comparing to the healthy controls, CoA pts group presented superior LV wall thickness (ventricular septum: 8.9 ± 1.4 vs. 7.6 ± 1.7mm, $p = 0.033$; posterior wall: 8.5 ± 1.7 vs. 7.3 ± 1.2, $p = 0.026$). Regarding the diastolic function parameters the E/e' is significantly higher in the CoA pts (7.9 ± 1.8 vs. 5.5 ± 1.4, $p = 0.04$). Despite the absence of differences in LV ejection fraction, CoA pts presented a significantly reduced LVGLS (-16.2 ± 4.2 vs. -18.6 ± 1.7, $p = 0.043$). There was no significant correlation between LVGLS and current systolic blood pressure or age of CoA repair.
Conclusion: In spite of a low percentage of LV hypertrophy, significant reduction of GLS was found, consistent with persistent subclinical myocardial dysfunction even long after correction of the defect. Although the significant prevalence of hypertension in these pts, this factor did not appear to play a significant role.

Pulmonary Circulation, Pulmonary Embolism, Right Heart Failure – Clinical

P1917

The effect of obstructive sleep apnea on in hospital outcomes of patients with acute pulmonary embolism

M Mario Rodriguez[1]; W Rzechorzek[1]; B Sabharwal[1]; X Wei[1]; A Manguba[1]; C Krittanawong[1]; C Godoy Rivas[2]; E Herzog[1]; J Puma[3]
[1]*Icahn School Of Medicine at Mount Sinai/ Mount Sinai St. Lukes-West Hospital, Department of Medicine, Division of Cardiology , New York, United States of America*; [2]*Cleveland Clinic Foundation, Cleveland, United States of America*; [3]*Columbia University Medical Center, New York, United States of America*

Background: Obstructive sleep apnea(OSA) has been found to be a risk factor for development of pulmonary embolism. Nevertheless, data reporting the in hospital outcomes of patients with obstructive sleep apnea that are admitted with acute pulmonary embolism is limited. There is some data suggesting decreased mortality in patients with OSA and acute myocardial infarction and we might be facing a new paradox in cardiovascular disease.
Purpose: describe the inhospital outcomes of patients with obstructive sleep apnea admitted for pulmonary embolism.
Methods: A retrospective analysis using the 2014 United States Nationwide Inpatient Sample was done. Patients above the age of 18 years with a primary diagnosis of acute pulmonary embolism were included. Patients with secondary diagnosis of pulmonary embolism (surgical) were excluded. Primary outcome was in-hospital mortality. Secondary outcomes included length of stay, cost of stay, shock, use of mechanical ventilation, acute kidney injury, acute kidney injury requiring dialysis(AKID), use of non-invasive ventilation(NIV), cardiac arrest, rate of heparin induced thrombocytopenia, rate of transfusion, rate of inferior vena cava filter use, use of thrombolysis and thrombectomy. Multivariate logistic regression analysis was performed adjusting for obesity, age, race, gender and hospital location using STATA IC 15.
Results: 33,927 patients with primary diagnosis of PE were identified of which 16,275 had a secondary diagnosis of OSA. 42% were female and mean age was 60 years. There was decreased odds of mortality (OR 0.72 $p = 0.03$) along with decreased rates of hemorrhage requiring transfusion(OR 0.68 $p = 0.001$) and cardiac arrest (OR 0.63 $p = 0.02$) in patients with OSA compared to those without. There was also an increased NIV utilization (OR 5.1 $P < 0.001$) along with increased length of stay. A non statiscally significant decreased odds of obstructive shock (OR 0.61 $p = 0.22$), invasive mechanical ventilation (OR 0.85 $p = 0.20$), AKID (OR 0.78 $p = 0.694$), rate of heparin induced thrombocytopenia (OR 0.48 $p = 0.10$), thrombectomy (OR 0.65 $p = 0.42$) and inferior vena cava filter placement (OR 0.92 $p = 0.3$) was also found.
Conclusions: Patients with OSA and pulmonary embolism showed decreased odds of mortality, cardiac arrest and transfusion needs, but an increased NIV utilization and length of stay after adjustment for obesity on multivariate regression analysis. A possible OSA paradox in cardiovascular disease that warrants further studies might be in front of us.

P1918

Acute pulmonary thromboembolism, a manifestation of oncologic disease to be diagnosed?

L Luisa Malvar Goncalves[1]; HUGO Antunes[1]; LUÍS Abreu[1]; JULIO Pereira[1]; INÊS Pires[1]; DAVIDE Moreira[1]; INÊS Almeida[1]; BRUNO Rodrigues[2]; COSTA Cabral[1]
[1]*Hospital Sao Teotonio, Department of Cardiology, Viseu, Portugal*; [2]*Centro Hospitalar Cova da Beira, Cardiologia, Covilha, Portugal*

Introduction: Neoplasia (N) is a risk factor (RF) for mortality (M) of any cause after venous thromboembolism (VTE). Acute pulmonary embolism (PE) may be the first manifestation of a N. Unprovoked (U) PE occurs in the absence of a reversible or temporary RF in the 6 weeks to 3 months preceding. Since VTE is the second cause of death in patients (P) with N, it is important to suspect a N in a P with PE. The differentiation of the type of PE has impact on the duration of the treatment, as so the prothrombotic potential of a N.
Objective: To evaluate the prevalence of N in the follow-up (FU) of PE and its impact on M.
Methods: Selected P admitted in a ICU by PE between 2007-2014, with division in two groups: N in FU (NF) and without N in FU (WF). FU up to 5 years. The active N status was measured in the hospital clinical process and in the computerized process of primary health care in the post-hospitalization period. Were excluded P who died or had active N during the episode, those who lost hospital follow-up and those who did not undergo oncological screening with their primary care physician.
Results: Of 175 P, were selected 126. Average age of 68 ± 18.3 years, 61.1% female. NF group 15.1% (n = 19) and WF 84.9% (n = 107). M in 1 year of 8.7% (n = 11) and in 5 years of 15.1% (n = 19). The most frequent N were the prostate and the lung (2.4% each, n = 3). U PE in 57.8% (n = 68) with 21.4% secondary to trauma / surgery, 10.9% to immobilization and 5.6% to pregnancy / contraceptives.
No differences in admission symptoms or blood tests between the groups. Compared with the WF group, the NF group was characterized by higher prevalence of previous heart failure (31.6% vs 12.3%, $p = 0.042$) and COPD (15.8% vs 3.8%, $p = 0.036$) and older age (69.42 ± 11.24 vs. 61.65 ± 19.1 years, $p = 0.003$). At admission, they had higher systolic blood pressure (129.32 ± 6.9 vs 117.01 ± 2.23 mmHg, $p = 0.042$). They revealed more AF (15.8% vs 3.8%, $p = 0.037$) and less T-wave inversion in V1-V3 (15.8% vs 41.5%, $p = 0.033$) on the ECG. There were no differences in the characteristics of the transthoracic echocardiogram but there was higher prevalence of inferior vena cava reflux (80% vs 40.4%, $p = 0.020$) and greater diameter of the coronary sinus (13.04 ± 0.90 vs 10.95 ± 0.31mm, $p = 0.049$) on CT angiography. The NF group was more frequently associated with PE classified as U (84.2% vs 15.8%, $p = 0.010$) and PESI risk III-V (89.5% vs. 64.5%, $p = 0.031$). No difference in M for any cause at 1 or 5 years after diagnosis.
Conclusion: The presence of N after the diagnosis of PE was 15.1% (22.2% in U PE). The EP may be a first sign of an asymptomatic N. The extensive screening of an hidden N after a TEV appears in the literature as having high sensitivity, although without impact on long-term survival. The integration of more holistic specialties will allow a better identification of those to whom a PE was the first manifestation of a pathology with important vital prognosis.

P1919

Non-invasively assessed pulmonary artery systolic pressure predicts short-term rehospitalizations in acute dyspnea patients

D Gabartaite[1]; J Bugaite[1]; E Paleviciute[2]; K Cerlinskaite[2]; R Norvilaite[3]; D Verikas[3]; G Ziubryte[3]; G Balciunaite[2]; A Krivickiene[3]; J Motiejunaite[3]; D Zaliaduonyte-Peksiene[3]; D Zakarkaite[2]; A Mebazaa[4]; A Kavoliuniene[3]; J Celutkiene[2]
[1]*Vilnius University, Faculty of Medicine, Vilnius, Lithuania*; [2]*Vilnius University, Clinic of Cardiac and Vascular diseases, Center of Cardiology and Angiology, Vilnius, Lithuania*; [3]*Lithuanian University of Health Sciences, Kaunas, Lithuania*; [4]*University Paris Diderot , U942 Inserm, Hospital Lariboisiére, Paris, France*

On behalf of: GREAT network

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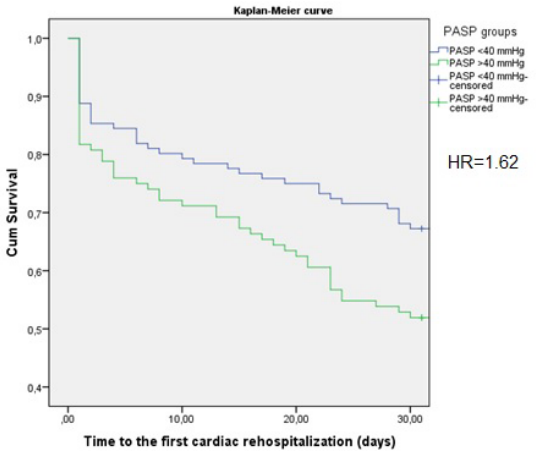
Introduction: Pulmonary hypertension (PH) is common among patients with heart failure (HF) and predicts worse outcomes. PH may also occur in patients with pulmonary and other diseases causing chronic or acute dyspnea. Significance of non-invasively diagnosed PH in predicting readmissions in the so called "vulnerable phase" (30 days after index hospitalization) has not been analysed.

Table 1	Hazard ratio	Confidence interval	P value
Patients with PASP ≥40 mmHg compared to patients with PASP <40 mmHg			
RH due to all causes in 1-month period	1.54	1.07 to 2.22	0.02
RH due to all causes in 1-month period (adjusted)	1.86	1.23 to 2.82	0.03
RH due to cardiac causes in 1-month period	1.62	1.06 to 2.46	0.026
RH due to cardiac causes in 1-month period (adjusted)	1.78	1.11 to 2.86	0.017



Kaplan-Meier curve

Objective: To investigate the prognostic value of non-invasively assessed PASP for rehospitalizations (RH) at follow up of 30 days in patients with acute dyspnea.
Design and Methods: During the period of 32 months 1482 acutely dyspneic patients were prospectively enrolled in the observational cohort study in two university hospitals. Causes of acute dyspnea were acutely decompensated HF, exacerbation of COPD, pneumonia, pulmonary embolism (PE) and others. In the first 48 hours after admission echocardiography was performed in 482 (32.5%) patients. Patients were divided in two groups: having PASP < 40 mmHg (no and mild PH) and with PASP = 40 mmHg (moderate and severe PH). Hazard ratio was adjusted to gender, age, LVEF and causes of dyspnea.
Results: Of 482 examined patients (mean age 68.6 ± 12.9 years) 193 (40.0%) were female. 64% had acute HF, 6.9% PE. Pulmonary hypertension (PASP >25 mmHg) was detected in 69.3% (n = 334) of patients. Mean PASP was equal to 46.54 ± 16.19 mmHg. The proportion of patients with PASP < 40 and = 40 mmHg was 56.6% (n = 273) and 43.4% (n = 209) respectively. Increased PASP = 40 mmHg was associated with higher rate of RH due to all and cardiac causes in 1-month period (Table 1). In 118 (24.5%) patients, first rehospitalization occured in the first 30 days after discharge, 88 (74.58%) of them were rehospitalized due to cardiac causes (HF 22.9%, atrial fibrillation 11.9%, acute coronary syndromes 5.9%, cerebrovascular diseases 5%, aortic stenosis 5%, PE 4.2%) and 30 (25.4%) due to non-cardiac causes (pneumonia 5.9%, exacerbation of COPD/asthma 3.4%, sepsis 3.4%). 55.08% of rehospitalized patients had PASP = 40 mmHg.
Conclusion: The higher pulmonary artery systolic pressure is a significant short-term predictor of rehospitalizations in acute dyspnea patients admitted to the emergency department.

P1920

In-depth hemodynamic phenotyping of pulmonary hypertension due to left heart disease

C Christian Gerges[1]; M Gerges[1]; P Fesler[2]; D Celermajer[3]; IM Lang[1]
[1]Medical University of Vienna, Department of Internal Medicine II, Division of Cardiology, Vienna, Austria; *[2]University Hospital of Montpellier, Department of Internal Medicine, Division of Nephrology, Montpellier, France*; *[3]University of Sydney, Department of Cardiology, Sydney, Australia*

Background: The commonest cause of pulmonary hypertension (PH) is left heart disease (LHD). However, current definitions of PH-LHD are under scrutiny. Therefore, we performed prospective in-depth invasive hemodynamic phenotyping in order to assess the site of increased pulmonary vascular resistance (PVR) in PH-LHD subsets.
Methods: Based on pulmonary artery occlusion waveforms yielding an estimate of the effective capillary pressure (Pc'), we partitioned PVR in larger arterial (Rup, upstream resistance) and small arterial plus venous components (Rds, downstream resistance). In case of small vessel disease Rup decreases and Rds increases concordantly. Inhaled nitric oxide (iNO) testing was used to assess acute vasoreactivity.
Results: Right ventricular (RV) afterload was significantly higher in combined post- and pre-capillary PH (Cpc-PH, n = 35) than in isolated post-capillary PH (Ipc-PH, n = 20). RV afterload decreased during iNO in Cpc-PH and idiopathic pulmonary arterial hypertension (iPAH, n = 31), but remained unchanged in Ipc-PH. Rup was low in Cpc-PH (66.8 ± 10.8%) and iPAH (65.0 ± 12.2%, p = 0.530) suggesting small vessel disease, and high in Ipc-PH (96.5 ± 4.5%, p < 0.001) suggesting upstream transmission of elevated left atrial pressures (LAP).
Conclusions: RV afterload is driven by elevated LAP in Ipc-PH and is aggravated by elevated small vessel resistance in Cpc-PH. Cpc-PH is responsive to iNO. Our data support current definitions of PH-LHD.

P1921

First collaborative registry of pulmonary hypertension in argentina (RECOPILAR)

D F Echazarreta[1]; ER Perna[2]; ML Coronel[2]; ML Diez[3]; A Lescano[3]; N Atamanuk[3]; JA Mazzei[4]; JA Caneva[4]; A Nitsche[5]; D Haag[6]; ML Cazalas[6]; C Stepffer[6]
[1]FAC, Buenos Aires, Argentina; *[2]FAC, Corrientes, Argentina*; *[3]SAC, Buenos Aires, Argentina*; *[4]AAMR, Buenos Aires, Argentina*; *[5]SAR, Buenos Aires, Argentina*; *[6]SAP, Buenos Aires, Argentina*

On behalf of: RECOPILAR
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Introduction: The First Collaborative Registry of Pulmonary Hypertension in Argentina (RECOPILAR) is an inter-institutional project developed between the Argentine Federation of Cardiology (FAC), the Argentine Society of Cardiology (SAC), the Argentine Association of Respiratory Medicine (AAMR), the Argentine Society of Rheumatology (SAR) and the Argentina Society of Pediatrics (SAP) of a multicenter, prospective, observational nature that included patients diagnosed with pulmonary hypertension (PH) including the 5 groups of the Nice 2013 classification. Method: From Jul-14 to Oct-16, incident and prevalent patients with pulmonary hypertension (PH) were prospectively included by 62 investigators from 22 provinces of Argentina. The inclusion criteria were: 1-patients over three months of age; 2 - mean pulmonary arterial pressure (mPAP) at rest = 25 mmHg by right heart catheterization and 3 - clinical stability in the absence of hospitalization in last month.
Results: A total of 627 patients were included, 338 (53.9%) before and 289 (46.1%) after Jul-15 Mean age was 50.8 ± 18.7 years, 434 (69.2%) were females, ethnicity was Caucasian 92.3%, native 7.5% and Asian 0.2%. Referral cases represented 22%, 53% were incident cases and 17.5% did not have social security. WHO functional class III-IV was 69.1% at the time of diagnosis, 33.3 at inclusion and 24.9% at the follow-up. Classification of PH in groups 1 to 5 (Nice) was the following: 64%; 16%; 8%; 10% and 2%. The clinical manifestations were dyspnea 82%, fatigue 54%, syncope 11%, chest pain 15%, palpitations 20% and heart failure in 21%, with previous hospitalization in 33% (half due to heart failure). The overall hemodynamic profile showed a mean pulmonary arterial pressure of 48.30 ± 16.51 mmHg, cardiac index 2.65 ± 0.89 l/min/m2, right atrial pressure 11.75 ± 1.4 mmHg, and vascular pulmonary and systemic resistances of 685.16 ± 456.96 and 1414.86 ± 579.97 dynes/sec/cm-5, respectively. Pulmonary vasorreactivity test was performed in 73% and it was positive in 10%. In patients with pulmonary arterial hypertension (PAH) vs other groups, the use of specific therapy was 80.5 vs 40.8% (p <0.001), including PDF5i in 71 vs 39%, endothelin receptor antagonists in 54.4 vs 14.5, and prostanoids in 14.3 vs 3.1% (all p <0.001). The follow-up was available in 422 patients (67%), with an 3-year overall survival of 74%.
Conclusion: In this collaborative Argentinean registry of PH, the epidemiological profile was similar to other Latin American series, with two thirds of patients with pulmonary arterial hypertension. The diagnostic work-up and therapeutic interventions, with a high use of specific therapy in PAH, were consistent with current recommendations of national and international guidelines. Despite the severity of the disease, the outcome was comparable to other contemporary registries.

P1922

Pulmonary arterial hypertension in the elderly: insights from a new group of patients with an old disease

E R Eduardo Perna[1]; ML Coronel[1]; E Calegari[2]; A Lescano[3]; G Giacomi[4]; M Diez[5]; L Favaloro[6]; M Cordova[4]; D Garcia Brasca[7]; C Huerta[8]; C Stepffer[9]; LL Lobo Marquez[10]; N Naval[10]; A Nitsche[11]; D Echazarreta[12]

[1]J.F. Cabral Cardiology Institute, Corrientes, Argentina; *[2]Hospital Fernandez, Buenos Aires, Argentina*; *[3]Finochietto Clinic, Buenos Aires, Argentina*; *[4]HIGA Mar del Plata, Mar del Plata, Argentina*; *[5]Cardiovascular Institute of Buenos Aires (ICBA), Buenos Aires, Argentina*; *[6]Favaloro Foundation University Hospital, Buenos Aires, Argentina*; *[7]Hospital Italiano, Cordoba, Argentina*; *[8]Hospital Cordoba, Cordoba, Argentina*; *[9]Hospital de Niños Pedro de Elizalde, Buenos Aires, Argentina*; *[10]Instituto de Cardiologia, Tucuman, Argentina*; *[11]Hospital Aleman, Buenos Aires, Argentina*; *[12]Hospital San Juan de Dios, La Plata, Argentina*

On behalf of: RECOPILAR Investigators

A demographic transition to older age in patients with pulmonary arterial hypertension (PAH) has been recently identified. We evaluate the prevalence, clinical profile and management of elderly with PAH in Argentina.
Method: From Jul-14/Oct-16, 399 incident/prevalent patients with PAH were prospectively included by 62 investigators from 22 provinces of Argentina, if they fulfilled all following inclusion criteria: Age >3 months; mean pulmonary arterial pressure = 25 mmHg by right heart catheterization (RHC) and clinical stability with no hospitalization in last month. Elderly group (EG) was defined by age >60 years.

Table 1

Variables	EG	NoEG	p
Pulmonary arterial pressure (Syst/Diast/Mean) (mmHg)	72/30/46	85/38/54	<0.001
Cardiac Index (l/min/m2)	2.7±1	2.8±1	NS
Wedge (mmHg)	12±4	11±5	NS
Right atrial pressure (mmHg)	11±8	12±11	NS
Pulmonary vascular resistance (WU)	8.4±5.6	10.4±6.2	0.012
Distance in 6 Min Walk Test (mts)	313±108	387±116	<0.001

Results: The prevalence of elderly was 26.6% (N = 106). The mean age in EG and noEG was 70 ± 7 vs 39 ± 14 years, females were 85 vs 77% (p = NS), and incident cases were 52 vs 49% (p = NS), respectively. Cardiovascular comorbidities in EG vs noEG were different in hypertension 17 vs 5.5% (p < 0.001), dyslipemia 8.5 vs 3.4% (p = 0.03), diabetes 6.6 vs 2.4 (p = 0.04) and chronic renal failure 3.8 vs 0% (p = 0.005). Subgroups of PAH in EG vs noEG were idiopathic 31.1 vs 43.3% (p = 0.028), heritable 1.9 vs 1% (p = NS), connective tissue disease 42.5 vs 17.1% (p < 0.001); portal hypertension 7.5 vs 2.7% (p= 0.042); HIV 0 vs 6.8% (p = 0.006) and congenital heart disease 17 vs 28.3% (p = 0.021). Clinical characteristics were similar between EG and noEG, with WHO class III-IV in 67.7 vs 63.8%, but with a lower proportion of syncope 5.7 vs 16% (p = 0.007). RHC and functional capacity are in Table 1. The use of specific therapy was similar in EG vs noEG, with no drugs in 19.8 vs 19.5%; monotherapy 33 vs 28.3% and combined treatment 47.2 vs 52.2 % (p = NS). The follow up was obtained in 65% of cases, and the survival in EG vs noEG at 3 years was 72 vs 75% (p = NS).
Conclusion: Nowadays, an important proportion of PAH patients are elderly. They have a particular profile: more cardiovascular comorbidities, similar severity of symptoms, better hemodynamic but worse functional capacity. Despite these differences, specific therapy and outcomes were comparable. These findings suggest an earlier diagnosis and faster decline in elderly with PAH.

Cardiovascular Surgery - Other

P1923

Prevention of periprocedural kidney ingury by loading doses of statins in elective percutaneous coronary interventions

EO Vershinina[1]; AN Repin[1]

[1]State Research Institute of Cardiology of Tomsk, department of rehabilitation, Tomsk, Russian Federation

Purpose of the study. To compare the effect of loading doses of atorvastatin and rosuvastatin on the value of the acute kidney injury and acute inflammatory response to elective percutaneous coronary interventions.
Materials and methods. An open prospective comparative study included 68 patients referred for elective percutaneous coronary intervention (PCI). At baseline, all patients had been taking statins for a long time as a standard lipid-lowering therapy. The first group included 33 patients who received a loading dose of 80 mg of atorvastatin (As) 12 hours before the intervention with saving this dose for 2-6 days. The second group included 35 patients treated with rosuvastatin (Rs) 40 mg / day in the same manner. The levels of creatinine and cystatin C in the blood were determined at baseline and 12, 24, 48 and 72 hours after the intervention. HsCRP level was determined at baseline and 5 days after PCI.
Results: AKI was diagnosed in 5 patients (7.94%): 4 patients (12.1%) in group As and 1 patient (3.3%) in group Rs (p = 0.36). The increase of serum creatinine level in the group As patients was 43.4% higher than one in the Rs group patients (p = 0.024). The decrease of glomerular filtration rate (GFR) in group As was 15.5% higher than one in group Rs (p = 0.09). Initially, the level of cystatin C in the groups did not differ (698.9 (560.2-869.6) ng / ml in group As vs 759.5 (673.8-899.9) ng / ml in group Rs, p = 0.75). Significant intergroup differences were found in the level of serum cystatin C 12 hours after PCI (718.3 (555.6-839.6) ng / ml in group As vs 470.6 (378.2-689.4) ng / ml in the Rs group, p = 0.007) that persisted 24 hours after the intervention (732.1 (632.3-887) ng / ml vs 526.4 (357.4-802.7) ng / ml, respectively, p = 0.02). From the second day after PCI, intergroup differences in serum cystatin C disappeared. The level of hsCRP significantly increased 72 hours after the intervention in group As (1.65 (0.9-4) mg / l at baseline vs 4.55 (1.6-8.7) mg / l 72 hours after PCI, p = 0.01). The level of hsCRP did not change significantly at the same time in the Rs group (2.8 (0.8-6.8) mg / l at baseline vs 2.75 (1.5-6.5) mg / l 72 hours after PCI, p = 0.16).
Conclusion. The loading dose of rosuvastatin better prevents periprocedural kidney injury in PCI and more significantly reduces the overall inflammatory response to intervention compared to the loading dose of atorvastatin.

P1924

Va-ecmo for the treatment of cardiac failure in post-cardiotomy patients with infective endocarditis

F S Floris Stefan Van Den Brink[1]; U Sonker[2]; R Van Tooren[1]; MJ Swaans[1]; P Klein[2]; FD Eefting[1]; NJ Breet[1]; E Scholten[3]

[1]St Antonius Hospital, Cardiology, Nieuwegein, Netherlands; *[2]St Antonius Hospital, Cardiothoracic Surgery, Nieuwegein, Netherlands*; *[3]St Antonius Hospital, Intensive Care, Nieuwegein, Netherlands*

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Introduction: Treatment of Infective Endocarditis (IE) consists in about a third of the patients of surgical intervention. Surgery for IE is often difficult with great challenges in post-operative circulatory and pulmonary support. Veno-Arterial Extra-Corporal Membrane Oxygenation (VA ECMO) could play a role in improving outcome in these patients, yet data in this regard is virtually non-existent.
Purpose: To gain insight in outcome of patients undergoing surgery for IE and subsequent treatment with VA-ECMO for circulatory support.
Methods: An in-hospital registry was kept between 2009 and 2016 on all patients receiving VA ECMO for circulatory support in our Hospital. All patients undergoing VA-ECMO were analysed retrospectively and were scored on age, gender, medical history, microorganisms involved, clinical outcome, complications, surgical procedure and length of stay.
Results: Between 2012 and 2016, 13 patients were treated with VA-ECMO following surgery for IE. The majority of patients was male (8/13). The median age was 62 years (33-73). A medical history concerning cardiac surgery was present in 9 patients: 8 had previous valvular surgery of whom 2 received concomitant coronary bypass surgery (CABG) as well, 1 patient had coronary bypass surgery alone. Surgical intervention consisted of a Bentall procedure in 10 patients, 2 of which received concomitant mitral valve surgery and another 2 received concomitant CABG. Valvular surgery without aortic involvement was performed in 3 patients: 1 mitral valve replacement, 1 aortic valve replacement and 1 combined procedure. All patients had positive cultures: S. Aureus in 3 cases, E. Faecalis in 3 cases, E. Faecium in 2 cases, E. Coli in 1 case, S. Epidermis in 1 case, S. Mitis in 1 case, H. Parainfluenzae in 1 case and Candida Albicans in 1 case.
Mortality while on VA-ECMO was 62% (8/13). Mortality during ICU stay was 77% (10/13). Survival to the ward was 23% (3/13) and all these patients had survival to discharge. One patient reached the one year survival point. The other two patients who have survived to discharge have not yet reached the one year survival point but are still alive. Patient related complications occurred in 54% (7/13) patients and consisted of haemorrhage at the cannula site in 4 patients, leg ischaemia in 1 patient, haemorrhage at another site in 1 patient and infection of the cannula in 1 patient. ECMO hardware related complications occurred in 1 case consisting of clot formation in the oxygenator. The median time on VA-ECMO was 5 (1-15) days, the median time spent on ICU was 6 (2-29) days and the median time spent in hospital was 16 (5-78) days.
Conclusion: VA-ECMO for the treatment of cardiac failure in post-cardiotomy patients who were operated on for infective endocarditis is feasible but outcome is poor. It could improve survival in selected patients

P1925

Technical approach to endovascular treatment of patients with ostium lesion of coronary arteries

Z KH Shugushev[1]; D A Maximkin[1]; AG Chepurnoy[1]; OO Safonova[1]; AV Mambetov[1]
[1]*RUDN University, Moscow, Russian Federation*

Aim: to increase the effectiveness of endovascular treatment in patients with ostium coronary artery lesions.
Methods: 150 patients were included in the study. Inclusion criteria: ostium atherosclerotic lesions of LAD or LCx > 70% according to QSA and IVUS; stable angina II-III functional class (CCS); silent myocardial ischemia; positive stress test. The main included 108 patients, who were randomized into 2 groups. In I group (n = 54) according to IVUS, atherosclerotic plaque spread from the ostium of LAD and/or LCx to the LMCA, and in group II (n = 54) - the plaque did not spread into the LMCA. In Group I all patients were initially treated with 'Provisional T' stenting of the LMCA, and in Group II - stenting of the ostium LAD or LCx. In retrospectively, the third (III) control group (n = 42) was formed, where the stenting of the ostium of LAD or LCx was performed without IVUS. Drug-eluting stents were implanted in all patients. Long-term results were evaluated on average over a period of 30.04 ± 12.04 months in 50 patients from group I, in 48 patients from group II and in 40 - from group III. Primary endpoints: frequency of MACE (death, MI, revascularizations). Secondary endpoints: frequency of restenosis and late stent thrombosis according to QSA and IVUS.
Results: during hospitalization of complications associated with PCI was not, survival was 100% in all groups. There was no conversion to complete bifurcation stenting. Survival in the long-term period was 100% in all groups. In all patients, in comparison with preoperative data, tolerance to physical activity significantly increased. Nonfatal MI was observed in 7.5% of patients from group III ($p < 0.05$), in the I and II group of cases MI was not recorded. The incidence of stent restenosis and target lesion revascularization (TLR) according to QSA and IVUS was observed in 1 patient (2%) in group I, in 1 patient (2.1%) in group II and in 4 patients (10%) in III group ($p < 0.05$). Frequency of target vessel revascularization (TVR) occurred in group I in 2% of patients, in group II in 2.1%, and in group III in 7.5% ($p < 0.05$). The total frequency of MACE in groups I, II and III was 2; 2.1 and 25%, respectively ($p < 0.05$). Among patients in group III, 1 case of stent thrombosis (2.5%) was verified 12 months after PCI.
Conclusion: the use of IVUS for the analysis of the ostium lesions of coronary artery allows us to choose the optimal stenting technique and also reliably improve the long-term results of endovascular intervention by reducing the incidence of stent restenosis and MACE.

P1926

Oxidative stress and endothelium dysfunctin in patients with coronary artery bypass grafting

YN Maksimovich[1]; TP Pronko[1]; YA Kashcheyeu[1]; NY Maksimovich[1]
[1]*Grodno state medical university, propaedeutics of internal diseases, Grodno, Belarus*

Introduction: It is known that the NO molecule has both pro- and anti-oxidant properties. Since the nitric oxide (NO) is a vascular endothelial anti-thrombotic factor, that can convert in the highly toxic peroxynitrite (ONOO-) it is obvious need to study the changes in nitric oxide level in patients during perioperative period of Coronary Artery Bypass Graft surgery (CABG).
Purpose: The aim of our study was to investigate the role of NOx and Malonic dialdehyde (MD) change in blood serum and the condition of endothelium in of patients with coronary artery disease in the perioperative period of coronary bypass surgery performed with pump on.
Methods. It was investigated the content of nitrites and nitrates, MD in the blood plasma and endothelium dysfunction of 26 patients with coronary artery disease and cardiac ischemia (CI) in condition grafting performed with pump on.
Results: The studies revealed a decrease in [NOx], increase of malonic dialdehyde level as an indicator of oxidative stress in blood plasma of the patients after coronary bypass surgery in period of coronary blood flow restoration in comparison with the period before pump on device was connected. The patients levels of nitrite and nitrate in the recovery period cardiac activity (pump on) was lower (74%, $p < 0,05$), as compared with their concentration in the initial period of operation (before pump on). Decrease of NOx indicates either a low production of NO by vascular endothelium or an increase in its utilization in reaction with superoxide anion and its conversion to peroxynitrite.
Increase in the levels of malonic dialdehyde is the result of the oxidative processes due to increased hemolysis.
In the patients with coronary artery bypass grafting we noticed decrease of endothelium dependent vasodilation in post-surgical period in comparison with the pre-surgical period. This creates conditions for the occurrence of coronary vascular endothelial dysfunction in patients with CABG, thereby predisposing to the development of thrombosis due to a decrease of antithrombotic properties of vascular endothelium generated NO.
Conclusion Decrease of NO levels, appearance of oxidative stress and endothelial dysfunctions are pathogenetic factors of perioperative Myocardial Infarction as the most frequent and dangerous fatal complications in patients with decreased antithrombotic properties of coronary arteries and implanted bypass.

P1927

Similar long-term clinical outcomes after percutaneous coronary intervention in grafts versus native vessels in prior coronary artery bypass grafting patients with diabetes mellitus

D Dong Liu[1]
[1]*Fuwai Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Cardiology, Beijing, China People's Republic of*

Background Atherosclerosis in diabetic patients with prior CABG progresses fastly. Data on how to choose target vessels of post-CABG PCI in diabetic pateints is sparse.
Methods 157 patients with diabetes and previous CABG, who underwent PCI of either a graft (n = 44) or a native (n = 113) vessel between January 1st 2009 and June 1st 2014 in the National Center for Cardiovascular Disease, China, were studied. In-hospital and long-term clinical outcomes were compared between the groups.
Results Diabetic patients with prior CABG had more percutaneous interventions (PCI) to native arteries, but the proportion of grafts PCI increased as time went on. Both groups had similar baseline characteristics. Group graft vessel (GV) patients compared with group native vessel (NV) had more totally occluded native vessels, less totally occluded grafts and more in-stent restenosis. However, there was no difference in in-hospital mortality and long-term incidence of major adverse cardiac event, cardiac death, nonfatal myocardial infarction (MI), or revascularization. Multivariate logistic regression analysis showed that PCI success (OR = 11.488, 95%CI = 1.135-116.303, $P < 0.05$) was independent predictor of MACE. **Conclusions:** It suggested similar long-term clinical outcomes after PCI in GV or NV in prior CABG patients with diabetes. Thus the vessel with higher estimated PCI success rate should be prioritized by operators.

Hypertension - Other

P1928

Assessment of left atrial mechanical function by two-dimensional echocardiography in hypertensive patients

S Antit[1]; S Slama[1]; S Chenik[1]; A Amri[1]; I Boussabeh[1]; M Thameur[1]; L Zakhama[1]; S Benyoussef[1]
[1]*Interior Security Forces Hospital, Department of Cardiology, Marsa, Tunisia*

Aim : To compare left atrial (LA) mechanical function, assessed by two-dimensional echocardiography, in patients with essential hypertension with healthy controls.
Methods : LA volumes were measured echocardiographically in 50 hypertensive patients and 50 age-matched healthy controls using biplane Simpson method. LA volume measurements were done at the time of mitral valve opening (Vmax), at the onset of atrial systole (p wave at the electrocardiogram = Vp) and at mitral valveclosure (Vmin). All volumes were indexed for body surface area, and the following left atrial emptying functions were calculated: LA passive emptying volume = Vmax-Vp, LA passive emptying fraction = LA passive emptying volume/Vmax, conduit volume = left ventricular stroke volume-(Vmax-Vmin), LA active emptying volume = Vp-Vmin, LA active emptying fraction = LA active emptying volume/Vp, LA total emptying volume=(Vmax-Vmin), LA total emptying fraction = LA total emptying volume/Vmax.
Results: Hypertension was associated with an increase of all LA volumes: Vmax ($p < 0.001$), Vp ($p < 0.001$) and Vmin ($p < 0.004$). LA booster pump function was significantly greater in hypertensive patients than in controls with an increase of LA active emptying fraction (35 ± 12% versus 30 ± 12%respectively; $p = 0.032$). The increase of LA booster pump function was found to be greater in hypertensive patients with impaired diastolic function compared to those with normal diastolic function ($p = 0.029$). LA conduct function assessed by LA passive emptying fraction was found to be significantly greater in control group than in hypertensives (32 ± 11% versus 22 ± 12% respectively; $p < 0.001$). There was a negative correlation between left ventricular mass index and LA passive emptying fraction ($r=-0.37$; $p = 0.007$). LA reservoir function evaluated by LA total emptying fraction was similar in both groups while LA total emptying volume was greater in hypertensives than in control group ($p = 0.03$).

Conclusion: Hypertension was associated with a decrease in left atrial passive emptying function, and an increase of systolic pump function. Left ventricular hypertrophy and diastolic dysfunction probably played a major role in these modifications.

P1929

Predictive models for major renal events in patients with significant atherosclerotic renal artery stenosis after renal angioplasty with stent implantation

DO Geavlete[1]; C Beladan[1]; D Deleanu[1]; O Tautu[2]; MR Zaharia[3]; BA Popescu[1]; C Ginghina[1]; O Chioncel[1]
[1]*Institute of Cardiovascular Diseases Prof. C.C. Iliescu, Cardiology, Bucharest, Romania*; [2]*Emergency Clinical Hospital Floreasca, Cardiology, Bucharest, Romania*; [3]*Emergency Clinical Hospital St John, Internal Medicine, Bucharest, Romania*

Introduction: Renal artery stenosis (RAS), due to poor prognosis remains a matter of debate regarding the selection of patients who would benefit the most from renal artery stenting, natriuretic peptide being suggested to be useful in patients' selection.
Purpose: The study was aimed to analyze the response of renal function 12 months' after renal angioplasty with stent in selected patients diagnosed with significant RAS in order to find predictors for major renal events (acute renal failure and need for dialysis).
Methods: 78 hypertensive patients diagnosed with significant uni- and bilateral RAS were prospectively enrolled, resulting in 3 groups (34-unilateral, 28-bilateral RAS and 16-RAS in solitary kidney). Cardiac and renal history, blood pressure, biological profile (including BNP), vascular diseases, comorbidities and hospitalization after revascularization were evaluated. A complete echocardiography was performed in all patients. Renal function was estimated based on the serum creatinine level and glomerular filtration rate (eGFR-CKD-EPI). The mean extended follow-up period was 24.27 ± 12.16 months.
Results: Baseline renal dysfunction was significantly higher in solitary kidney RAS cases when compared to bilateral and subsequently to unilateral RAS($p = 0.001$). Improvement in renal function 12 months' after stenting was observed in 52.7% of all patients, preservation in 43.1% and deterioration in 4.1%, without significant differences between groups (p?0.05). The prevalence of major renal events was 14%. Although a wide range of clinical, biological and echocardiographic parameters were significantly correlated with major renal events, the multivariate regression analysis confirmed only baseline LnBNP as an independent predictor for renal major outcomes ($p = 0.002$). The accuracy of the emerged predictive model as quantified by the area under the receiver-operating characteristics curve (AUC) was 0.95 (95% CI, 0.83-1.01, $p = 0.002$). By removing BNP from the model, an alternative model which included 3 independent predictors was emphasized: history of renal disease, post-revascularization eGRFCDK-EPI value and hospitalization for decompensated cardiac failure. The accuracy of the predictive model as quantified by AUC was 0.95 (95% CI, 0.89-1.00, p?0.001). The presence of preexistent renal disease in the model did not correlate with blood pressure nor with renal function evolution after revascularization.
Conclusions: The present findings demonstrated that BNP could be a valuable biomarker in the assessment of renal deterioration after revascularization as an unique predictor. The alternative model with higher prediction sensitivity was related to the strong relationship between renal events, poor renal function response to renal stenting and cardio-renal syndrome. Preexistent renal disease is distinctively marked in the model, as it probably refers to irreversible parenchyma and vascular renal diseases that lead to renal insufficiency progression.

P1930

The clinical profile and outcomes of acute decompensated heart failure in patients with history of hypertension

S Sergey Kozhukhov[1]; A Alexander Parkhomenko[1]
[1]*NSC "Institute of Cardiology", Kiev, Ukraine*

Background: Most patients with acute heart failure present with history of hypertension (HTN). The aim was to investigate baseline characteristics and impact of HTN in patients with acute decompensated heart failure (ADHF).
Methods: 117 consecutive patients (73.5% hypertensive and 26.5% non-hypertensive) presenting with ADHF were enrolled in a prospective open-label study. The diagnosis of ADHF was classified according to European Society of Cardiology guidelines.
Results: Patients with HTN were older (69.3 vs 62.7 years, $p < 0.05$), more likely to be female, to have diabetes, hyperlipidemia, cerebrovascular disease, prior history of coronary artery disease, but less likely to be smokers when compared with patients without HTN. On admission, HTN patients had lower glomerular filtration rate, hemoglobin and higher blood glucose level. In-hospital mortality was 2.6% without significant difference between groups. The incidence of cardiovascular death and rehospitalization due to heart failure did not differ among patients with HTN in overall ADHF group ($p = 0.212$ by Log rank).
Conclusion: In cohort of ADHF patients HTN was not associated with an increased rate of in-hospital mortality, cardiovascular death and rehospitalization during 2-years follow up.

P1931

The role of epigenetic factors by men with arterial hypertension in the formation of disorders of the central nervous system

V S Potaskalova[1]; NV Khaitovych[1]; MN Seliuk[2]; AP Burlaka[3]; NN Kozachok[2]; OV Seliuk[2]
[1]*National O.O. Bohomolets Medical University, Kiev, Ukraine*; [2]*Ukrainian military medical academy, Kiev, Ukraine*; [3]*R.E. Kavetsky Institute of Experimental Pathology, Oncology and Radiobiology of NAS Ukraine, Kiev, Ukraine*

The effect of ultra-high frequency electromagnetic radiation (UHF-EMR) can be considered as an epigenetic factor in the development of arterial hypertension and worsening of the prognosis of the disease. It is known that during the prolonged exposure of UHF EMR developing disturbances of the central nervous and cardiovascular systems. The study purpose was determining the features of cognitive functions (CF) and sleep of patients with arterial hypertension (AH), working in conditions of UHF EMR.
The study included 125 men, 35 - with AH, who worked under the influence of UHF EMR (group 1), 30 - were healthy men worked in the same conditions (group 2), 30 patients with AH and 30 healthy men without the long-term influence of UHF EMR (group 3, 4). The average age of the subjects $31,2 \pm 5,4$ years. The dose of UHF EMR was within the range of 4320-31065 kW ($17151,7 \pm 7102,4$ kW average). Patients of 1 and 3 groups were treated with antihypertensive therapy according to the recommendations of the European Society of Cardiology 2007, revision 2009. CF were determined by means of neuropsychological tests, specially designed questionnaire of sleep quantity and quality.
Patients of 1 group compared with patients of 3 group showed a reduction in motor function (MF) ($6,4 \pm 1,2$) against ($7,5 \pm 0,8$) points, $P < 0,001$; successive functions (SF) ($7,2 \pm 1,3$) against ($8,2 \pm 0,8$) points, $P < 0,05$ and functions of writing (WF) ($10 \pm 2,4$) against the ($12,6 \pm 1,4$) points, $P < 0,005$. Men from the 2 group also identified changes in the central nervous system: MF was ($8,2 \pm 0,4$) against ($9,2 \pm 0,8$) scores of healthy men, $P < 0,05$; SF - ($8,6 \pm 0,5$) against ($9,6 \pm 0,4$) points, $P < 0,05$, WF - ($13,4 \pm 1,5$) against the ($17,0 \pm 1,6$) points, $P < 0,05$. Diagnosed an inverse correlation between the level of MF ($r = -0,63$; $P < 0,05$), SF ($r = -0,75$; $P < 0,005$) and WF ($r = -0,51$; $P < 0,05$) and time under the conditions of UHF EMR exposure. Among the patients of 1 group sleep less than 6 hours reported 92% (including at least 5 hours - 38%), from 6 to 7 hours - 8% of patients, just 80% of patients of 1 group noted the quality of sleep disturbance. Sleep duration of patients from 2 group duration of 6 to 7 hours reported 86%, 8 and more hours - 14% of patients.
Conclusion: Those men, who worked in conditions of UHF EMR, were diagnosed disturbances of cognitive function, the degree of which correlated with the duration of work in these conditions. Most patients with AH (80%) had insufficient sleep duration and impaired quality of it, which perhaps along with other factors determined the propensity of increasing blood pressure.

Sleep Disorders

P1932

Impact of sleep apnea on five-year prognosis in patients after acute myocardial infarction

O Ludka[1]; R Stepanova[1]; T Kara[2]; J Spinar[3]
[1]*International Clinical Research Center, St. Anne's University Hospital, University Hospital Brno, Masaryk University, Brno, Czech Republic*; [2]*Division of Cardiovascular Diseases, Department of Internal Medicine, Mayo Clinic and Foundation, Minnesota, United States of America*; [3]*Department of Internal Medicine and Cardiology, University Hospital Brno, Brno, Czech Republic*

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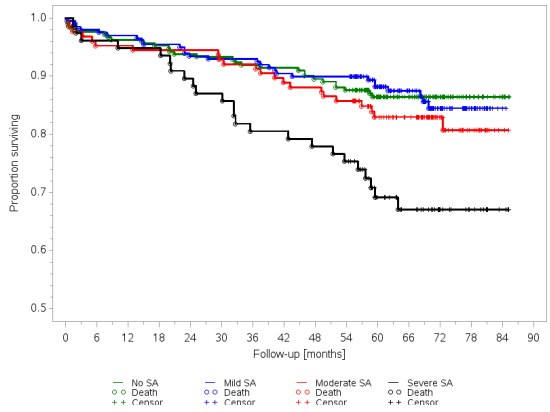
Purpose: Sleep apnea (SA) has a high prevalence in patients after myocardial infarction (MI). While SA might be a modifiable risk factor, recent data suggest that SA is severely underdiagnosed in patients after MI. There is also limited evidence about long-term prognosis of patients after MI according to SA categories. Therefore we sought to determine the relationship between SA and long-term prognosis among patients presenting with MI.
Methods: We prospectively studied 782 consecutive patients admitted to the hospital with the diagnosis of acute MI. The study was conducted in two tertiary care

institutions, where primary percutaneous coronary intervention (PCI) is the standard of care in the treatment of acute MI. All subjects underwent sleep evaluations using a portable diagnostic device after at least 48 hours post-admission, provided they were in stable condition. Patients were followed for median follow-up of 66 months.
Results: Almost all patients (98%) underwent urgent coronary angiography and 91% of patients underwent primary PCI. 175 (22.4%) patients had technically inadequate limited sleep studies (less than 4 h recording time or inability to score study due to excessive artifact). We therefore analyzed the data from 607 patients who had good quality sleep study records. Using a threshold of AHI > 5 events/hour, SA was present in 65.7% of patients after acute myocardial infarction. Mild SA was present in 32.6%, moderate in 20.4% and severe in 12.7%. There was a relation between the severity of SA and long-term prognosis. Patients after MI with increasing severity of SA had higher total mortality (p = 0.002, log-rank test). The Kaplan-Meier survival curves are presented. There was also a higher total mortality in reduced than in preserved left ventricular ejection fraction patients after MI in the group of moderate to severe SA (p = 0.033). Conclusion: Mortality of patients after MI significantly increased with increasing severity of SA. Whether treatment of SA after MI will significantly improve outcomes in these patients remains to be determined.



Kaplan-Meier survival curves

P1933

Improved sleep apnoea management in patients newly diagnosed with severe sleep apnoea via device-based pre-screening: a sub-analysis of the RESPIRE study

P Pascal Defaye[1]; A Ghuran[2]; S Vittadello[3]; V Russo[4]; I Heurtebise[5]; D Dey[6]; W Amara[7]
[1]University Hospital of Grenoble, Department of Cardiology, Grenoble, France; *[2]Lister Hospital, Stevenage, United Kingdom*; *[3]Osp. Civile Montebelluna, Treviso, Italy*; *[4]OSP. SS. Annunziata ASL Taranto, Taranto, Italy*; *[5]Centre Hospitalier de Bourges, Bourges, France*; *[6]LivaNova, Clamart, France*; *[7]Centre Hospitalier Intercommunal Le Raincy-Montfermeil, Le Raincy-Montfermeil, France*

On behalf of: RESPIRE Study Investigators
Funding Acknowledgements: LivaNova

Background/Introduction: The diagnosis of sleep apnoea (SA) with polysomnography is costly and often lengthy, making the use of pre-screening methods for SA attractive. The SA monitoring feature in REPLY 200 DR pacemakers detects, analyses and records abnormal breathing events (apnoea and hypopnoea), allowing pre-screening of SA via the measurement of a respiratory disturbance index (RDI).
Purpose: The RESPIRE study investigated the prevalence of severe SA and rates of associated referrals, examinations and treatment in an unselected pacemaker population.
Methods: The study was an 18-month international, single-arm, open-label study of patients implanted with REPLY 200 pacemakers. SA severity was determined from device memory using RDI, the sum of abnormal respiratory events divided by sleep duration. Severe SA was defined as a mean RDI = 20 over 12 months. SA referrals, examinations and treatment were determined at 12 months for patients with versus without severe SA. Patients already receiving SA treatment were excluded from the analysis.
Results: Of the 1147 enrolled patients (56.3% male; 75.7 ± 10.3 years), 1024 patients were analysed. At 12 months, 313 (30.7%) patients had severe SA. In patients with severe SA, 24.6% were referred to a sleep specialist, 21.7% were referred for an SA exam, and 15.3% were treated for SA (Table).
Conclusion(s): Severe SA is prevalent in unselected pacemaker patients. Thanks to pre-screening with device-based SA monitoring, more newly diagnosed patients with severe SA were able to benefit from specialist SA follow-up and subsequent examination and treatment.

	Patients with severe sleep apnoea* N = 313	Patients without severe sleep apnoea* N = 706
Referred to sleep specialist at 12 months	N = 77 (24.6%)	N = 74 (10.5%)
Pneumologist	69 (22.0%)	67 (9.5%)
Neurologist	5 (1.6%)	1 (0.1%)
Ear Nose Throat specialist	0 (0%)	4 (0.6%)
Cardiologist	1 (0.3%)	2 (0.3%)
Other	5 (1.6%)	5 (0.7%)
Referred for a sleep apnoea exam at 12 months	N = 68 (21.7%)	N = 65 (9.2%)
Polysomnography	55 (17.6%)	46 (6.5%)
Polygraphy	12 (3.8%)	17 (2.4%)
Other	5 (1.6%)	4 (0.6%)
Treated for sleep apnoea at 12 months	N = 48 (15.3%)	N = 62 (8.8%)

*Five patients overall were not evaluable at 12 months

P1934

Incidence of severe sleep apnoea and its association with significant atrial fibrillation in an unselected pacemaker population: results from the RESPIRE observational study

J Julio Marti Almor[1]; L Jesel[2]; R Garcia[3]; P Defaye[4]; E Di Girolamo[5]; F Locati[6]; A Dompnier[7]; P Venables[8]; H Burri[9]; G Askamp[10]; P Marques[11]
[1]Hospital del Mar, Barcelona, Spain; *[2]Nouvel Hôpital Civil, Strasbourg, France*; *[3]University Hospital of Poitiers, Poitiers, France*; *[4]University Hospital of Grenoble, Grenoble, France*; *[5]SS. Annunziata Hospital , Chieti, Italy*; *[6]Osp. G. Salvini-Garbagnate Milanese, Milan, Italy*; *[7]Centre Hospitalier d'Annecy, Pringy, France*; *[8]Ipswich Hospital NHS Trust, Ipswich, United Kingdom*; *[9]Geneva University Hospitals, Geneva, Switzerland*; *[10]LivaNova, Clamart, France*; *[11]Hospital de Santa Maria, Lisbon, Portugal*

On behalf of: RESPIRE Study Investigators
Funding Acknowledgements: LivaNova

Background/Introduction: Patients (pts) with atrial fibrillation (AF) are often affected by sleep apnoea (SA). The diagnosis of SA with polysomnography is costly and often lengthy. Pre-screening of SA in paced pts, based on the measurement of a respiratory disturbance index (RDI), is possible with certain pacemakers, such as the REPLY 200 DR.
Purpose: The RESPIRE study evaluated the incidence and severity of SA and its association with significant AF in unselected pacemaker pts, and whether the severity of SA affected the occurrence of major serious adverse events (MSAEs).
Methods: RESPIRE was an international, observational, single-arm, open-label study that followed pts for 18 months after implant with REPLY 200 pacemakers. SA severity was ascertained from device memory using RDI, the sum of abnormal respiratory events divided by sleep duration. Severe SA was defined as mean RDI = 20 over 12 months. Significant AF was defined as a cumulative time in AF = 24 hours over 2 consecutive days. The efficacy co-primary endpoint was the difference in significant AF between pts with severe versus non-severe SA at 12 months. The safety co-primary endpoint was all investigator-reported MSAEs. The analysis reports mean intergroup differences [95% confidence intervals] estimated using a one-sided Z test with significance set at $P < 0.025$.
Results: Of 1147 enrolled pts (56.3% Male; 75.7 ± 10.3 years), 1024 were analysed. At 12 months, severe SA was detected in 321 pts (31.3%), and 172 pts (16.8%) had significant AF. Pts with severe SA had a higher incidence of significant AF; there was no difference in the percentage of MSAEs (Table).
Conclusion(s): With pre-screening, almost a third of unselected pacemaker pts were found to have severe SA at 12 months. Severe SA was significantly associated with a higher incidence of significant AF. No relationship was found between severity of SA and occurrence of MSAEs.

	Patients with severe sleep apnoea	Patients with non-severe sleep apnoea	Difference [95% CI], P-value
Efficacy*	N = 321	N = 698	
Significant AF at 12 months, % (n)	24.9% (80)	13.2% (92)	11.7% [6.4;17.1], P = 0.018‡
Safety	N = 312	N = 712	
Major serious adverse events, % (n)	6.7% (21)	3.9% (28)	2.8% [-0.3; 5.9], P = 0.040
Death	3.5% (11)	1.4% (10)	
Myocardial infarction	0.6% (2)	0.1% (1)	
Stroke	0.6% (2)	0.1% (1)	
Re-intervention	1.9% (6)	2.2% (16)	

*Five patients were not evaluable. ‡Tested for an expected difference of 6%.

Cardiovascular Rehabilitation

P1935

Physical training reduces microvascular ischemia and improves left ventricular systolic function in patients with non-ischemic dilated cardiomyopathy and microvascular dysfunction

MV Marcus Vinicius Simoes[1]; EEV Carvalho[1]; JC Crescencio[1]; DM Tanaka[1]; LFL Oliveira[1]; PV Schwartzmann[1]; CQ Bertini[1]; A Schmidt[1]; L Gallo-Junior[1]; JA Marin-Neto[1]

[1]Medical School of Ribeirão Preto - University of São Paulo, Brazil, Ribeirão Preto, Brazil

Background: Myocardial ischemia with normal coronary arteries at angiography, characterizing the presence of coronary microvascular dysfunction (CMD), may be detected in 30-50% of patients with non-ischemic dilated cardiomyopathy (DCM) and is a marker of worse prognosis. However, there is a lack of studies assessing the impact of therapeutic measures targeting CMD in this clinical context.
Purpose: We aimed at testing the effect of physical training over the extent/severity of myocardial perfusion defects and left ventricular systolic function in patients with CMD associated to DCM.
Methods: We prospectively investigated 20 patients with DCM presenting CMD characterized by chest pain, normal coronary arteries at angiography, and detection of = 2 myocardial segments with reversible perfusion defects during stress-rest Tc-99m-Sestamibi myocardial perfusion-SPECT imaging (MPI). Patients were assigned to a Training Group (TG - n = 11, 5 men, age = 60.0 ± 7,8 y. o., mean NYHA functional class = 1.8 ± 0.4) and Control Group (CG - n = 9, 5 men, age = 55.8 ± 12 y.o., mean NYHA functional class = 2.0 ± 0.5). At baseline and 3 months afterwards, both groups underwent MPI including evaluation of left ventricular ejection fraction (LVEF) by using gated-SEPCT images, cardiopulmonary exercise test (CPT) and quality of life (QOL) evaluation by using the SF36 questionnaire. The patients of the TG were submitted to aerobical physical training during 3 months, consisting of 1-hour treadmill sessions, 3 times/week, moderate intensity (60 to 85% of the peak-VO2). The myocardial perfusion defects were visually graded using a semi-quantitative score (0 = normal uptake; 4 = absent uptake) in a left ventricular 17-segment model. Summed reversibility score (RS) was calculated by subtracting the rest summed score from the stress summed score.
Results: The CG presented no significant difference between the baseline and post 3 months evaluation for all investigated variables. However, the TG patients exhibited significant reduction of the RS from baseline to the post-training evaluation (7.7 ± 3.9 to 2.4 ± 4.7, respectively, p = 0.003), reduction of the number of segments with reversible defects (6.9 ± 2.9 to 2.9 ± 4.1, respectively, p = 0.007), increasing of the LVEF (39.6 ± 20.5 to 44.8 ± 20.7%, respectively, p = 0.02), increasing of the physical capacity measured by the peak-VO2 (16.3 ± 3.9 to 18.7 ± 3.5 ml/Kg/min, respectively, p < 0.003) and by the VO2 at the anaerobic threshold (10.4 ± 2.0 to 12.9 ± 3.0 ml/Kg/min, respectively, p = 0,001). We observed significant improvement in all domains of the SF-36 scores.
Conclusions: Physical training was associated to significant reduction of the extent/severity of reversible myocardial perfusion defects in patients with DCM and coronary microvascular dysfunction. This positive effect was also associated to improvement of the LVEF and QOL scores. Our results suggest that physical training is a relevant therapy for coronary microvascular dysfunction in DCM patients.

P1936

The Efficacy of Exercise-Based Cardiac Rehabilitation in heart failure patients with mid-range ejection fraction

I Burazor[1]; R Sakurai[2]; S Stevovic[1]; M Moraca[1]; A Kovacevic[1]; Y Adler[3]

[1]Institute for Rehabilitation, Cardiology, Belgrade, Serbia; [2]International University of Health and Welfare, Tokyo, Japan; [3]Chaim Sheba Medical Center, Tel Hashomer, Israel

Heart failure is a major cause of morbidity, mortality and re- hospitalizations and is highly prevalent in myocardial infarction survivors. Cardiac rehabilitation based on exercise training and heart failure self-care counseling have each been shown to improve clinical status and clinical outcomes. We aimed to evaluate the usefulness of exercise based in house cardiac rehabilitation in patients with heart failure with mid-range ejection fraction (HFmrEF) after myocardial infarction.
Patients and Methods: Out of 2253 patients who were admitted to our three weeks in- hospital secondary prevention program - exercised based cardiac rehabilitation, we analyze a total of 109 patients who were admitted early after coronary revascularization (percutaneus coronary interventions or coronary bypass surgery) with HFmrEF. The majority of patients were males (67%).R isk factors and co morbidities were noted. Patients were selected for exercise training after six minute walking testor exercise stress test (cardiopulmonary dominantly to evaluate unexpected exertional dyspnea) . After 3 weeks in house cardiac rehabilitation the patients were re-tested.
Results: The major comorbidities in our patient population were as follows: hypertension, diabetes and dyslipidemia. Six minutes walking test was performed and the total distance walked ranged from 120 to 480 meters and the beginning of the program. Patient had 7 -days a week training program. After the 3 weeks in hospital exercise rehabilitation the improvement in the test was ˜32%. Cardiopulmonary test showed also improvement of functional capacity.We noted several rhythm disturbance complications by telemetry (VES, SVES). None had acutisation of heart failure (with peripheral edema and congestion). All patients fulfilled cardiac rehabilitation program.
Conclusions: Supervised multidisciplinary cardiac rehabilitation program, including an individualized exercise component is effective and can improve functional status and exercise tolerance in patient with HFmrEF after myocardial infarction.

P1937

Erectile dysfunction: a forgotten determinant of cardiac rehabilitation program success

H Helena Nascimento[1]; A Rocha[1]; M Braga[1]; R Pinto[1]; M Tavares-Silva[1]; G Pestana[1]; P Araujo[1]; A Nunes[1]; S Torres[1]; J Rodrigues[1]; V Araujo[1]; F Parada[1]; MJ Maciel[1]

[1]Sao Joao Hospital, Porto, Portugal

Introduction: In order to improve cardiac rehabilitation program (CRP) success, it is of paramount importance to identify vulnerable groups of patients. Erectile dysfunction (ED) is a powerful indicator of cardiovascular risk and poor outcome. Therefore, our study main goal was to evaluate ED role as a predictor of functional capacity as a surrogate of CRP success.
Methods: From a registry of 840 consecutive patients (pts) enrolled in a cardiac rehabilitation program after an acute coronary syndrome (ACS), between 2008 and 2016, we studied the male pts. Sociodemographic and clinical data was prospectively collected. Depression was assessed using the HospitalAnxiety and Depression Scale (HADS) and ED through the 5-Questions International Index of Erectile Function (IIEF). ED was defined as an IIEF < 17.
Results: From a total of 637 male pts studied, ED was present in 300 patients (47%). Cardiac event was a ST-elevation ACS in 45.7% and a non-ST-elevation ACS in 54.3%. ED group of pts was significantly older (56.8 ± 9.4 vs. 52.0 ± 9.3 years-old, p < 0.001), has lower educational level (8.0 ± 4.6 vs. 9.1 ± 5.0, p = 0.005) and higher levels of HADS-depression (5.1 ± 3.9 vs. 3.6 ± 3.7, p < 0.001). Regarding the cardiovascular risk factor, hypertension and diabetes were significantly more prevalent in ED pts (p < 0.005). Also,coronary artery disease was more severe in this group (number of coronary vessel disease: 1.5 ± 0.8 vs. 1.3 ± 0.6, p = 0.001). In terms of functional capacity, the ED pts performed worse both at the beginning (METs 8.6 ± 2.3 vs. 9.5 ± 2.2, p < 0.001) and at the end of the CRP (METs 10.2 ± 2.0 vs. 11.4 ± 2.4, p < 0.001). Nevertheless, the CRP program significantly improved the functional capacity (degree of METs improvement 1.6 ± 1.8, p < 0.001) and reduced the HADS depression levels (1.1 ± 4.2, p = 0.014) in these pts.
Conclusion: ED is a highly prevalent condition inACS population and its impact on quality of life is undeniable. Moreover, it must be recognized as a predictor of poorer performance in CRP programs. Therefore, sexual function assessment should

integrate ACS patient evaluation,and tailored strategies ought to be conceived in order to achieve CRP success.

P1938
The role of the cardiac rehabilitation program in improving functional capacity

A Alzira Nunes[1]; P Maia Araujo[1]; H Nascimento[1]; M Braga[1]; R Pinto[1]; M Tavares Silva[1]; G Pestana[1]; A Rocha[2]; V Araujo[1]; M Belchior Campelo[1]; M Julia Maciel[1]
[1]Sao Joao Hospital, Cardiology Service, Porto, Portugal; [2]Sao Joao Hospital, Physical Medicine and Rehabilitation, Porto, Portugal

Introduction: The Cardiac Rehabilitation Programs (CRP) occupy a prominent position in the prevention of cardiovascular disease and in the control of its risk factors. A significant part of its effectiveness is due to its positive impact on the functional capacity (FC) of patients (pts), which results in a significant improvement in their prognosis.
Purpose: To assess the functional capacity of pts with ischemic heart disease undergoing a CRP over a 12-month follow-up.
Methods: We retrospectively analyzed pts who integrated the CRP between August 2008 and August 2016. We compared two groups of pts: those who maintained their FC and those who lost = 10% of their FC, taking into account the difference between the duration of the exercise testing at the end of the PRC and at the end of the 12-month follow-up. Then we performed univariate and multivariate analysis in order to found the predictors of that evolution.
Results: We recruted a total of 549 pts, 86.5% of whom were men, with an average age of 54 ± 9.8 years. In 49.1% of the cases, the diagnosis that led to hospitalization was an acute myocardial infarction with ST segment elevation. We performed a univariate analysis with sociodemographic, clinical and physical activity variables. The family history of coronary disease (p = 0.056), systolic function at the first echocardiogram (p = 0.055) and moderate physical activity in the 12-month review (p = 0.037) were identified as predictors of functional capacity loss. After a multivariate analysis, the previous history of coronary disease (p = 0.056) and the number of damaged vessels (p = 0.033) were the only predictors of this evolution.
Conclusions: This study reinforces the excellence of CRPs in the secondary prevention of cardiovascular disease by demonstrating that the majority of pts who integrate that ones show a significantly favorable evolution of FC. It is imperative to identify the different predictors of this outcome in order to enhance the effectiveness of the CRP.

P1939
Cardiac rehabilitation after an acute coronary syndrome: eight years of a real-life experience

M Marta Braga[1]; A Rocha[1]; H Nascimento[1]; P Araujo[1]; A Nunes[1]; S Torres[1]; R Pinto[1]; J Rodrigues[1]; V Araujo[1]; F Parada-Pereira[1]; MJ Maciel[1]
[1]Sao Joao Hospital, Porto, Portugal

Background: Cardiac rehabilitation programs (CRP) are essential interventions in secondary prevention of patients with acute coronary syndrome (ACS). Contemporary CRP includes baseline patient assessments, psychosocial and nutritional counselling, cardiovascular (CV) risk factor management, and exercise training. The purpose of this study was to describe the baseline characteristics and evaluate the impact of a CR in CV risk profile and functional capacity (FC) in patients after ACS.
Methods: We prospectively collected data from patients who underwent a CR program after an ACS, from 2008 to 2016. FC was assessed using a standard exercise test (ET), including exercise duration and intensity in metabolic equivalents (METs). We used paired sample T-Test to study the effect of a CR program.
Results: Among the 867 patients included, 85.1% were males. The mean age was 54.7 ± 10.0 years. About 16.2% were unemployed. Regarding to the prevalence of CV risk factors, hypertension was present in 42.7%, smoking in 54.3%, dyslipidemia in 60.2%, and obesity in 25.5% of patients. Mean LDL-cholesterol was 122.8 ± 38.9 mg/dL, while HDL-cholesterol was 41.6 ± 11.8 mg/dL. Mean body mass index was 27.8 ± 4.0. Only 18.8% of cohort were diabetic, and their mean glycated haemoglobin was 7.6 ± 1.5%. Main diagnosis of patients was ST-segment elevation myocardial infarction. Percutaneous myocardial revascularization (MR) was performed in 80.9% of patients, and only 8.4% of patients had been submitted to a surgical MR. Most patients had preserved left ventricular systolic function. The results of the first ET showed mean maximal ET duration of 8.4 ± 2.1 min and mean intensity of 9.0 ± 2.3 METs. Approximately 85% of the patients completed an exercise training, showing a statistically significant improvement of FC after the CRP. Final ET showed mean maximal ET duration of 10.2 ± 2.2 min and mean intensity of 10.7 ± 2.1 METs. After a CRP there was a significant reduction in LDL-cholesterol, and in mean body mass index. There was also a reduction in mean glycated haemoglobin in diabetic patients, as well as a tendency for increase in HDL-cholesterol (without statistically significance).
Conclusions: Patients with ACS had a high prevalence of CV risk factors. CRP had an important role in reduction of modifiable CV risk factors and improvement of FC , as wel as in reducing CV morbidity and mortality. This study emphasizes the need to increase referral of ACS patients to the CRP.

P1940
Left ventricle systolic dysfunction and physical training: efficacy of secondary prevention cardiac rehabilitation program

I Burazor[1]; R Sakurai[2]; M Moraca[1]; S Stevovic[1]; A Kovacevic[1]; Y Adler[3]
[1]Institute for Rehabilitation, Cardiology, Belgrade, Serbia; [2]International University of Health and Welfare, Tokyo, Japan; [3]Chaim Sheba Medical Center, Tel Hashomer, Israel

Secondary prevention based on cardiac rehabilitation (CR) exercise training programm and chronic heart failure (CHF) self-care counseling have each been shown to improve clinical status and clinical outcomes in CHF. The aim of this study was to evaluate the efficacy of exercise based in hospital cardiac rehabilitation in patients with left ventricle dysfunction
Patients and Methods: A total of 217 patients who were admitted to our three weeks in- hospital rehabilitation program, early after coronary revascularization (percutaneus coronary interventions or coronary bypass surgery) with ejection fraction below 40%. The majority of patients were males (60%). The oldest patient was 75 years of age. Ejection fraction below 25% was detected in 15%. We noted risk factors and co morbidities. Patients were selected for exercise training after six minute walking test (92%) or cardiopulmonary exercise test. After 3 weeks in hospital cardiac rehabilitation the patients were re-tested.
Results: The major comorbidities in our patient population were as follows: diabetes, hypertension, atrial fibrillation. Six minutes walking test was performed and the total distance walked ranged from 120 to 400 meters and the beginning of the program. Patient had 7 -days a week training program. After the 3 weeks in hospital exercise rehabilitation the improvement in the test was ˜33%. Cardiopulmonary test showed also improvement of functional capacity. We noted several rhythm disturbance complications by telemetry (VES, SVES) and when needed beta blockers were added. None had acutisation of chronic heart failure (with peripheral edema and congestion). The majority of patients fulfilled cardiac rehabilitation program (99%).
Conclusions: Supervised secondary prevention program based on exercise, including an individualized exercise component is safe and improve functional status and exercise tolerance in patient with left ventricle dysfunction after myocardial infarction.

Autoimmune/Chronic Inflammatory Disorders and Heart Disease

P1941
Familial dilated cardiomyopathy in a 32-year-old woman diagnosed with Mucolipidosis III Alpha/Beta by Whole Exome Sequencing

H W Lee[1]; SH Lee[1]; JC Choi[1]; JY Shin[1]; JH Ahn[1]; JS Park[1]; JH Oh[1]; JH Choi[1]; HC Lee[1]; KS Cha[1]; TJ Hong[1]
[1]Pusan National University Hospital, Department of Cardiology, Busan, Korea Republic of

Introduction: Familial DCMP is sometimes combined with systemic genetic syndromes. Among them, for the patients who have skeletal dysplasia, appropriate diagnostic examination should be performed.
Case Report: A 33-year-old woman was presented with cardiac arrest from ventricular fibrillation. She had been diagnosed with DCMP 2 years ago, but she stopped taking medicine for recent 8 months. Although she has been given optimal medication and implantable cardioverter/defibrillator (ICD) several months after resuscitation, her cardiac function remained severely decreased . She was listed for heart transplantation and get transplanted soon. Pathologic examination of explanted heart showed severely dilated left ventricle with severe fibrosis and some inflammatory change, but showed no remarkable coronary and valvular abnormalities. Clinical course after transplantation was good without complications. During hospitalization, a physician noticed her unique morphologic features. She had mild coarse face, low nose, large tongue, and claw hands with contracted major joints in upper and lower extremities. Her height and weight were 153cm and 56kg, respectively. But had no intellectual and sexual dysfunction. She had been treated with spinal surgery from unknown lumbar degenerative disease 8years ago. Her older sister was also diagnosed with DCMP and spinal disease at the age of 35, and died of sudden cardiac death. Turner and Noonan syndrome was ruled out by array Comparative Genomic Hybridization and genetic mutation test. Under the suspicion of mucopolysaccharidosis (MPS) I, diagnostic tests were done. Urine glycosaminoglycans test and a-L-iduronidase activity in serum was marginally diagnostic. Direct sequencing showed c.1898C>T (p.Ser633Leu) heterozygote mutation. Because

such heterozygote mutation was discovered in a patient who was finally diagnosed with MPS I, we started treatment for the patient with enzyme replacement therapy for several months. However, her mother and younger sister who were functionally and morphologically normal were known to have same heterozygote mutation with the patient. Therefore, we performed whole exome sequencing to diagnose genetic mutations which have correlation with familial DCMP and skeletal dysplasia. Heterozygote mutation in GNPTAB gene with c.2715+1G>A and c.3173C>G was found. Mucolipidosis III alpha/beta was finally diagnosed after confirmation of elevated plasma enzyme activity of arylsulfatase A and hexosaminidase, and not elevated plasma activity of ß-glucosidase. Since then, she has been treated with pamidronate. Summary:This is the case of familial dilated cardiomyopathy in a young woman diagnosed with mucolipidosis III alpha/Beta by Whole Exome Sequencing. If several test reveals not to be conclusive, whole exome sequencing may give additional information, and can be sometimes diagnostic as in this case.

P1942

Coronary artery calcium score in rheumatoid arthritis patients: associations with apolipoproteins and disease biomarkers

M Bernardes[1]; A Madureira[2]; A Oliveira[3]; MJ Martins[4]; R Lucas[4]; L Costa[1]; JG Pereira[3]; F Ventura[4]; I Ramos[2]; E Martins[4]
[1]Sao Joao Hospital, Rheumatology, Porto, Portugal; *[2]Sao Joao Hospital, Radiology, Porto, Portugal*; *[3]Sao Joao Hospital, Nuclear Medicine, Porto, Portugal*; *[4]University of Porto, Faculty of Medicine, Porto, Portugal*

Aims and Methods: In rheumatoid arthritis (RA), cardiovascular (CV) comorbidities are a major cause of mortality. Coronary calcium score (CCS) assessed by computed tomography has been associated with RA prognosis. In this work, we aimed to assess CCS in RA patients and determine their associations with different clinical, laboratory and imaging disease parameters.
Results: We evaluated 78 patients, with a mean age of 53.4 ± 11.1 years, 76. 9% females, with a mean Disease Activity Score (DAS28) four variables (4v) and Stanford Health Assessment Questionnaire (HAQ) of 4.359 ± 1.309 and 1.375 ± 0.664, respectively, and disease duration of 14.1 ± 9.9 years.
Mean CCS value was 46.133 ± 122.892. CCS > 10 was significantly associated to CV risk factors [age (OR= 1.076; p = 0.004), BMI = 30 Kg/m2 (OR= 0.072; p = 0.017), HDL (OR= 0.016; p = 0.015), LDL/HDL ratio (OR= 1.767; p = 0.045), apolipoprotein A1 (ApoA1) (OR = 0.970; p = 0.009); apolipoprotein B/ApoA1 (ApoB/ApoA1) ratio (OR= 28.657; p = 0,011), homocysteine (OR= 1.176; p = 0.038), statins use (OR = 3.413; p = 0.03) and diabetes (OR= 13.429; p= 0,019)], disease activity [C Reactive-Protein (CRP) (OR= 1.046; p = 0.022), DAS(4v) (OR= 1.584; p = 0.019) and modified Sharp/van der Heijde Score (SHS) erosion score (OR= 1.012; p = 0.018)], biomarkers [(Dkk-1 (OR = 1.014; p = 0,017) and osteoprotegerin (OR= 1.381; p = 0.031)], bone mineral density [femoral (OR = 0.012; p = 0,014), lumbar spine (OR = 0.009; p = 0,006)] and osteoporosis (OR = 5.476; p = 0,012). After adjustment for age, gender and BMI, significant associations were maintained with ApoA1, ApoB/ApoA1 ratio, statins use, CRP, DAS(4v) and Dkk-1.
Conclusions: Our work reinforces the hypothesis that in RA, CCS may be a useful tool in cardiovascular risk assessment, particularly valuable in poorer controlled patients with certain lipoprotein profile.

P1943

Heart failure needs to be ruled out in HIV-infected patients on antiretroviral therapy

M Maria De Las Nieves Montoro Lopez[1]; C Soto[2]; I Ponz[1]; JJ Rios[2]; G Guzman Martinez[1]
[1]University Hospital La Paz, Department of Cardiology, Madrid, Spain; *[2]University Hospital La Paz, Internal Medicine, Madrid, Spain*

Background: Highly active antiretroviral therapy (HAART) has greatly improved life expectancy among HIV-infected patients, nevertheless, cardiovascular disease has become its first mortality cause in high-income countries. It is known that HIV-patients present higher risk of coronary artery disease but there is scarce data about the prevalence of symptomatic heart failure due to HIV-related cardiomyopathy in the HAART era.
Methods: We conducted a prospective observational study in a tertiary hospital in Spain. A randomized sample of HIV+ outpatients on HAART was selected from the specialized HIV clinic. We performed a test of dyspnoea to select symptomatic patients, in whom we determined NT-proBNP levels, considering positive a value above 125 pg/mL. Patients underwent a transthoracic echocardiogram (TTE) to assess the left ventricle (LV), the right ventricle (RV) and to rule out pulmonary hypertension (PH).
Results: A total sample of 75 HIV+ patients on HAART with dyspnoea was analysed (median age 47y, male 74%; smokers 54%; years on HAART-mean- 15.5; Hepatitis C virus 51%). Ten patients (13%) showed NT-proBNP levels above the upper limit. Out of them, five cases (7%) were diagnosed with either HF or PH: one case mild LV systolic and diastolic dysfunction (DD); one case LV hypertrophy and DD; two cases RV systolic dysfunction (one of them associated with PH); and one case was compatible with isolated HIV-related PH. Five did not present significant cardiac disease by TTE (table).
Conclusion: In our sample of symptomatic HIV+ individuals in routine follow-up, 7% were diagnosed with either HF due to HIV-related cardiomyopathy or PH. Furthermore, this proportion could have risen up to 13% if more sophisticated cardiac tests had been undertaken. This result reinforces the need of cardiac screening protocols and collaboration between cardiologists and HIV-specialists in order to improve the prognosis of this vulnerable population.

Cardiovascular Nursing - Other

P1944

Development of providing care of heart failure patients who are in need of extra support

NP Kato[1]; N Takayama[2]; J Iwaki[3]; E Nogami[3]; K Kinugawa[4]; T Jaarsma[1]
[1]Linkoping University, Department of Social and Welfare Studies, Linkoping, Sweden; *[2]University of Tokyo Hospital, Department of Nursing, Tokyo, Japan*; *[3]University of Toyama Hospital, Department of Nursing, Toyama, Japan*; *[4]University of Toyama, The Second Department of Internal Medicine, Toyama, Japan*

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Background: Some heart failure (HF) patients do not fit the standard HF management model and might be in need of extra support, for example patients with cognitive disorders, patients with frequent readmissions for HF, and patients with a low level of health literacy.
Purpose: The purpose of this study was to summarize nurses' opinions about how to take care of HF patients who might be in need of extra support.
Methods: The study used an explorative, descriptive design. Two focus group discussions were performed in Japan, including a total of 19 nurses who took care of HF patients. Three cases were discussed: (1) a patient (87 years old, female) with cognitive disorders who lives alone, (2) a patient (91 years old, male) with frequent readmissions due to HF who lives with an elderly family caregiver, (3) a patient (82 years old) with low health literacy who lives alone. The focus groups were led by a moderator and an interview guide was used with questions addressing the care needed, the role of family members and health care professionals and possible use of information and communication technology (ICT) as a tool to support patient's self-care. Data was analysed using qualitative content analysis.
Results: The opinions about how to take care of HF patients who might be in need of extra support could be summarized into four categories, namely 'share goals with patients and their family', 'tailor-made self-care support', 'effective resource utilization' and 'manage social support' The category 'shared goals' included two sub categories: share treatment/care goals and share life goals, describing especially found important for an elderly patient who had frequent HF readmissions. The second category 'tailor-made self-care' included suggestions for the help for taking medication , symptom monitoring, and a healthy balanced diet and these were considered to be relevant in all three cases. A third category 'effective resource utilization' described use of social service (e.g., food delivery service) and healthcare service (e.g., continuous support by home visit nurses and/or outpatient clinics). The fourth category 'manage social support' described a need for social connection and collaboration with other family members. Some nurses thought that ICT would not work for these HF patients with special needs, but other nurses thought that it was up to the ICT devices whether the ICT could support patient's self-care.
Conclusions: HF nurses had specific and dedicated ideas on adaptation of HF management models for patients with special needs. Suggestions included sharing goals with patients and their family, tailoring self-care support, use and develop existing and available resources effectively and to manage social support.

P1945

A new tool to promote preventive behaviours in patients at risk of heart failure.

A Annamaria Bagnasco[1]; M Zanini[1]; G Catania[1]; G Aleo[1]; L Sasso[1]
[1]University of Genoa, Health Sciences, Genoa, Italy

Background. Nurses play an important role in helping patients improve self-management, make sure they confidently and safely manage therapy at home, and consequently contribute to reducing readmissions and costs. We identified the Barrows Cards method, originally used to test decision-making skills and critical thinking in medical students. In this study, we designed a new tool to improve preventive behaviors in patients at risk of developing heart failure.

Purpose: To develop and validate a tool to educate patients already affected by some form of heart disease, but without cardiac structure alterations, to avoid risk behaviours, identify risk factors (e.g. hypertension, diabetes, obesity) and safely manage cardiotoxic drugs at home.
Methods. The Barrows Cards-also known as the 'Portable Patient Problem Pack'-uses a situational card that describes a complex problem and learners can choose from a deck of at least 15 cards each of which describes a possible solution to that problem with the support of a picture. The Barrows Cards method is based on problem-based learning, and we applied this to patients to improve self-management and preventive behaviours through therapeutic education.
Two focus groups with 15 cardiac nurses were conducted to identify the educational competencies to include in the HF Prevention Barrows Cards.
The instrument development and validation process included the following steps:
1) A review of the literature to retrieve scientific evidence to support the purpose of our study.
2) Obtaining support and advice from a group of cardiologists.
3) Obtaining support and advice from a psychologist with regard to the sentences to include in the cards.
4) Checking the nursing records of 30 patients at risk of heart failure.
5) Using a short questionnaire to obtain feedback from patients on their level of satisfaction with the statement and picture on each card in terms of clarity and appropriateness.
6) Check the efficacy of the tool in correcting risk behaviours.
Results: This tool was successfully tested on 30 heart failure patients and all the indications that emerged from the test have been applied in corrective terms and an updated version is currently being tested.
The Barrows Cards aroused in HF patients a good level of interest and compliance, consequently contributing to a higher level of self-care educational efficacy. This was confirmed a reduced number of calls and accesses to the cardiology outpatients clinic requiring major information about drug treatment.
Conclusion: Despite the benefits provided by the new systems that evaluate the ability to prevent risks, there are still important issues linked to the incorrect management of patients at risk of heart failure and who live at home. Therapeutic patient education performed by nurses based on a validated structured model such as the Barrows Cards, can significantly contribute to improve outcomes in vulnerable chronic populations, such as patients with heart diseases.

P1946
Adhere risk model in a public healthy institution in brazil: preliminary data

E R Eneida Rejane Rabelo-Silva[1]; D De Souza Bernardes[1]; C Wahast Avila[1]; C Mirapalheta Ernandes[2]; MA Lumertz Saffi[1]; L Lopez Pedraza[1]
[1]Federal University of Rio Grande do Sul, Heart Failure Clinic and Transplant Group at Hospital de Clinicas de Program at the Nursing School, , Porto Alegre, Brazil; *[2]Hospital de Clínicas de Porto Alegre, Multidisciplinary residency, Porto Alegre, Brazil*

Introduction: Patients admitted for acute decompensated heart failure (ADHF) are likely to develop episodes of worsening during hospitalization that require more complex interventions, such as inotropic drugs and / or intravenous vasodilators, or transfer to intensive care units. In this sense, the ADHF requires careful evaluation in the first hours of hospital admission, a practice that is often performed by screening nurses. The "ADHERE risk model" is a score that predicts risk of worsening in-hospital in patients with ADHF. In Brazil, this score has not yet been used in studies.
Objective: To apply the "ADHERE risk model" risk prediction model in hospitalized patients.
Methods: A cohort study conducted in a public and university hospital in Brazil from January 2013 to October 2017 through a retrospective collection in a database of electronic medical records. Data on clinical, laboratorial and sociodemographic variables were extracted at the time of admission. Subsequently, the "ADHERE risk model" was applied, which designated the sample risk. The patients were followed up during hospitalization, in order to verify if some group became worse according to the prediction of the score.
Results: A preliminary analysis of 673 patients from a sample estimated in 1234 was performed. The predicted risk model showed that 320 (47.5%) of the included patients presented risk of developing a worsening of the ADHF during long hospitalization. Of these, 156 (49%) actually worsened ADHF during hospitalization, while in the non-risk group, 271 (77%) of the patients did not develop worsening ($p < 0.001$). Based on the risk estimate, the at-risk group had 3.14 (2.2 - 4.3, 95% CI) times greater risk of worsening of ADHF compared to the non-risk group. Comorbidities, mortality and length of hospital stay were associated with clinical worsening in-hospital.
Conclusion: Preliminary data indicated that the score was shown to be applicable to identify patients at risk of worsening of ADHF. Approximately 50% of the at-risk cases evolved to worsening in-hospital. Only mortality was significant for patients who developed worsening in both groups. The group with risk of in-hospital worsening presented longer hospitalization time.

P1947
Home visits for a cohort of heart failure patients who otherwise could not attend a heart failure clinic, an observation of their management after referral for home visit.

B Bronagh Travers[1]; C Keane[2]; R O Hanlon[3]; P Campbell[1]; S Zhou[2]; M Ledwidge[2]; K Mcdonald[1]
[1]St. Vincent's University Hospital, Heart Failure Unit, Dublin, Ireland; *[2]Heart Failure Unit, Dublin, Ireland*; *[3]Blackrock Clinic, Dublin, Ireland*

Background: Heart failure (HF) is a chronic disease which affects 2% of population, prevalence increases with age . Aging, co-morbidities and or progression of HF, mean some patients find it increasingly difficult to attend hospital appointments for management of HF. Home visits are provided to a small cohort of patients who require nursing home care, lack family support or physically cannot attend HF service.
Method: This observational report looks at a group of HF patients (82) diagnosed with HF either following admission to hospital with ADHF (24.3%) or are referred using other pathways, for diagnosis and management of HF. As a result of aging, increased care requirements, progression of HF or other chronic diseases, a percentage of our patients, who otherwise would refuse follow-up are offered home visits from a HF Nurse Specialist.
Results : Over a five year period, 82 patients have benefitted from home visits, (48 female (49%), 37 (45%) HF with reduced ejection fraction (HFREF). NYHA Class II 10 (12%) at time of referral to home visits. Mean age at time of first review in HF Unit 81.63 years $\pm$ -9.03 and mean age at time to referral for home visits 84.79 $\pm$ -9.02. Mean follow-up from time of referral to service 3.8 years (1-14). Thirty (36.5%) patients required input from specialist palliative care services for management of HF symptoms. In total, 29 (35%) patients died, of these 20 patients (24%) had input from specialist palliative care services, the remainder for non- HF related reasons. Over the five year period, 8 (9.7%) patients were readmitted with one ADHF admission, 5 patients (6%) had more than 2 ADHF admissions. Twenty seven patients (32%) required at least one additional visit, 9 (10.9%) required more than two additional visits and 5 (6.09%) patients required more than 3 home visits outside of routine reviews for further management of their HF symptoms. At time of initial referral to HF service, 9 (10%) were on diuretic, with 72 (87 %) requiring diuretics at time of referral to home visit. Changes in BNP by more than 100pg/ml increased in 9 patients (36%).
Conclusion: A complex cohort of HF patients who otherwise would not be able to continue their link with specialist HF service can be managed at their place of residence, maintaining continuity of care with HF service and quality of life.

P1948
Prediction of risk and diagnostic accuracy in nursing in patients hospitalized for decompensated heart failure

E R Eneida Rejane Rabelo-Silva[1]; C Mirapalheta Ernandes[2]; D De Souza Bernardes[1]; L Lopez Pedraza[1]
[1]Federal University of Rio Grande do Sul, Heart Failure Clinic and Transplant Group at Hospital de Clinicas de Program at the Nursing School, , Porto Alegre, Brazil; *[2]Hospital de Clínicas de Porto Alegre, Multidisciplinary residency, Porto Alegre, Brazil*

Introduction: The risk model of the Acute Decompensated Heart Failure National Registry (ADHERE) is a risk prediction model for in-hospital worsening heart failure. In many referral centers, a screening of patients in ready care is performed by nurses. It would be interesting if nurses could combine the use of a score with their clinical evaluation in order to improve their clinical reasoning in the establishment of nursing diagnoses.
Objective: To analyze the diagnostic accuracy in nursing in patients with predicted risk of clinical worsening during hospitalization for acutely decompensated heart failure (ICAD).
Methods: A total of 43 patients were analyzed through an electronic medical record in a retrospective cohort, hospitalized by ICAD in a public university hospital, Brazil (period 2013-2017), which presented a clinical health risk defined by the ADHERE risk model. After the application of the escore and definition of the patients at risk, the Accuracy Scale of Nursing Diagnostics version 2 (EADE v.2) was applied to the nursing diagnoses established during the first 24 hours of hospitalization. The EADE v.2 evaluates and points out the diagnostic accuracy from the analysis of clues (signs and / or symptoms), specificity, relevance and consistency of these, at the end is added the score to establish the category of accuracy: null, low, moderate or high of confirmed diagnoses.

Results: Of the patients with risk of worsening, 22 (51%) did not worsen and 21 (49%) worsened; in both patients with a moderate / high quality diagnosis in 22 (89%) and 16 (88%) of the nursing diagnoses, respectively. The established nursing diagnoses were ineffective respiratory pattern in 27 patients, with 21 (78%) in the High category and 15% in the Moderate accuracy category. Cardiac output decreased and Excess fluid volume was 100% in the high accuracy category with seven and two patients, respectively. Ineffective tissue perfusion: cardiopulmonary with 57% in the category of High Accuracy.
Conclusions: These data allow to conclude with patients with ICAD and risk of clinical worsening during hospitalization are identified with good diagnostic accuracy by nurses. This enables effective planning of interventions.

P1949
Development and implementation of an integrated diagnostic and therapeutic care model for outpatients with pulmonary hypertension

DL Vadala'[1]; C Bessone[1]; C Piccinino[1]; S Miccioni[1]; C Clementi[1]; J Zanaboni[1]; A Dimagli[1]; A Ailia Giubertoni[1]; PN Marino[1]
[1]*Hospital Maggiore Della Carita, Cardiology, Novara, Italy*

Introduction: Pulmonary hypertension (PH) is a severe life-limiting disease. Guidelines recommend early diagnosis for a timely menagement that has proven to be effective in improving prognosis. They also recommend a multidisciplinary approach wich should be referred to an expert centre.
Purpose: To explore the roles of nurses in optimising a patient-centred multidisciplinary model care.
Methods: Patients are referred to our centre because at high risk of developing PH or because already followed-up. The naive patients are recruited by a dedicated specialised nurse who calls back patients in less than 24-48 hours after voicemail or electronic mail massages. She arranges the meeting, provides informations on how they can access the centre and the procedures she planned. The diagnostic pathway includes many interdisciplinary activities previously scheduled in hourly time windows, ending in a clinical summary of findings. Specifically, they undergo comprehensive clinical evaluation including EKG and physical examination, a 6 minute walk test, conventional transthoracic echocardiography, pulmonary function tests (PFTs), gas transfer analyses - diffusion lung CO (DLCO), arterial blood gases and chest X-ray, evaluation of brain natriuretic peptide (BNP). The nurse herself does some tests and works the whole time alongside the medical equipe. All results are stored in a dedicated database. The patients already in specific therapy are enrolled in a nursing telephone follow-up. The nurse ensures that informations to patients and care-givers are updated and plans next meeting. This model has been implemented since 2014.
Results: We recruited 386 patients, 47 new patients in 2017. In 21 cases we started a telephone follow-up. The planned pathway enabled patients to udergo a thorough diagnostic assessment including at least 8 tests and final report in a single day. This policy avoided multiple access to hospital laboratories, provided a better selction of patients to address to right heart catheterization and offset unplanned hospital admissions.
Conclusions: A medical-nursing unit model with the help of an integrated computerised system would allow a higher qualified and more timely diagnostic and therapeutic approach in patients with PH.

P1950
Impact of standardized therapeutic hypothermia protocol on neurological performance after resuscitation from cardiac arrest

T Okasha[1]; W Morsy[1]; H Zaghla[2]
[1]*Cairo University, Critical care and emergency nursing department, Cairo, Egypt*;
[2]*Cairo University, critical care medicine, Cairo, Egypt*

Background: Cardiac arrest remains one of the most dramatic, unexpected, and life threatening events worldwide. Survival and neurological outcome vary widely.Current evidence supports that induction of therapeutic hypothermia in selected patients after cardiac arrest can improve neurological outcome.
Aim: The aim of the study is to evaluate the impact of standardized therapeutic hypothermia protocol on neurological performance after resuscitation from cardiac arrest.
Research hypothesis: Post cardiac arrest patients with GCS score of less than (8) and who will be exposed to therapeutic hypothermia protocol will exhibit improvement in their neurological performance.
Sample:Purposive sample of 17 patients who were fulfilling the inclusion criteria. Design:Quasi-experimental design was used in this study.Setting:critical care units at AlkasarAlaini hospitals.
Tools: Demographic and medical data sheet, Post cardiac arrest health assessment sheet, Bedside Shivering Assessment Scale (BSAS), and Glasgow Pittsburgh cerebral performance category scale (CPC).Result: the mean age was 53 years, 47.1% were arrested because of cardiac aetiology. 35.3% with initial arrest rhythm VT, 23.5% with VF, and 29.4% with A-Systole. a favorable neurological outcome was seen among 70.6% (CPC of 1-2).there was significant difference in WBC, Platlets, PaO2, PaCo2, HCo3, RBS. There was significant difference in ventilator hours across the CPC categories. Initial arrest rhythm, aetiology of cardiac arrest, and shivering status were significantly correlated with CPC
Conclusion: therapeutic hypothermia has positive effects on neurological performance among post cardiac arrest patients with GCS score of less than (8).
Key wards: therapeutic hypothermia, neurological performance, cardiac arrest.

Basic Science - Cardiac Biology and Physiology

P1951
Segmental analysis of longitudinal contractility in assessing left ventricular function

A Alexey Kuchmin[1]; EP Galova[1]; MV Zubakova[1]; DA Galaktionov[1]; KB Evsukov[1]; AA Kazachenko[1]; DY Epelshtein[1]
[1]*The Kirov Military Academy, St-Petersburg, Russian Federation*

Background: Speckle tracking is an important method in assessing left ventricular function along with ejection fraction and parameters of diastolic function. To date the contribution of different segments to the systolic and diastolic functions of the left ventricle has not been studied sufficiently.
Purpose: evaluation of the role of various segments of the left ventricle in the performance of left ventricle systolic and diastolic function in healthy individuals.
Methods: 56 volunteers without signs of cardiovascular pathology, 48 men and 8 women, mean age 33.6 ± 9.3 years were examined. All patients underwent an echocardiographic study using the GE "VividE95" device (USA) in accordance with the recommendations of the European echocardiographic association and the American echocardiographic society. The analysis of longitudinal deformations of the myocardium was carried out, which was determined by the percentage of shortening of the fibers in each segment of the left ventricle, and was visualized on the device with the help of the "bull's eye" technique.
Results: Based on the results of the correlation analysis, the magnitude of longitudinal deformation in the lower-septal segments (3 and 9) correlated with the thickness of the interventricular septum ($r = -0.46, -0.44$, respectively, $p < 0.05$), the thickness of the posterior stack ($r = -0.45$, $p < 0.05$), myocardial mass index ($r = -0.41, -0.44$, respectively, $p < 0.05$), as well as the anterior-posterior size of the LP ($r = -0, 4, -0.48$, respectively, $p < 0.05$).
A negative correlation was found between the left ventricular ejection fraction and the longitudinal strain in the basal anterior-septal (2), basal lower-septal (3), lower basal (4), basal lower-lateral (5), medial lower septal (9) and lower medial (10) segments ($r = -0.24, -0.30, -0.21, -0.19, -0.34, -0.21$, respectively, $p < 0.05$).
Also, correlated with each other, the parameters reflecting the diastolic function of the left ventricle with the values of longitudinal deformation in the segments 2, 3, 4, 9, 10. Moreover, if the correlation was positive for the indicator E '($r = 0.56$, $p < 0.05$), then for E/E 'connection it was negative ($r = -0.52$, $p < 0.05$).
It is important to note that almost all the segments except the basal anterior-septal part comprise the heart area, which is blood supplying from the right coronary artery system.
Conclusions: Not all segments of the left ventricular myocardium have the same effect on the pumping function of the heart. According to our data, the smallest value to healthy individuals has segments of the left ventricle, blood supplying the right coronary artery. The revealed correlation links between the index of longitudinal deformation and the parameters of diastolic function of the heart confirm the relationship between the processes of contraction and relaxation of the myocardium.

P1952
Increased interleukin 6 levels at 24 hours after ST-elevation myocardial infarction are associated with decreased cardiac function at 4 months

HE Hilde Groot[1]; L Al Ali[1]; ICC Van Der Horst[2]; E Lipsic[1]; DJ Van Veldhuisen[1]; JC Karper[1]; P Van Der Harst[1]
[1]*University Medical Center Groningen, Cardiology, Groningen, Netherlands*;
[2]*University Medical Center Groningen, Critical Care , Groningen, Netherlands*

Introduction: Inflammation is considered to be an important player in the pathogenesis of ischemic heart failure (HF). However, the exact mechanism remains to be elucidated. We would like to focus on the role of the interleukin 6 (IL-6) cascade in the development of HF.
Purpose: In order to provide more insight we aimed to investigate the time course and the association of members of the IL-6 cascade (IL-6, soluble IL-6 receptor

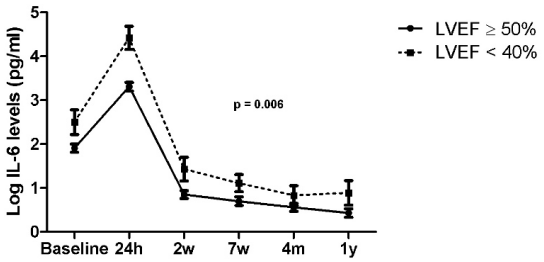
(sIL-6R), soluble glycoprotein 130 (sgp130)) with IS and cardiac function measured at 4 months after ST-elevation myocardial infarction (STEMI).

Methods: In 379 consecutive STEMI patients of the GIPS-III trial IL-6, sIL-6R, and sgp130 levels were measured at baseline, 24 hours, 2 weeks, 7 weeks, 4 months, and 1 year post-PCI. In multivariate models sex, age, BMI, hypercholesterolemia, TIMI (pre- and postintervention), MBG, and ischemic time were included. At 4 months, IS and left ventricular ejection fraction (LVEF) were assessed by magnetic resonance imaging and the ratio of transmitral early flow to early mitral annulus velocity (E/e') was determined by echocardiography'. A 2-tailed p-value of < 0.005 was considered significant. P-value between 0.05 and 0.005 was considered suggestive.

Results: Baseline levels of IL-6, sIL-6R, sgp 130 were 3.7 pg/ml (IQR 2.1 - 6.7 pg/ml), 51.6 ng/ml (IQR 37.3 - 69.0 ng/ml), and 332 ng/ml (IQR 280 - 399 ng/ml) respectively. At 24 hours IL-6 had increased threefold compared to baseline ($p < 0.001$) and subsequently decreased to 1.8 pg/ml (IQR 1.1 - 2.9; $p < 0.001$) at 2 weeks. sIL-6R and sgp130 levels at 24 hours stayed at the same level compared to baseline, and increased at 2 weeks. All biomarkers remained stable between 2 weeks and 1 year.

Regarding the association of biomarkers and IS/cardiac function at 4 months, IL-6 and sIL-6R/IL-6 ratio measured at 24 hours after myocardial infarction, remained independently associated with IS (ß 5.4 (95% CI 3.3 - 7.5); $p < 0.001$, ß -4.0 (95% CI -6.1 - -1.9); $p < 0.001$, respectively). Also, the Q4 of IL-6 at 24 hours remained significantly associated with reduced LVEF after adjustment (ß -4.2 (95% CI -6.7 - - 1.8); $p = 0.001$). Over time course, sIL-6R/IL-6 ratio was lowest in patients with systolic and diastolic dysfunction, measured by LVEF and E/e', compared to other patients ($p = 0.003$; $p = 0.005$ respectively). IL-6 was suggestively higher in these patients (systolic dysfunction: $p = 0.006$; diastolic dysfunction: $p = 0.013$ respectively) (Figure 1). We did not find significant associations with E/e', or associations between sIL-6R levels or sgp 130 alone with either IS or cardiac function, although suggestive associations were observed.

Conclusion: IL-6 and sIL-6R/IL-6 ratio at 24 hours after STEMI are strongly independently associated with IS and cardiac function at 4 months.



Log IL-6 levels in STEMI patients

Basic Science - Vascular Diseases

P1953

Cardiac allograft vasculopathy: the way for early diagnosis

M Marzia Cottini[1]; FB Fabio Sbaraglia[2]; VB Vitaliano Buffa[2]; PLM Paola Lilla Della Monica[2]; GDS Giada Distefano[2]; AP Amedeo Pergolini[2]; VP Vincenzo Polizzi[2]; FM Francesco Musumeci[2]

[1]University of Insubria, Department of Surgical and Morphological Sciences, Cardiac Surgery Unit, Varese, Italy; *[2]San Camillo Forlanini Hospital, Rome, Italy*

Background: CAV limits long-term survival after heart transplantation, and screening for CAV is generally performed on an annual or biannual basis. It is usually detected by CCA. CCTA is currently not recommended for CAV screening due to the limited accuracy reported by early studies. Technological advances such as 64-slice dual-source CCTA might justify re-evaluation of this recommendation.

Methods: A retrospective, observational analysis has been conducted on 90 consecutive patients undergone cardiac transplantation at the Cardiac Surgery and Heart Transplant Unit of S. Camillo Forlanini Hospital in Rome, from January 2001 to December 2017. 196 CCTA scans were performed with a multisegment reconstruction in a minimum interval time of 2,7 months (mean time $32,5 \pm 15,1$ months) on the other hand the CCA minimum interval time was 1 month (mean time $9,5 \pm 13,7$ months) after heart transplantation. We considered significant CAV any identifiable plaque at CCTA and any stenosis >50% of the coronary lumen at CCA.

Results: The mean age of the population was $48,3 \pm 12,4$ years (age range 16-67 years), males 74.5% (n = 67), females 25.5% (n = 23). The mean time from heart transplant was $8,32 \pm 4,78$ years. The incidence of CAV in our group was 20%, (n = 18) with mean age $44,9 \pm 11,7$ years, males 80% (n = 12), and mean time from heart transplantation $14,83 \pm 7,93$ years. We evaluated a total of 1991 coronary artery segments with a axial image reconstruction of 0,75 mm slice thickness. CCTA versus CCA showed a mean sensitivities of 98,2% and 95%, specificities of 98.5 and 94.1%, a negative predictive value (NPV) of 98.1% and 99% and a positive predictive value of 87.1% and 88%, respectively.

Conclusions: In clinical practice CCTA could be a valid alternative to coronary angiography for detection of CAV and our experience documented a reliable data of CCTA quality in detection CAV versus CCA.

Poster Session 3 - Basic Science

Basic Science - Cardiovascular Development and Anatomy

P1954

Impact of right ventricular hypertrophy on left ventricle anatomy and function, in an experimental animal model.

J Jairo Montemor[1]; E Luiz Antonio[1]; LFN Santos[1]; CT Picollo[1]; AJ Serra[1]; SSM Ihara[1]; PJF Tucci[1]; VM Ambrosio[1]
[1]Federal University of Sao Paulo (UNIFESP), Lab. experimental cardiology physiology , Sao Paulo, Brazil

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Left ventricle (LV) may have anatomic and functional alterations secondary to right ventricular hypertrophy.Objective To analyze the anatomical and functional characteristics of the LV in rats with pulmonary artery banding(BAP).
Methods: Wistar-EPM rats were submitted to BAP (BAP = 69 animals) to produce right ventricular hypertrophy (RV) or sham procedure (controls, 56 rats). From 72hours, 2,4,6 and 8 weeks after the procedure, the animals were submitted to echocardiogram(echo)to identify RV hypertrophy and to analyze (LV) echo variables and later to invasive hemodynamic study of the LV and RV. Analysis with mean, standard deviation, and t-test or Wilcoxon; significant if $p < 0.05$.
Results: in the Echo analysis, there was a difference between sham and BAP in the wall thickness (0.12cm, 0.15cm), diastolic diameter (0.76cm, 0.73cm)in D% of the diameters (46.9 %, 49.1%) and in the isovolumic relaxation time TRIV (0.03 sec: 0.06 sec). At catheterization, there was difference between sham and BAP in dP/dt(+) (8745 mmhg: 7801 mmhg) and in dP/dt(-) with (6422 mmHg: 5615 mmHg).
Conclusion: Despite of all these differences, statistical significance was found only in the variable TRIV of the echo. Echo and catheterism at this evaluation did not present a significant performance to characterize structural and functional alterations of the LV in the proposed BAP model in rats.

P1955

Adult sox10+ cells contribute to myocardial regeneration in the zebrafish

M Marcos Sande[1]; IM Ines Marques[1]; MG Maria Galardi[1]; NM Nadia Mercader[1]
[1]University of Bern, Developmenta Blology and Regeneration, Bern, Switzerland

During heart regeneration in the zebrafish, fibrotic tissue is replaced by newly formed cardiomyocytes that derive from pre-existing ones. It is unclear whether all cardiomyocytes have an equal capacity to replace lost myocardium. In opposition to mammals, sox10+ neural crest cells were proposed to contribute to the embryonic zebrafish myocardium. Here we examined the contribution of sox10-derived cells to the adult heart. Embryonic sox10-derived cardiomyocytes persisted in adult hearts but did not participate during regeneration. Surprisingly, a resident sox10+ cell pool in the adult heart expanded massively after cryoinjury. Inhibition of collagen maturation impaired this cell expansion and blocked heart regeneration. Finally, genetic ablation of sox10+ cells severely impaired cardiac regeneration. Thus, our results show that rather than being detrimental, transient fibrosis is necessary for regeneration and that sox10 marks a subset of cardiomyocyte with high regenerative potential.

P1956

Relationship between polymorphism of NOS3 gene and primary cardiac conduction disorders

A Anna Chernova[1]; S YU Nikulina[1]
[1]Krasnoyarsk State Medical University named prof. V. F. Voino-Yasenecky, Krasnoyarsk, Russian Federation

Background: Inherited cardiac conduction diseases (CCD) are rare but are caused by mutations in a myriad of genes. Nitric oxide (NO) derived from endothelial NO synthase (NOS3) plays a central role in ??D. Nitric oxide is a reactive free radical which acts as a biologic mediator in several processes, including neurotransmission and cardiac activities. Nitric oxide is synthesized from L-arginine by nitric oxide synthases. Multiple transcript variants encoding different isoforms have been found for this gene.
Material and Methods: A family examination was performed in 69 patients with atrioventricular block (AVB). The control group consisted of 220 patients without clinical ECG manifestations of cardiac diseases. All the examinees have undergone ECG, echocardioscopy, electrophysiological examination of the heart.
Results: by results of research it is established that the frequency of carriers of a homozygous genotype on rare allel (4b/4b) among patients with AVB (26,1% ± 5,3) was higher in comparison with control selection (3,2% ± 1,2). The obvious tendency to decrease in carriers of a homozygous genotype on extended allel (4a/4a) among patients with AVB (47,8% ± 6,0) in comparison with group of control (71,4% ± 3,0) is also noted.
Conclusions: In this work we for the first time revealed on clinical - genetic material association between hereditary disturbances of cardiac conduction, such as AVB and polymorphism of NOS3 gene.

Genotypes:	AVB (n = 69)	Control group (n = 220)	?		
n	%±m	n	%±m		
4a/4a	33	47,8±6,0	157	71,4±3,0	? <0,001
4a/4b	18	26,1±5,3	56	25,5±2,9	?>0,05
4b/4b	18	26,1±5,3	7	3,2±1,2	? <0,001
Allels:					
Allel 4a	84	60,9±4,2	370	84,1±1,7	? <0,001
Allels 4b	54	39,1±4,2	70	15,9±1,7	? <0,001
?R; 95% CI OR	3,401;2,217-5,208				
Genotype 4a/4a	33	47,8±6,0	157	71,4±3,0	? <0,001
Genotypes 4a/4b+4b/4b	36	52,2±6,0	63	28,6±3,0	? <0,001
?R; 95% CI OR	2,717;1,560-4,739				

P1957

Relationship between polymorphism of Connexin40 gene and primary sick sinus syndrome

A Anna Chernova[1]; S YU Nikulina[1]
[1]*Krasnoyarsk State Medical University named prof. V. F. Voino-Yasenecky, Krasnoyarsk, Russian Federation*

Background: Sick sinus syndrome refers to a collection of disorders marked by the heart's inability to perform its pacemaking function. Predominantly affecting older adults, sick sinus syndrome comprises various arrhythmias, including bradyarrhythmias with or without accompanying tachyarrhythmias. Intrinsic causes include degenerative fibrosis, ion channel dysfunction, and remodeling of the sinoatrial node.
Material and Methods: A family examination was performed in 67 patients with sick sinus syndrome (SSS). The control group consisted of 615 patients without clinical ECG manifestations of cardiac diseases. All the examinees have undergone ECG, echocardioscopy, electrophysiological examination of the heart.
Results: by results of research it is established that the frequency of carriers of a homozygous genotype on rare allel (44AA) among patients with SSS (35,8 ± 5,9) was higher in comparison with control selection (4,7 ± 0,9). The obvious tendency to decrease in carriers of a homozygous genotype on extended allel (44GG) among patients with SSS (22,4 ± 5,1) in comparison with group of control (57,1 ± 2,0) is also noted.
Conclusions: In this work we for the first time revealed on clinical - genetic material association between hereditary SSS and polymorphism of Connexin40 gene.

Genotypes:	SSS (n = 67)	Control group (n = 615)	?		
n	%±m	n	%±m		
44AA	24	35,8±5,9	29	4,7±0,9	? <0,0001
44AG	28	41,8±6,0	235	38,2±2,0	?>0,05
44GG	15	22,4±5,1	351	57,1±2,0	? <0,0001
Allels:					
Allel 44A	76	56,7±4,3	293	23,8±1,2	? <0,0001
Allels 4?	58	43,3±4,3	937	76,2±1,2	? <0,0001
?R; 95% CI OR	4,19;2,906-6,043				
Genotype 44AA	24	35,8±5,9	29	4,7±0,9	? <0,0001
Genotypes 44AG+44GG	43	64,2±5,9	586	95,3±0,9	? <0,0001
?R; 95% CI OR	11,278;6,048-21,033				

P1958

Effect of gender on myocardial reverse remodeling in a rat model of banding and debanding of the abdominal aorta

M Mihaly Ruppert[1]; T Radovits[1]; S Korkmaz-Icoz[2]; S Loganathan[2]; W Jiang[2]; LH Lehmann[3]; A Olah[1]; BA Barta[1]; B Bodi[4]; Z Papp[4]; B Merkely[1]; M Karck[2]; G Szabo[2]
[1]*Semmelweis University Heart Center, Budapest, Hungary*; [2]*University of Heidelberg, Department of Cardiac Surgery, Heidelberg, Germany*; [3]*University Hospital of Heidelberg, Department of Cardiology, Angiology and Pulmonology, Heidelberg, Germany*; [4]*University of Debrecen, Division of Clinical Physiology, Faculty of Medicine, Debrecen, Hungary*

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Background: Gender differences have been intensively investigated during the development of pressure overload-induced left ventricular (LV) myocardial hypertrophy (LVH). However, it is less clear whether female sex also affects the regression of LVH after pressure unloading therapy.
Purpose: In the present study we aimed to investigate the effect of gender on myocardial reverse remodeling following pressure unloading in male and female rats utilizing a rat model of banding and debanding of the abdominal aorta.
Methods: Pressure overload of the left ventricle was induced in male (M) and female (F) Sprague-Dawley rats by abdominal aortic banding (AB) for 6 or 12 weeks. Sham operated animals served as controls. Pressure unloading was evoked by removing the aortic constriction after week 6 (debanded). Serial echocardiography and LV pressure-volume analysis was performed to assess the morphological and functional alterations. In addition, histological and molecular biological measurements were also carried out.
Results: In male (M) and female (F) AB groups, development of LVH at a similar extent was confirmed by increased left ventricular mass, heart weight-to-tibial length ratio (HW/TL) and cardiomyocyte diameter (CD). On the functional level, LVH was associated with diastolic dysfunction in both genders. However, impairment of systolic function could be only detected in male aortic-banded rats. In contrast to the sex-dependent differences in LVH, removal of the aortic constriction resulted in a similar morphological (HW/TL: 0.38 ± 0.01 debanded-M vs. 0.47 ± 0.01 AB-M, $p < 0.05$; 0.28 ± 0.01 debanded-F vs. 0.36 ± 0.02 AB-F, $p < 0.05$), histological (CD: 16.4 ± 0.5 debanded-M vs. 18.2 ± 0.6 AB-M, $p < 0.05$; 14.7 ± 0.4 debanded-F vs. 17.7 ± 0.6 AB-F, $p < 0.05$) and functional reverse remodeling in both genders.
Conclusion: Our results provide evidence that pressure unloading therapy at a relatively early time point leads to myocardial reverse remodeling at a comparable degree in male and female rats.

P1959

Gse1, a new player in cardiac development

F Alnour[1]; X Xu[1]; E Baier[1]; M Drignath[1]; M Zeisberg[2]; EM Zeisberg[1]
[1]*University Medical Center Goettingen, Cardiology department, Goettingen, Germany*; [2]*University Medical Center Goettingen, Nephrology department, Goettingen, Germany*

Purpose: Hypoplastic left heart syndrome (HLHS) is one of the most severe congenital heart diseases. KIAA0182 gene (Gse1 in mouse) was found to be de novo mutated in HLHS. While the function of this gene has not been elucidated yet, Gse1 is known to produce one circular RNA isoform that is highly abundant. Gse1-knockdown in zebrafish revealed a cardiac phenotype. We therefore aimed to explore the biological role of Gse1 gene using a newly generated Gse1 knockout mouse.
Methods: By using targeted gene-trapping strategy we established Gse1-knockout-first mice with the mutated allele (Gse1-tm1a(EUCOMM)Wtsi) as a knockout model for Gse1 on expression level. In these mice the trapping cassette is located just downstream from the second exon of Gse1 that generates its circularized isoform.
Results: After confirming the correct targeting of Gse1 by the trapping cassette, offspring of matings between heterozygous (Gse1 tm1a/+) parents was analyzed, and within 134 newborn mice no homozygous (Gse1 tm1a/tm1a) mice were detected, indicating embryonic lethality. Systematic embryological analysis revealed that the time of lethality spans over the last trimester of pregnancy. Histological analysis revealed cardiac abnormalities comprising hypoplastic and non-compacted myocardium and ventricular septum defect in the majority of homozygous embryos. Gse1 linear mRNA was surprisingly downregulated by less than 50% in homozygous embryos compared to wild type, without any clear difference on protein level. To exclude the possibility of off-target effects due to the trapping cassette in Gse1-tm1a allele, the genes upstream and downstream from Gse1 were tested and none of them was found to be dysregulated in the homozygous embryos. We found, however, a significant upregulation of Gse1 circular RNA in homozygous as compared to wild type embryos, suggesting that the trapping cassette affects the backsplicing process within the circular RNA forming region, and that this circular RNA may be responsible for the observed abnormalities. We next used miRBase database to identify 12 miRNAs that can be bound by Gse1 circular RNA, and the online database miRDB to identify more than 4000 genes potentially affected by these miRNAs. Among these genes, we focused on 5 candidates (WT1, Mef2c, Tfap2b, Hey2 and GATA4), which were previously linked to cardiac development. We found upregulation of WT1 and downregulation of GATA4 in heart samples from homozygous embryos as compared to wild type. This potentially reflects two known functions of circular RNA to either sequester or to protect miRNAs, providing a possible link between Gse1-circular RNA and the cardiac phenotype.
Conclusions: Homozygosity of Gse1-tm1a allele causes embryonic lethality. The observed cardiac phenotype may be caused, at least in part, by the upregulated circular RNA isoform of Gse1. The biological mechanisms behind our results and the exact functions of Gse1 and its circular RNA are still to be further elucidated.

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P1960

Advantages of prophylactic versus conventionally scheduled heart failure treatment in doxorubicin induced cardiomyopathy

M Lodi[1]; D Priksz[2]; GA Fulop[1]; B Bodi[1]; J Kocsis[3]; I Edes[4]; Z Csanadi[4]; I Czuriga[4]; Z Kisvarday[5]; B Juhasz[2]; A Toth[1]; Z Papp[1]; D Czuriga[6]
[1]University of Debrecen, Faculty of Medicine, Department of Cardiology, Division of Clinical Physiology, Debrecen, Hungary; *[2]University of Debrecen, Faculty of Medicine, Department of Pharmacology and Pharmacotherapy, Debrecen, Hungary*; *[3]Semmelweis University, Department of 3rd Internal Medicine, Budapest, Hungary*; *[4]University of Debrecen, Clinical Centre, Department of Cardiology, Debrecen, Hungary*; *[5]University of Debrecen, Faculty of Medicine, Department of Anatomy, Histology and Embryology, Debrecen, Hungary*; *[6]University of Debrecen, Faculty of Medicine, Department of Cardiology, Division of Cardiology, Debrecen, Hungary*

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Background: Despite intense research efforts, chemotherapy induced left ventricular dysfunction remains a clinical problem in the field of oncocardiology. Optimal timing of heart failure treatment may play an important role in the prognosis of patients. Still, there is no hard evidence for a prophylactic cardioprotective approach for the vast majority of oncological treatments.
Purpose: In this study we set out to investigate whether a prophylactic or a conventionally scheduled heart failure therapy is more effective in preventing doxorubicin (DOX) induced cardiotoxicity.
Methods: Previously, we developed a rat model for the investigation of the adverse myocardial effects of iv. DOX using concentrations extrapolated from human oncotherapeutic protocols. Here we had 4 groups of animals: saline treated negative controls (CON), DOX treated positive controls, and DOX treated animals scheduled for prophylactic (PRE, started a week before DOX exposure) or conventional cardioprotection (POST, started 1 month after DOX exposure). The cardioprotection was achieved by orally administered, combined heart failure therapy (2.5 mg/kg bisoprolol, 2 mg/kg perindopril, 6.25 mg/kg eplerenone). Baseline as well as follow-up blood pressure, heart rate and echocardiographic measurements were performed. At 2 months the animals were sacrificed, their hearts were excised and frozen for further electronmicroscopic scanning and in vitro force measurements in isolated, skinned cardiomyocytes.
Results: Prophylactic treatment significantly reduced the blood pressure and heart rate of animals in the PRE group compared to all other groups. Similarly to CON, the survival of PRE animals was significantly better than that in the DOX and POST groups. Ejection fraction and longitudinal strain remained preserved in the PRE group. DOX treatment did not result in significant desensitisation of the myofilaments to Ca2+. However, the DOX induced lower rate of the actin-myosin cross-bridge cycle could not be reverted by any drug intervention. The DOX related adverse myocardial remodelling also manifested in pronounced ultrastructural changes such as myofibrillolysis, mitochondrial disintegration and chromatin fragmentation. A substantial reduction of the above abnormalities could be seen in the PRE, but not in the POST group.
Conclusions: Prophylactic cardioprotective treatment has many advantages compared to conventional therapy applied at a later stage in preventing or attenuating adverse myocardial effects induced by DOX.

P1961

Hypertrophic cardiomyopathy: variable expression of mutant and wildtype protein from cell-to-cell leading to contractile imbalance - a possible trigger for pathogenesis

T Kraft[1]; D Aldag-Niebling[1]; A Radocaj[1]; J Montag[1]; K Kowalski[1]; M Makul[1]; B Keyser[1]; C Dos Remedios[2]; A Perrot[3]; A Francino[4]; F Navarro-Lopez[4]; B Brenner[1]
[1]Medical School, Hannover, Germany; *[2]University of Sydney, Dept. of Anatomy, Sydney, Australia*; *[3]Charité - Campus Berlin Buch (CBB), Berlin, Germany*; *[4]Hospital Clinic i Provincial, Barcelona, Spain*

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Hypertrophic Cardiomyopathy (HCM) is caused by mutations in mainly sarcomeric proteins. HCM pathogenesis is assumed to result from functional alterations due to the respective mutation. Yet, a common mechanism how different mutations trigger HCM is still unclear. We hypothesize that myocyte disarray and fibrosis in HCM are triggered by cell-to-cell variation of the fractions of mutated and wildtype protein leading to contractile imbalance among individual cardiomyocytes (CMs).
By analyzing CMs isolated from heterozygous HCM patients' cardiac tissue we could show that mutations in ß-myosin (ß-MyHC) alter calcium-sensitivity, which, however, was highly variable from cell-to-cell. Also, the fractions of mutated and wildtype MYH7-mRNA were highly variable, ranging from cardiomyocytes expressing essentially pure mutant to others with essentially pure wildtype mRNA. As mechanism we propose that stochastic, burst-like transcription which is independent for the two MYH7-alleles produces variable fractions of mutated and wildtype mRNA and protein from cell-to-cell. This was corroborated by analysis of activity of MYH7-transcription sites in individual CMs and by model simulations.
Here we extended our studies to cardiac tissue from a heterozygous HCM-patient with cMyBP-C-mutation c.927-2A>G, which creates a premature stop-codon. Again, calcium-sensitivity of individual CMs was determined. Variable expression of cMyBP-C-protein from cell-to-cell was tested by immunofluorescent labelling against cMyBP-C and a-actinin. For this mutation calcium-sensitivity was increased with a large variability of force from cell-to-cell at submaximal, physiological activation levels. Some cells were essentially indistinguishable from controls, while others generated substantially increased force suggesting reduced levels of cMyBP-C. Fluorescence intensity ratio (IMyBPC/IAlpha-Actinin) was 35% lower in patient's CMs and significantly more variable from cell-to-cell compared to donors. cMyBP-C-fluorescence appeared much patchier in patient CMs, suggesting variable abundance of wildtype-cMyBP-C within patient CMs. No truncated cMyBP-C was found, consistent with mRNA-decay of the mutated transcript.
We propose that the lower fluorescence intensity ratio and patchier appearance of cMyBP-C fluorescence in the HCM-CMs results from random, burst-like transcription of cMyBPC, which is independent for the mutant and wildtype alleles. The resulting highly variable levels of wildtype cMyBP-C in the individual CMs could be the underlying cause of the functional imbalance among the individual CMs. Overall expression of cMyBP-C seems reduced, consistent with the frequently observed haploinsufficiency for cMyBP-C-mutations in HCM.
In the long run, for both, cMyBP-C-mutations and the previously studied ß-MyHC-mutations such contractile imbalance may well induce structural distortions like cellular/myofibrillar disarray and fibrosis, as they are typically observed in HCM.

P1962

Mitigation of anthracycline cardiotoxicity through liposomal formulation is mediated by activation of interferon-inducible genes in pigs

J Johannes Winkler[1]; M Gyongyosi[1]; D Lukovic[1]; K Zlabinger[1]; A Spannbauer[1]; A Gugerell[1]; N Pavo[1]; D Traxler[1]; A Jakab[1]; J Bergler-Klein[1]
[1]Medical University of Vienna, Department of Cardiology, Vienna, Austria

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Background: Compared to the free drug (DOX), liposomal doxorubicin (LDOX) has shown comparable antitumor efficacy and reduced cardiotoxicity, thereby increasing the therapeutic index. LDOX has been developed to reduce drug exposure of healthy tissues. The precise molecular mechanisms of anthracycline-induced toxicity remain incompletely understood.
Purpose: We performed transcriptomic profiling of myocardial samples of a translational pig model after treatment with LDOX or free DOX in order to investigate alterations in gene expression and to identify strategies for cardioprotection.
Methods: We treated juvenile domestic pigs with either DOX (n = 6), LDOX (n = 6), or saline (n = 5, controls) in doses equivalent to human treatment regimes. Heart function and the extent of myocardial fibrosis were assessed by cardiac magnetic resonance imaging with gadolinium late enhancement and transthoracic echocardiography. Serial plasma levels of NT-proBNP and Troponin I were quantified by ELISA. After the completion of three treatment cycles, gene expression profiles of the left and right ventricles were determined by global RNA sequencing with validation by quantitative PCR. Cardiac fibrosis and protein biomarkers were analyzed with immunohistochemistry and immunofluorescence.
Results: We identified an increase of plasma markers NT-proBNP (569 ± 144 and 499 ± 116 vs. 44 ± 5 pg/mL) and Troponin I (1.30 ± 0.85 and 1.39 ± 0.18 vs. 0.01 ± 0.01 ng/mL) in both DOX and LDOX groups, and an impact on body weight of the growing animals after DOX treatment (46 ± 11 and 73 ± 8 vs. 75 ± 3 kg, DOX and LDOX vs. Co, respectively), as indications of anthracycline-induced cardiotoxicity. Altered left ventricular systolic function (LV enddiastolic volume 1.96 ± 0.24 and 1.62 ± 0.41 vs. 1.20 ± 0.13 mL/kg) and E/e' ratio (8.9 ± 1.4 and 5.8 ± 1.3 vs. 5.0 ± 1.3) were found after DOX. In both ventricles, LDOX but not DOX treatment resulted in upregulation of a distinct signature of interferon-inducible genes (IFIT 1, 2, 3, 5, ISG 15, IRF 7 and 9, and others), which are mediating DNA damage repair and promote cell survival. Gene network analysis identified the cardioprotective translocator protein (TSPO) as a central node of differentially regulated genes, linking interferon-induced genes to transcription factors and cell survival genes. While TSPO expression was not significantly altered by LDOX compared to controls, it was inhibited 2.7-fold by DOX. Immunohistochemistry showed slightly increased cytosolic localization of TSPO after LDOX application with persisting predominantly mitochondrial staining.
Conclusions: Our data show transcriptional activation of a DNA damage response pathway through activation of interferon-inducible genes by LDOX, but not DOX,

presumably caused by reduced exposure of the myocardium to the drug. Translocator protein TSPO as a central gene in the identified network might be a feasible target for development of specific strategies for cardioprotection from anthracyclines.

P1963

Shock wave therapy improves cardiac function in a model of chronic ischemic heart failure-evidence for a mechanism involving VEGF signaling and the extracellular matrix

J Holfeld[1]; D Lobenwein[1]; M Theurl[2]; U Primessnig[3]; D Lener[2]; E Kirchmair[1]; W Mathes[1]; M Graber[1]; L Polzl[1]; P Paulus[4]; W Schaden[5]; M Grimm[1]; R Kirchmair[2]; C Can Tepekoylu[1]

[1]Innsbruck Medical University, Department of Cardiac Surgery, Innsbruck, Austria; *[2]Innsbruck Medical University, Department of Internal Medicine III, Innsbruck, Austria*; *[3]Charité - Universitätsmedizin Berlin, Department of Internal Medicine and Cardiology, Berlin, Germany*; *[4]General Hospital (AKH) of Linz, Department of Anesthesiology, Linz, Austria*; *[5]Trauma Hospital Meidling, Vienna, Austria*

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Background: Mechanical stimulation of acute ischemic myocardium by shock wave therapy (SWT) is known to improve cardiac function by induction of angiogenesis. However, SWT in chronic heart failure and underlying mechanisms are poorly understood.
Objective: To study if mechanical stimulation upon SWT improves heart function in a model of chronic ischemic heart failure by induction of angiogenesis and postnatal vasculogenesis and to dissect underlying mechanisms.
Methods: Three weeks after ligation of the left anterior descending coronary artery, SWT was applied to chronic ischemic myocardium. Cardiac function was evaluated using echocardiography and pressure/volume measurements. To study effects of SWT on postnatal vasculogenesis wild-type mice received bone marrow transplantation from GFP donor mice after sublethal irradiation. Functional angiogenesis assays with human umbilical vein endothelial cells and a murine aortic ring assay were used to specify underlying mechanisms.
Results: Echocardiography and pressure/volume measurements revealed improved left ventricular ejection fraction, myocardial contractility and diastolic function and decreased myocardial fibrosis after treatment. Concomitantly, we found upregulation of myocardial vascular endothelial growth factor (VEGF), vascular endothelial growth factor receptor 2, fibroblast growth factor and placental growth factor expression with increased numbers of capillaries and arterioles in treated hearts consistent with induction of angiogenesis. In vitro, SWT enhanced activation of extracellular-signal regulated kinase and protein kinase B/Akt. This resulted in endothelial cell proliferation, enhanced survival, and induction of capillary sprouting in an ex-vivo aortic ring assay. The effects were abolished by the vascular endothelial growth factor receptor 2 inhibitor Vandetanib or by pre-incubation with heparin or heparinase indicating involvement of VEGF signaling and heparan sulfate proteoglycans (HSPGs) in SW-induced angiogenesis. To study effects of SWT on postnatal vasculogenesis wild-type mice received bone marrow transplantation from GFP donor mice after sublethal irradiation. SWT resulted in enhanced expression of the chemoattractant stromal cell derived factor 1 in ischemic myocardium and serum of treated animals. Treatment induced recruitment of endothelial progenitor cells from the bone marrow to the site of injury shown by higher numbers of GFP-positive endothelial cells in treated hearts.
Conclusions: The mechanical stimulus of SWT positively affects heart function in chronic ischemic heart failure by induction of angiogenesis and postnatal vasculogenesis. SWT upregulated pivotal angiogenic and vasculogenic factors in the myocardium in-vivo and induced proliferative and anti-apoptotic effects on endothelial cells. Mechanistically, these effects depend on VEGF signaling and HSPGs. SWT could become a promising treatment option for regeneration of ischemic myocardium.

P1964

Non-hypertrophic and hypertrophic human cardiomyocytes secrete unprocessed ANP and BNP precursors (proANP/proBNP) and exhibit a similar efficiency in their processing

A Semenov[1]; E Feygina[2]; N Tamm[2]; V Filatov[2]; A Katrukha[1]

[1]HyTest Ltd, R&D department, Turku, Finland; *[2]M.V. Lomonosov Moscow State University, Biological faculty, Moscow, Russian Federation*

Background: A- and B-type natriuretic peptides (ANP and BNP) are key cardiac hormones of cardiorenal homeostasis. ANP and BNP are produced as prohormones, proANP and proBNP, which are enzymatically converted to biologically active peptides ANP and BNP, and N-terminal fragments, NT-proANP and NT-proBNP. The diseased heart (e.g. under hypertrophy in heart failure (HF)) secretes high amounts of unprocessed precursors resulting in the lack of physiological natriuretic response in HF patients. The appearance of intact precursors in the circulation can be attributed to their inefficient processing. However, the mechanism of proANP and proBNP secretion and processing in the normal heart remains elusive, since the levels of ANP and BNP under normal conditions are very low and often beyond the detection limits of available assays. One may suggest that a robust and physiologically relevant cell-based model can be used to address these issues.
Purpose: To explore the secretion and processing efficiency of proANP and proBNP in human cardiomyocytes, in both normal and hypertrophic conditions.
Methods: Human induced pluripotent stem (iPS) cell-derived cardiomyocytes were used as an in vitro model to study proANP and proBNP secretion and processing in normal and hypertrophic conditions. Hypertrophy of cardiomyocytes was induced by treatment of cells with endothelin 1 (ET-1) at different concentrations (0.004-1000 pM). The levels of intact proANP and proBNP (i.e. [precursor]) as well as the total levels of the corresponding peptide (i.e. [N-terminal fragment + precursor]) were measured by means of sandwich-type immunoassays in condition media after 20 hours post induction. Antibodies specific to (i) both N- and C-terminal parts of either proANP or proBNP (to measure [precursor] levels), or (2) N-terminal parts only (to measure [N-terminal fragment + precursor] levels) were employed. Recombinant proANP and proBNP expressed in E. coli were used as calibrators. The rate of processing was calculated using the formula: (1 - [precursor]/[N-terminal fragment + precursor])*100%.
Results: ET-1 treated iPS cell-derived cardiomyocytes exhibited dose-dependent increases in total ANP and BNP production: up to 5-fold for ANP and 8-fold for BNP. Secretion of intact proANP and proBNP was observed in both non-induced and ET-1 induced cardiomyocytes. The processing rate of proANP and proBNP in both normal and hypertrophic cells was similar: ˜30% for proANP and ˜60% for proBNP. There was no alteration of processing efficiency in the cells treated with different ET-1 concentrations.
Conclusions: The increases in ANP and BNP production observed in cardiomyocytes under hypertrophy do not result in the alteration of the processing rate of precursor molecules. The present data suggest that intact proANP and proBNP may be also secreted by normal hearts (similarly to what is observed in HF patients) and enable to assume a specific role of intact precursors in the circulation.

P1965

The effect of free fatty acids on endogenous angiotensin converting enzyme inhibition

M Fagyas[1]; B Varga[1]; IT Altorjay[1]; A Csongradi[1]; ZS Polik[1]; SI Manyi[1]; Z Papp[1]; A Toth[1]

[1]University of Debrecen, Department of Cardiology, Division of Clinical Physiology, Debrecen, Hungary

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Angiotensin converting enzyme (ACE) inhibitors have the potential to reduce cardiovascular mortality by up to 40%. We have recently reported that ACE activity is endogenously inhibited by human serum albumin (HSA). We hypothesize that decreased endogenous ACE inhibition associates with development and progression of cardiovascular diseases. Here we aimed to identify and characterize factors influencing HSA-mediated endogenous ACE inhibition.
68 patients with documented cardiovascular diseases were involved into the study. Besides routine laboratory parameters, the extent of endogenous ACE inhibition, free fatty acid (FFA) concentration and composition were also measured.
The extent of endogenous ACE inhibition varied considerably among patients (62-83%, n = 68), but it had no relation with albumin concentration in the samples ($r2 = 0{,}149$). Hence we postulated, that other factors could also influence the extent of endogenous ACE inhibition. Removal of hydrophobic molecules from the surface of albumin significantly decreased the capacity of albumin to inhibit ACE activity (before treatment: $IC50 = 9.91 \pm 1.0$g/L, n = 3, after treatment: $IC50 = 35.8 \pm 2.7$g/L, n = 3, $p < 0.001$). FFA concentrations were measured from the samples and we found no relationship between FFA concentration and the extent of endogenous ACE inhibition ($r2 = 0.089$). We concluded that different types of FFAs may modify the endogenous ACE-inhibiting capacity of albumin to various extents. Treatment of FFA free HSA with different types of FFAs confirmed this hypothesis. Among the examined saturated and unsaturated FFAs, C18:3 cis,cis,cis,?6,9,12 had the most potent ACE-inhibitor modifying effect ($IC50 = 5.5 \pm 0.4$g/L), while the effect of C10:0 treated albumin ($IC50 = 32.3 \pm 1.6$ g/L) was not different from that of FFA free albumin. Our results revealed that FFA-binding to albumin is essential for endogenous ACE inhibition. There are several FFAs, which are able to increase significantly the ACE-inhibitory effect of HSA. Therefore, intake of these FFAs via functional foods may decrease cardiovascular risk and delay the development of cardiovascular diseases.

P1966

Beneficial effect of intravenous iron, ferric carboxymaltose, in heart failure

A Paterek[1]; J Kolodziejczyk[1]; M Kepska[1]; U Mackiewicz[1]; M Maczewski[1]
[1]*The Medical Centre of Postgraduate Education, Department of Clinical Physiology, Warsaw, Poland*

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Introduction: Iron deficiency (ID) occurs in up to 50% of patients with chronic heart failure (HF). Unfortunately, causes of this ID in HF remain largely unknown and probably are multifactorial. ID is associated with poor prognosis in HF patients, whereas iron supplementation had beneficial symptomatic effects. The effect of iron on hard endpoints and left ventricular remodeling parameters fundamental for patient's prognosis is still unknown. On the other hand iron is a highly toxic, can participate in the Fenton reaction to form the most reactive oxygen species- hydroxyl radical, so its level in the human body must be strictly controlled. Therefore treatment with intravenous iron in HF is still an open question.
Purpose: To characterize iron status in the rat model of post-myocardial infarction (MI) chronic HF and to assess the effect of 4-week intravenous iron supplementation on post-MI HF.
Methods: Rats were subjected to induction of MI or sham operation and after 4 weeks were randomized into two groups, one received intravenous (i.v.) iron (ferric carboxymaltose, 10 mg/kg body weight) (HF+Fe, Sh+Fe), whereas the other received saline (HF, Sh), a total of 4 doses in 1-week intervals. Echocardiography was performed weekly. Eight weeks after surgery rats underwent final echocardiographic imaging and left ventricular catheterization. Blood was collected and subsequently hearts were excised for biochemical and cellular studies. Serum and liver were also collected for further analysis.
Results: MI alone did not cause anemia, ID or abnormalities of iron turnover (no abnormalities of either myocardial or systemic iron). Iron therapy increased serum Fe, ferritin and transferrin saturation as well as cardiac and hepatic iron content in HF+Fe rats. This was accompanied by: (1) better preservation of left ventricular (LV) ejection fraction and smaller LV dilation, (2) preservation of function of Ca2+ handling proteins in LV cardiomyocytes and (3) reduced level of inflammatory marker, CRP. Furthermore, iron supplementation did not potentiate oxidative stress or have toxic effects on cardiomyocyte function.
Conclusions: Although we did not find any evidence of anemia or iron deficiency in the rat model of post-MI HF, we observed positive effect of iron supplementation in such setting and we confirmed that such supplementation is safe.

P1967

Dipeptidyl peptidase 4 inhibitor sitagliptin ameliorates renal function in a model of hypertension-induced cardiorenal disease

D Cappetta[1]; A De Angelis[1]; LP Ciuffreda[1]; G Esposito[1]; A Cozzolino[1]; D D'amario[2]; A Siracusano[2]; F Rossi[1]; F Crea[2]; L Berrino[1]; K Urbanek[1]
[1]*University of Campania "Luigi Vanvitelli", Department of Experimental Medicine, Naples, Italy*; [2]*Catholic University of the Sacred Heart, Department of Cardiovascular and Thoracic Sciences, Rome, Italy*

Background: heart failure with preserved ejection fraction (HFpEF) and chronic kidney disease often share co-morbidities like hypertension and diabetes. Moreover, renal dysfunction in HFpEF is common and is associated with increased mortality. Co-existence of heart and kidney failure is a clinical challenge, because of diagnostic and therapeutic difficulties, since many HF medications may cause, or are contraindicated in the presence of renal failure. Experimental studies have suggested a cardio and renoprotective role of dipeptidyl peptidase 4 (DPP4) inhibitors in various experimental models, which may be independent of lowering blood glucose levels.
Purpose: to examine the effects of DPP4 inhibitor sitagliptin treatment on the progression of heart and kidney disease independently from the effects on glycaemia. To identify molecular mechanisms involved with a particular focus on the potential renal protection. For this purpose, Dahl salt-sensitive (Dahl/SS) rats, reported as an experimental model of HFpEF, were used.
Methods: seven-week-old Dahl/SS rats fed a high salt diet (8% NaCl) for 5 weeks to induce hypertension. Then, rats continued with a high salt diet and were administered with either sitagliptin (10 mg/kg by oral gavage) or vehicle for the following 8 weeks.
Results: treatment with sitagliptin ameliorated both cardiac and kidney injury. During 8 weeks of the treatment with sitagliptin, blood pressure remained markedly elevated, with a slight, but significant reduction observed only at 19 weeks of age. Because of a non-diabetic nature of our model and unaltered blood glucose levels, the cardio-renal protective action of sitagliptin certainly lays beyond its effect on glycaemia. At renal level, expression of pro-inflammatory markers like nuclear factor kappa B, tumor necrosis factor-a and interleukin-6 were elevated in Dahl/SS rats and partially reduced by sitagliptin treatment. Sitagliptin also reduced the grade of endothelial dysfunction as evidenced by the increase of eNOS and the decrease of E-selectin. Moreover, oxidative stress was attenuated by sitagliptin. Oxidative stress and pro-inflammatory status observed in Dahl/SS rats contribute to activation of pro-fibrotic pathways in the kidney. Increase of collagen deposition and activation of pro-fibrotic signalling that leads to a remarkable renal tubulointerstitial fibrosis and glomerulosclerosis in high salt diet-fed rats were reduced with administration of sitagliptin.
Conclusions: sitagliptin reduced inflammatory-related endothelial dysfunction and fibrosis in the kidney and positively modulated myocardial diastolic compliance. The concomitant damage at heart and kidney level puts in evidence the feature of cardio-renal syndrome of this experimental model whilst the protective effects of sitagliptin highlight its action at multi-organ level.

P1968

Neladenoson, a partial adenosine A1 receptor agonist shows renal protection in rodents

K Leineweber[1]; P Kolkhof[1]; A Kretschmer[2]; B E Albrecht-Kuepper[1]
[1]*Bayer AG , Drug Discovery - Cardiology/Heart Diseases, Wuppertal, Germany*; [2]*Bayer AG, Drug Discovery - Clinical Sciences-Global Biomarker Research, Wuppertal, Germany*

Background: Heart failure (HF) is often associated with renal impairment which in itself is also a strong predictor of mortality in HF. Adenosine A1 receptors (A1Rs) are expressed in heart and kidney and mediate several beneficial physiological effects. But A1R activation in the kidney also leads to anti-diuretic effects. Partial A1R agonists have the potential to selectively address only certain physiological effects and thereby show not only cardio- but also reno-protection without disturbances of diuresis in HF patients. Neladenoson is an oral partial A1R agonist currently in PhIIb clinical development for HF.
Purpose: The objective of the described studies was the characterization of acute renal effects of neladenoson in healthy rats and chronic effects in subtotal nephrectomised (SNX) rats, an animal model for chronic kidney disease.

Effects of neladenoson in SNX rats

	Control	Placebo	Neladenoson
n	10-12	10-12	10-11
Urine Volume [ml/kg/h]	1.2±0.1	1.8±0.1	1.8±0.2
Kidney injury marker-1 [rel. expr.]	11±4***	182±54	56±18**
Proteinuria [mg/ml urine/kg BW/h]	1.14±0.25*	2.19±0.51	0.97±0.12*
Heart rate [bpm]	320±10	316±7	291±9
Systolic blood pressure [mmHg)]	119±2***	127±4	126±3
Diastolic blood pressure [mmHg]	91±2***	98±3	95±2

Values are Mean+SEM. *p < 0.05, **p < 0.01 and ***p < 0.001 vs. Placebo. Statistics: One-way Anova with Newman Keuls Multiple Comparison post-hoc test.

Methods: Acute effects were measured in male Sprague Dawley rats treated with a single dose of neladenoson (3 mg/kg body weight, p.o.) and kept in metabolic cages for 24 hrs. Chronic effects were analysed in male Wistar rats randomly allocated to subtotal nephrectomy. Three weeks after SNX surgery, neladenoson (3 mg/kg body weight, p.o., once daily) was given for additional four weeks. At the end of the protocol heart rate and blood pressure and renal parameters were assessed.
Results: Acute treatment with neladenoson resulted in a significant increase of urine volume (neladenoson 77.5+7.4 ml/kg vs. control 35.4+4 ml/kg BW (p <0.001)) over 24 hrs. without any natriuretic effect. Chronic treatment of SNX rats significantly reduced renal expression of the kidney injury marker KIM-1 and proteinuria in comparison to placebo. Additionally, no change in blood pressure and urine volume was observed compared to placebo.
Conclusion: The partial A1R agonist neladenoson improves renal impairment without deterioration of diuresis.

P1969

Passive stiffness of ventricular myocardium in a mouse model of sleep apnea: effects of intermittent hypoxia and ageing

N Farre[1]; J Otero[2]; I Jorba[2]; I Almendros[2]; R Farre[2]; D Navajas[2]
[1]*Hospital del Mar, Department of Cardiology, Municipal Institute for Medical Research (IMIM), Barcelona, Spain*; [2]*University of Barcelona, Unitat de Biofísica i Bioenginyeria. Facultat de Medicina. , Barcelona, Spain*

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Introduction: Obstructive sleep apnea (OSA), characterized by intermittent hypoxia (IH), is a very prevalent disease associated with heart failure (HF). Diastolic dysfunction is a key feature of HF which can be caused by either prolongation of active myocardial relaxation or increased myocardial passive stiffness. Both the extracellular matrix (ECM) and the cardiomyocytes are potentially determining passive stiffness in the myocardium although their exact contribution in OSA is unknown.
Purpose: The aim was to study whether IH and ageing modulate the passive stiffness of the LV myocardium in an animal model of OSA.
Methods: Two-month and 18-month old mice (N = 10 each) were subjected to IH (20% O2 40s - 6% O2 20s) for 8 weeks (6h/day). Corresponding control groups for each age were kept under normoxia in room air (RA). After sacrifice the hearts were excised and frozen for subsequent analysis. After thowing at room temperature, a strip of ˜8x1x1 mm was cut from the LV wall. One end of the strip was glued with cyanoacrylate to a hook attached to the lever of a servocontroled displacement actuator and the other end was glued to a fixed hook. Stress-stretch (s-?) curves were recorded by measuring the stretched length and the applied force (Aurora Scientific, 300C-LR) after strips were preconditioned. The curves were analyzed with Fung's model which assumes that the Young's modulus (E) increases linearly with stress. The stiffness of the tissue was characterized by computing E at 20% stretch (? = 1.2). After measuring E in native samples, each strip was decellularized (1% sodium dodecyl sulfate solution and 1% Triton X-100). Stress-stretch curves for the decellularized strips were obtained and computed.
Results: E (m ± SE) was 17.28 ± 2.43 (RA) and 37.24 ± 6.53 (IH) (p = 0.007) for young mice and 16.65 ± 3.18 (RA) and 42 ± 5.85 (IH) (p = 0.003) for old mice. Two-way ANOVA analysis found no statistically significant effect of age (young vs. old, p = 0.489) and highly significant effect of respiratory challenge (IH vs. RA, p <0.001) on E. Virtually the same results were found on the decellularized tissue samples, indicating a negligible contribution of cells in E.
Conclusions: The passive elastance of myocardial strips measured before and after decellularization in a mouse model of OSA indicates that IH (but not age) significantly increased LV tissue stiffness and that this effect is mainly caused by changes the ECM.

P1970

Vardenafil can prevent the development of cardiomyocyte diastolic dysfunction complicating diabetes mellitus

J Judit Tamas[1]; B Bodi[1]; CS Matyas[2]; A Toth[1]; B Merkely[2]; T Radovits[2]; Z Papp[1]
[1]*Institute of Cardiology, Division of Clinical Physiology, Debrecen, Hungary*; [2]*Semmelweis University, Budapest, Hungary*

On behalf of: clinical physiology
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Introduction: Patients with diabetes mellitus exhibit diastolic dysfunction with decreased nitric monoxide production (diabetic cardiomyopathy). Elevated intracellular cyclic guanosine monophosphate (cGMP) levels can confer cardioprotection in different heart diseases. Here we investigated the effects of vardenafil, a phosphodiesterase-5A (PDE-5A) inhibitor in a rat model of diabetic cardiomyopathy on cardiomyocyte function.
Materials and Methods: Experiments were performed in male Zucker Diabetic Fatty (ZDF) and ZDF Lean (ZDFL) rats (as controls). Seven weeks old animals received either vehicle (ZDFLV) or 10 mg/bwkg vardenafil per os (ZDFV). Functional measurements were performed at the age of 32 weeks. Permeabilized left ventricular (LV) cardiomyocytes were used during isometric force measurements. Maximal Ca2+-activated active force production (Fmax), its Ca2+-sensitivity (pCa50), and Ca2+-independent passive force (Fpassive) were monitored. Western immunoblotting was applied to assess site-specific phosphorylation status of cardiac troponin-I (cTnI) and cardiac myosin binding proten C (cMyBP-C). Total phosphorylation status of titin protein was probed by a ProQ Diamond phosphoprotein staining kit.
Results: No significant differences were observed among Fmax values of the four groups. The pCa50 and Fpassive values were significantly higher in the ZDF rats than in the ZDFL, ZDFLV or ZDFV groups (pCa50 and Fpassive: ZDF: 5.88 ± 0.03 and 1.98 ± 0.12 kN/m2; ZDFL: 5.76 ± 0.01 and 1.02 ± 0.12 kN/m2; ZDFLV: 5.78 ± 0.03 and 1.03 ± 0.14 kN/m2; ZDFV: 5.76 ± 0.02 and 1.40 ± 0.13 kN/m2, P < 0.05, n = 6-7, mean ± SEM). In ZDF rats cTnI phosphorylation levels at Ser22/23, Ser43 and Thr143 sites were significantly lower than those in the ZDFV group (ZDF: 0.77 ± 0.05, 0.77 ± 0.08 and 0.68 ± 0.06; ZDFV: 1.01 ± 0.08, 1.35 ± 0.18 and 1.35 ± 0.16, in relative units, respectively, P < 0.05, n = 4). No significant differences in the site specific phosphorylation status of cMyBP-C at Ser282 and in the total phosphorylation status of titin between the ZDF and ZDFV groups were observed.
Conclusion: Increased passive force and Ca2+-sensitivity of force production developed in LV cardiomyocytes of rats with type 2 diabetes mellitus which could be limited by chronic phosphodiesterase-5A inhibition through increased protein phosphorylation.

P1971

Assessment of cardiomyocyte hypertrophy in rat myocardial infarction model using synchrotron X-ray phase contrast imaging

I Planinc[1]; P Garcia-Canadilla[2]; H Dejea[3]; E Guasch[4]; T Steigmeier[5]; M Stampanoni[3]; D Milicic[1]; B Bijnens[6]; A Bonnin[5]; M Cikes[1]
[1]*University of Zagreb School of Medicine, University Hospital Center Zagreb, Department of Cardiovascular Diseases, Zagreb, Croatia*; [2]*University Pompeu Fabra, Physense, DTIC, Barcelona, Spain*; [3]*Swiss Federal Institute of Technology Zurich (ETH Zurich), Zurich, Switzerland*; [4]*Hospital Clinic de Barcelona, Unitat de Fibrillació Auricular, Barcelona, Spain*; [5]*Paul Scherrer Institut, Villigen, Switzerland*; [6]*University Pompeu Fabra, ICREA, Barcelona, Spain*

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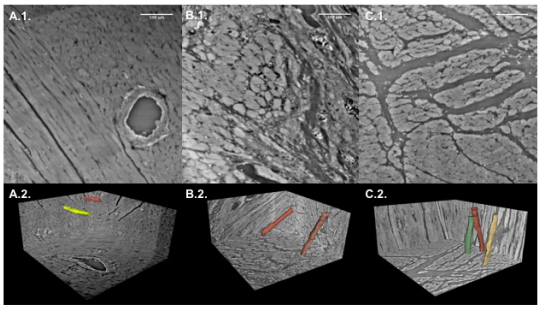
Background: Ischemic heart disease (IHD) is the leading cause of heart failure. The main pathogenic process is negative cardiac remodelling following myocardial infarction (MI). Global remodelling is easy to assess, yet no single technique can aggregate information on both cellular and entire organ level processes. A prominent technique under research is Synchrotron X-ray Phase Contrast Imaging (X-PCI) that can be used for both 3D analysis of whole hearts, as well as cardiomyocytes (CMCs) without tissue processing or destruction. We previously reported on the use of X-PCI for 3D data acquisition of whole rat hearts providing information on cardiac geometry and fibre orientation. We now aim to assess the ability of X-PCI to acquire information on cellular remodelling.



Top row, high resolution X-PCI images of selected areas and bottom row corresponding 3D rendering of selected cardiomyocytes in tissue volumes (400x550x550um). A.1 and A.2 healthy rat control, B.1 and B.2. peri-Mi area and C.1. and C.2 non-MI area of a MI heart

Methods: MI was induced in a well-established rat model of young adult (8-11 w.old) Wister rats by LAD artery ligation through a left thoracotomy. The rats were sacrificed in 2 weeks, and the hearts were excised, immersed in formalin and embedded in a tube with degassed deionized water. X-PCI was performed at an energy of 20 keV with 0.65 μm voxel size in selected regions of interest (ROIs)of the hearts. The projection sets were reconstructed using the Gridrec algorithm, leading to a 3D dataset. When ROIs were larger than the field of view, multiple scans were acquired to cover the full area; reconstructed volumes were merged into a single dataset. The high resolution level achieved by this technique allowed identification and analysis of individual CMCs which were segmented and analysed byopen-source software (3D Slicer and Fiji) allowing us to calculate cross sectional area (CSA). We analysed 2 post-MI rat hearts, and a control healthy rat heart. In post-MI hearts, the CMCs were analysed in the MI area (preserved cells adjoining fibrotic post-MI cardiac tissue - peri-MI zone), and in the contralateral region (the non-affected myocardium). CMCs of corresponding areas were quantified in the normal heart as well. CSA was expressed as the mean value with standard deviation of measurements of 10 CMCs per area.
Results: Average CSA of CMCs in the control rat was 321 ± 75 μm2. In MI rats, average CSA in peri-MI areas was 737 ± 127 μm2 and 499 ± 141 μm 2 in non-MI areas. The results indicate significant (p < 0.001) differences in CSA between peri-MI and non-MI areas of ischemic hearts, as well as compared to the healthy rat, indicating compensatory hypertrophy pronounced in peri-MI area as opposed to contralateral region. CMC CSA were consistent between MI hearts 1 and 2 (peri-MI: 773 ± 118 μm2 (MI rat 1) vs. 701 ± 125 μm2 (MI rat 2), p = 0.07 and non-MI area: 477 ± 53 μm2 (MI rat 1) vs. 521 ± 160 μm2 (MI rat 2), p = 0.255). Conclusion: X-PCI is a valuable imaging technique for assessing cellular hypertrophy in addition to whole organ remodelling in 3D. We showed marked differential compensatory hypertrophy in a rat model of IHD, which should be taken into account when evaluating post-MI hearts clinically.

P1972

Secretory products from pericardial adipose tissue of dietary-induced obese minipigs induce cardiomyocyte apoptosis via impairing mitochondrial homeostasis and autophagy

SJ Li[1]; TW Wu[1]; CY Ching-Yi Chen[1]
[1]*National Taiwan University, Taipei, Taiwan ROC*

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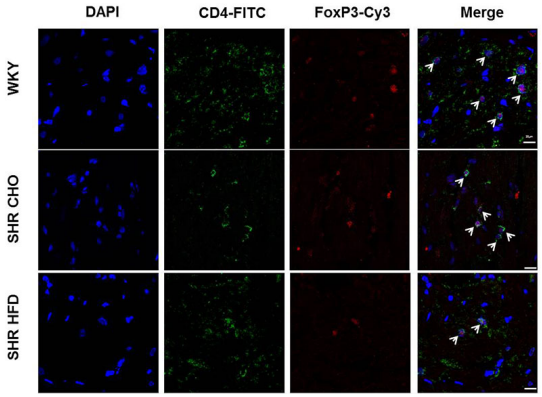
Objectives: Pericardial adipose tissue (PAT) is positively associated with the cardiovascular diseases and left ventricular remodeling. However, the underlying mechanism is still unknown. The objectives of this study was to examine the effect of PAT secretion from obese minipigs in H9C2 cardiomyoblasts with regard to mitochondrial homeostasis and autophagy.
Materials and Methods: The visceral adipose tissues (VAT) and PAT were collected from the Lee-Sung minipigs with high-fat diet feeding for six months. Conditioned medium (CM) generated from the explant of PAT and VAT were subjected to secretome profiling, or incubated with cardiomyocytes to assess the effect on mitochondrial functions and autophagy.
Results: A similar secretome profile was observed in PAT-CM and VAT-CM. Compared with the complete medium, PAT-CM and VAT-CM exhibited higher level of C16:0 and C18:1, greater lipid peroxidation products, and more inflammatory cytokine IL6 concentration. PAT-CM incubated with H9C2 cardiomyoblasts for 24 hrs induced cell apoptosis and reduced cell viability. A concordant effect was found in the VAT-CM treatment. A significant decrease in the mitochondrial fission-related proteins (Drp1 and Fis1) was found in the PAT-CM treatment. OPA1, a mitochondrial fusion-related protein, was downregulated in the PAT-CM treatment. Similarly, VAT-CM suppressed the expressions of mitochondrial fission and fusion-related proteins. These results suggested that both PAT and VAT impaired the mitochondrial dynamics in the H9C2 cells. Neither Parkin nor Pink1 (markers of mitophagy) was regulated by CM treatment. VAT-CM increased the LC3II/LC3I ratio, , while PAT-CM induced a greater ratio of LC3II to LC3I than VAT-CM did, suggesting that PAT-CM evoked a severer maladaptive autophagy than VAT-CM did.
Conclusion: The present study showed that PAT from obese minipigs displayed the cytotoxic potential as the VAT did. Secretion of pericardial fat evoked cardiomyocyte apoptosis via impairing mitochondrial dynamics and accumulating autophagosomes.

P1973

High fat diet downregulates regulatory T cells in the myocardium of spontaneous hypertensive rats.

S-H Sang-Hyun Ihm[1]; SK Hong[1]; EH Choo[1]; KY Chang[1]
[1]*Catholic University School of Medicine, Seoul, Korea Republic of*

Background: Obesity induced myocardial fibrosis may lead to diastolic dysfunction and ultimate heart failure. Cardiac inflammation may play a pivotal role in the pathogenesis of obesity-induced myocardial fibrosis. Regulatory T cells (Tregs) play an important role in cardiovascular complications and inflammatory action with the immune response. However, the role of Tregs and its associated anti-inflammation in obesity-induced myocardial fibrosis has not been elucidated to date. Therefore, we investigated whether high fat diet suppresses Tregs activation in the myocardium of spontaneously hypertensive rats (SHRs), which aggregates myocardial fibrosis.
Methods and Results: We assessed the extent of Tregs response and fibrosis in the myocardium. Eight-week-old male SHRs were fed to either high-fat diet (HFD) or control diet (CHO) groups for 12 weeks. We measured Tregs (CD4+FoxP3+) in the heart and mediastinal lymph nodes (LNs). The flow cytometry analysis confirmed that the SHR-HFD exhibited a decreased Tregs compared with that of the WKY in the heart and mediastinal LNs. In contrast, the SHR-CHO exhibited an increased Tregs compared to that of the SHR-HFD in the heart. Furthermore, SHR-CHO slightly increased the Foxp3+ compared with that of the SHR-HFD in the mediastinal LNs. The CD4 and FoxP3 antigens were used in the immunofluorescence microscopy of Tregs in the heart tissues. In the heart, dual staining for the Treg population was increased more in the SHR-CHO than it was in the SHR-HFD rats. In line with these findings, SHR-HFD significantly exacerbated myocardial fibrosis.
Conclusions: We found that diet-induced obesity typically showed an exacerbated myocardial fibrosis and down-regulation of Tregs pathway in the heart and mediastinal LNs. Therefore, we suggest that the up-regulation of Tregs may be a promising therapeutic approach to preventing obesity induced heart failure.



CD4 and FoxP3 and in rat hearts

P1974

Omega-3 fatty acids and melatonin affect activity of extracellular matrix metalloproteinase-2 in the plasma, aorta and heart of isoproterenol injured normotensive and hypertensive rats.

B Szeiffova Bacova[1]; C Viczenczova[1]; K Chaudagar[2]; M Sykora[1]; T Egan Benova[1]; M Barancik[1]; N Tribulova[1]
[1]*Slovak Academy of Sciences, Institute for Heart Research , Bratislava, Slovak Republic*; [2]*L. M. College of Pharmacy, Ahmedabad, India*

Rationale: Sustained activation of beta-adrenoceptors is accompanied by pathological remodeling and endangering the viability of cardiomyocytes, which increases the incidence of cardiac failure and sudden cardiac death. Our and other experimental studies as well as clinical trials suggest that melatonin and omega-3 fatty acids (PUFAs) are cardioprotective due to their anti-inflammatory, anti-oxidant, anti-hypertensive and anti-arrhythmic effects, but underlying molecular mechanisms are still not fully explored. We hypothesize that both compounds may affect extracellular matrix remodeling by modulation of extracellular matrix metalloproteinases (MMPase) activity.
Purpose: We aimed to explore MMP-2 activity in plasma, aorta and heart in normotensive and hypertensive rats after infarct-like cardiac injury induced by high dose of isoproterenol (ISO) as well as the effects of treatments with PUFA and melatonin.
Methods: In accordance with the rules issued by the State Veterinary Administration of the Slovak Republic and European Union Council Directive 86/609/EEC we used in our experiment Wistar and spontaneously hypertensive rats (SHR) which were divided into four groups. 1) Controls without treatment; 2) Iso-injured rats (118mg/kg totally, s.c., for 7days); 3) Iso-injured rats treated with melatonin (10mg/kg, p.o., 2-mo); 4) Iso-injured rats treated with PUFA (Omacor, 1.68g/kg, p.o.,2-mo). Samples from plasma, left and right ventricles and aorta were used to determine activity of MMP-2 by using gelatin zymography.
Key Results: There was higher plasma but lower heart tissue-related MMP-2 activity in non-treated SHR vs Wistar rats and no difference in aorta. ISO caused an increase of MMP-2 activity in plasma as well as in atria and decrease in left and right ventricles of Wistar rats. In contrast, ISO decreased MMP-2 activity in plasma, aorta and increased in left and right ventricles of SHR. Melatonin and Omacor suppressed plasma MMP-2 activity in Iso-treated Wistar but not in Iso-SHR. Both compounds lowered MMP-2 activity in atria of Iso-Wistar rats but elevated in iso-SHR as well as decreased MMP-2 activity in ventricles of Iso-treated SHR only.
In conclusion, data indicates that both melatonin and Omacor modulate circulating and cardiovascular tissue-related MMP-2 activity and there are strain- and tissue-related differences.
This work was supported by VEGA 2/0167/15, 2/0076/12, 1/0160/18, APVV-15-0119, SKS Egan Benová,

P1975

Effect of BGP-15 treatment on hypertension induced cardiac remodeling in an in vivo SHR model

K Katalin Ordog[1]; L Deres[1]; K Eros[2]; O Horvath[1]; T Habon[1]; B Sumegi[3]; K Toth[1]; R Halmosi[1]
[1]University of Pecs, Division of Cardiology and Angiology, 1 st Department of Medicine, Medical School, Pecs, Hungary; *[2]University of Pecs, Szentagothai Research Center, Pecs, Hungary*; *[3]University of Pecs, MTA-PTE Nuclear-Mitochondrial Interactions Research Group, Pecs, Hungary*

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Introduction: Based on previous studies BGP-15 improves cardiac function and reduces arrhythmic episodes in mouse model of atrial fibrillation. BGP-15 treatment improves mitochondrial function. In our present study we investigated the effect of BGP-15 on heart failure.
Methods: 15-month-old male SHR rats received 25 mg/kg/day BGP-15 (SHR-B) or placebo (SHR-C) treatment for 18 weeks. Age-matched Wistar rats (WKY) were used as normotensive control. Echocardiography was performed at the beginning and at the end of the treatment period. Plasma B-type natriuretic peptide (BNP) level was measured, and histological preparations were made from cardiac tissue. The levels of proteins involved in mitochondrial dynamics, the phosphorylation state of GSK-3ß, Akt, PKC and the MAPK cascade were monitored by Western blot technique.
Results: By the end of the study left ventricular (LV) wall thickness and LV mass increased significantly in SHR-C group compared to the initial values ($p < 0.05$), however in SHR-B group these parameters decreased markedly ($p < 0.05$). Ejection fraction (EF%) decreased in both SHR groups, however in SHR-B group this deterioration was only minimal. E/E' ratio - representing the diastolic function - increased in the control group, while in the treated group it decreased compared to the baseline values ($p < 0.05$). BGP-15 treatment reduced plasma BNP levels in the SHR-B group compared to the control animals ($p < 0.05$). The phosphorylation state of Akt-1Ser473 was slightly higher in the control group than in the WKY group, but in the treated group it increased markedly due to BGP-15 treatment ($p < 0.05$).
Discussion: BGP-15 treatment reduced the hypertension-induced cardiac remodeling and heart failure due to its favorable effect on intracellular signaling and mitochondrial function.

P1976

Assessment of heart transplant outcomes in long postoperative period

T Tatiana Chumarnaya[1]; A Bykov[2]; E Idov[3]; V Kochmasheva[2]; S Mikhailov[3]; O Solovoyva[4]
[1]Institute of Immunology and Physiology of Russian Academy of Sciences, Ekaterinburg, Russian Federation; *[2]Yekaterinburg Regional Clinical Hospital 1, Yekaterinburg, Russian Federation*; *[3]Urals State Medical University, Ekaterinburg, Russian Federation*; *[4]Ural Federal University, Yekaterinburg, Russian Federation*

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Cardiac transplantation is accepted as the best therapeutic option for end-stage heart failure patients who remain symptomatic despite optimal medical therapy. The function of the transplanted heart will be affected by acute allograft rejection, chronic rejection, high blood pressure and so on. All these factors may induce the remodeling of the left ventricle (LV) that will significantly affect the prognosis of heart transplantation (HT). The LV configuration changes from end diastole to end systole are an important factor of the heart pump function optimization. These changes could be described by the term LV "functional geometry".
The objective of this study is the assessment of outcomes in long time period after HT using parameters of LV functional geometry.
The LV functional geometry in myocardial diseases with different degrees of LV systolic dysfunction has been determined by using two-dimensional echocardiography. The control group (CG) consisted of 24 healthy volunteers without any signs of cardiovascular diseases. The second group(IHDG) with preserved LV systolic function (ejection fraction >50%) consisted of 52 patients suffering from ischemic heart disease. And third group(DCMG) with significant LV systolic dysfunction (ejection fraction < 35%) consisted of 35 patients with dilatational cardiomyopathy.
We used linear discriminant analysis (LDA) to build model for pattern recognition of our groups. The model was based on classic echocardiographic parameters, LV function geometry parameters (sphericity index, Fourier shape-power index showing the complexity of the LV shape, apical conicity index, spatio-temporal heterogeneity indexes), and speckle-tracking-derived LV longitudinal strain and strain rate.
We examined 31 patients after orthotopic HT who had postoperative period from 1 to 9 years. All HT patients underwent pairs of endomyocardial biopsy (EMB) and echocardiographic evaluation on the same day. Group of HT patients were stratificated of our LDA model. One quarter of HT group had normal systolic function and were defined in CG. 44% and 31% HT patients were defined in IHDG and DCMG respectively. In 97% of HT patients the predictions of the LDA model coincided with the state of the allograft obtained by EMB.
LDA model taking into account the parameters of LV functional geometry can facilitate the diagnosis of rejection and reveal deterioration of the allograft condition.

P1977

Main features of pathological myocardial remodeling in chronic heart failure and dilated cardiomyopathy

T Tatiana Kulikova[1]; O Stepanova[1]; A Voronova[1]; M Valikhov[1]; V Sirotkin[1]; A Samko[1]; V Masenko[1]; S Tereschenko[1]
[1]Russian Cardiology Research and Production Complex, cardiology department, Moscow, Russian Federation

Cardiac hypertrophy, fetal gene program reactivation and cardiac energy metabolism alterations are the main features of pathological myocardial remodeling in chronic heart failure (CHF). Although cardiac metabolic alterations are the consequence of the pathological state, they lead in turn to the disease development and contribute to the pathogenesis of CHF. Metabolic alterations ranging from changes in substrate utilization to mitochondrial dysfunction, ultimately resulting in energy deficiency and impaired contractility. Energy depletion is not the only consequence of metabolic alterations during CHF. By providing cellular building blocks and signaling molecules, metabolic pathways control essential processes such as cell growth and regeneration. Thus, alterations in cardiac metabolism may also affect the progression to CHF by mechanisms beyond energy supply. Peroxisome proliferator-activated receptor-gamma coactivator 1 alpha (PGC-1 alpha) controls the energy state and contractile function of heart. The expression of PGC-1 alpha is reduced in HF and during cardiac hypertrophy in vitro model of cardiac hypertrophy. The studies at animal model of CHF have shown the link between pathological cardiac hypertrophy, metabolic alterations and fetal gene program reactivation. PGC-1 alpha has an important regulator role in these processes and PGC-1 alpha expression level decreased. The aim of this work to study pathological cardiac hypertrophy, metabolic alterations and fetal gene program reactivation in patients with DCM and CHF.
Endomyocardial biopsies (18) were obtained from patients with CHF and DCM. RT-qPCR was used to measure gene expression levels. Hematoxylin and Eosin staining (H & E) was used for histopathology study.
Myocardial tissue H & E staining results have shown only the pathological hypertrophy of cardiomyocytes and the absence of fibrosis. PGC-1 alpha expression level decreased in CHF in comparison to human non-diseased myocardium autopsy specimens (5).
These data indicate the occurrence of metabolic alterations in CHF - an energy metabolism shifting from cardiac fatty acid oxidation as primary energy source to glucose. The results demonstrate the reactivation of the fetal gene program, features of fetal heart include the preference of carbohydrates over fatty acids as energy substrate.
Pathological hypertrophy of cardiomyocytes and PGC-1a expression level decreasing revealed by us in patients with HF are in line with data received in animal models that cardiac metabolic alterations, connected with PGC-1a downregulation, occur in cardiac pathological hypertrophic processes, and there is a close link. Metabolic alterations in CHF not only results in impaired cardiac energetics, but also induces other processes implicated in the development of CHF such as structural and cell remodeling. Accordingly, modulating cardiac metabolism in heart failure may have significant therapeutic relevance that goes beyond the energetic aspect.

P1978

Ubiquinol intravenous injection protects the myocardium from ischemic damage

O Oleg Medvedev[1]; O Kulyak[1]; E Gorodetskaya[1]; V Makarov[2]; E Kalenikova[1]
[1]M.V. Lomonosov Moscow State University, Pharmacology, Moscow, Russian Federation; *[2]Institute of Pharmacy, Pharmacy, Saint Petersburg, Russian Federation*

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Introduction: Coenzyme Q10 (CoQ10) is the endogenous compound essential for mitochondrial function and bioenergetics of cells. In the body CoQ10 exists in two forms - oxidized (ubiquinone) and reduced (ubiquinol). The main role in achieving the protective effects of CoQ10 is due to the antioxidant properties of ubiquinol. The innovative water-soluble form of ubiquinol for intravenous administration was developed.
Purpose: Experimental evaluation of the cardioprotective efficacy of the innovative drug form of ubiquinol for intravenous administration.
Methods: The experiments were carried out on the rat model of myocardial infarct (MI) induced by coronary artery ligation. In 10 min after occlusion solubilized

ubiquinol (10 mg/kg, group "MI + ubiquinol ", n = 10) or saline (group "MI + saline", n = 12) was administered by intravenous injection. Sham operated rats were given saline (group "Sham", n = 8). Severity of the myocardium damage, CoQ10 tissue levels were evaluated on the 21st day after coronary occlusion. The CoQ10 content was measured by HPLC with electrochemical detection.
Results: In group "MI + ubiquinol" aneurysm size of the left ventricle (13,19 ± 7,13 %) was much less than in group "MI + saline" (31,55 ± 17,9 %, p <0,05). The interventricular septum in group "MI + ubiquinol " (2,61 ± 0,03 mm) was thinner than in group "MI + saline" (2,83 ± 0,27 mm, p <0,05) and did not differ from "Sham" group (2,51 ± 0,29 mm). Only in the treated animals, there was a correlation between the thickness of the interventricular septum and the level of ubiquinol in the myocardium (R2 = 0.672, p <0.05), that shows that it was the administration of ubiquinol that caused the cardioprotective effect.
Conclusion: Intravenous administration of ubiquinol after coronary artery occlusion reduces the aneurysm size the left ventricle and prevents the development of left ventricular hypertrophy in rats.

P1979

Design of models for predicting the development of heart failure with reduced ejection fraction and preserved ejection fraction in patients with acquired heart diseases in the postoperative period

I I Irina Averina[1]; OL Bockeria[1]; MYU Mironenko[1]
[1]Bakoulev Center for Cardiovascular Surgery RAMS, Cardiosurgical , Moscow, Russian Federation

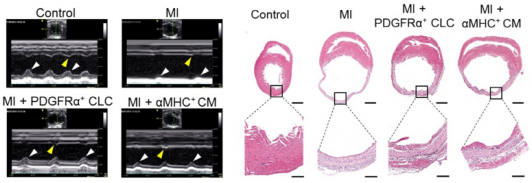
Background: Despite technically successful operations postoperative complications as heart failure are still observed.
Purpose: To identify models for the prediction of cardiac heart failure with reduced ejection fraction (HFrEF) and with preserved ejection fraction (HFpEF) in patients with acquired heart disease in the postoperative period.
Materials and Methods: The study was involved 144 patients (99 men and 45 women) with aortic and mitral valve disease. The median age was 46,7 ± 15,1 years (range from 18 to 72 years). 3 examinations were conducted: befor surgery, in the early postoperative period (8 - 14 days) and 12 - 36 months after the surgery. All patients underwent clinical examination, echocardiography, tissue Doppler (TD), the speckle tracking method (STE), 28 patients also had dynamic contrast-enhanced magnetic resonance imaging (MRI). The patients were divided into prognostic groups according to the presence of complications. Group 0 - favorable prognosis; Group 1 - evolved postoperative HFpEF; Group 2 - evolved postoperative HFrEF.
Results: MANOVA and Cox regression models were applied. The highest quality prognosis model for HFrEF and HFpEF was identified.
It includes the MRI anterior-posterior LV dimension at the papillary muscle level (p = 0,004), LV fraction of shortening (p = 0,001), the early-to-late LV diastolic velocity ratio E/A (p = 0,0005), the diastolic diameter of the mitral annulus (p = 0.001) (for HFrEF); the left atrium average global longitudinal strain GLSt av LA(p = 0,002) and early filling (Et) and early diastolic tricuspid annular velocity (E') ratio (Et/E' ratio) assessed by TD (p = 0,05) (for HFpEF).
All the parameters significantly determine the risk of postoperative HF complications.
Conclusion: HFrEF and HFpEF models from easily obtained variables for prediction in patients with acquired heart disease in the postoperative period were identified.

P1980

Regenerative potential of pluripotent stem cell-derived PDGFRa+ cardiac lineage committed cells in infarcted myocardium

S W Cho[1]; SY Sohn[2]; SP Hong[3]; S Song[4]; JH Park[5]
[1]Inje University, Seoul Paik Hospital, Division of Cardiology, Department of Internal Medicine, Seoul, Korea Republic of; *[2]Hospital Myongji, Division of Endocrinology, Department of Internal Medicine, Goyang, Korea Republic of*; *[3]Korea Advanced Institute of Science and Technology, Biomedical Science and Engineering Interdisciplinary Program, Daejeon, Korea Republic of*; *[4]Korea Advanced Institute of Science and Technology, Daejeon, Korea Republic of*; *[5]Chungnam National University Hospital, Daejeon, Korea Republic of*

Background: Pluripotent stem cell (PSC)-derived cardiomyocytes have become one of the most attractive cellular resources for cell-based therapy to rescue damaged hearts. However, the current yield of cardiomyocytes from PSC has still insufficient to meet clinical requirements because of the limited proliferative capacity of differentiated cardiomyocytes. We newly generated PSC-derived PDGFRa+ cardiac lineage committed cells (CLCs) having proliferative capacity, but morphologically and functionally immature state compared to differentiated cardiomyocytes.
Method: We induced PDGFRa+ CLCs from PSCs using a combination of the small molecules Cyclosporin A, the rho-associated coiled-coil kinase inhibitor Y27632, the antioxidant Trolox, and the ALK5 inhibitor EW7197. We implanted PDGFRa+ CLCs and differentiated aMHC+ cardiomyocytes (CMs) into myocardial infarction (MI) murine model and performed the functional analysis using transthoracic echocardiography (TTE) and histologic analysis.
Results: Compared with MI model, the anterior and septal regional wall motion and systolic functional parameters were notably and similarly improved in the MI hearts implanted with PDGFRa+ CLCs and aMHC+ CMs in TTE. In histologic analysis, the gross sizes of MI hearts implanted with PDGFRa+ CLCs and aMHC+ CMs were smaller than MI heart. Furthermore, MI heart had a thinner ventricular wall (0.20 mm) than did controls while the ventricular walls of MI hearts implanted with PDGFRa+ CLCs and aMHC+ CMs were similarly thicker (0.47 mm and 0.39 mm, respectively) compared to MI heart.
Conclusion: PDGFRa+ CLCs from PSCs having proliferative capacity showed the regenerative potential in infarcted myocardium. Therefore, PSC-derived PDGFRa+ CLCs could be an ideal and optimal cellular resource for cardiac regeneration.



P1981

Cardiac regenerative and metabolic processes in chronic heart failure

T Tatiana Kulikova[1]; O Stepanova[1]; M Valikhov[1]; A Voronova[1]; A Samko[1]; V Masenko[1]; S Tereschenko[1]
[1]Russian Cardiology Research and Production Complex, cardiology department, Moscow, Russian Federation

In chronic heart failure (CHF) occur metabolic alterations - an energy metabolism shifting in cardiomyocytes from fatty acid oxidation as primary energy source to glucose. Cardiomyocyte metabolic plasticity is unique metabolic feature of these cells. Plasticity of stem cells also reflects the plasticity of their energy substrate metabolism. There is a clear link between the self-renewal state of stem and dedifferentiated cells, in which cells proliferate without differentiation, and the activity of metabolic pathways. Cell dedifferentiation is accompanied by a shift from oxidative phosphorylation to glycolysis. Transcription factor nuclear receptor peroxisome proliferator-activated receptor alpha (PPARa) of is an important regulator of energy metabolism by regulating genes encoding enzymes involved in fatty acid and glucose utilization. We propose that myocardial metabolism shift results to cardiomyocyte dedifferentiation. As PPARa is a main regulator of energy metabolism, change in its activity shows metabolism alterations and may represent a marker of dedifferentiated cell state, the aim of the work to determine PPARa expression level in CHF, to detect dedifferentiated cardiomyocytes in CHF and the role of TNF-a in activation of cardiomyocyte dedifferentiation.
Human fetal cardiomyocytes were stimulated with inflammatory cytokine TNF-a for up to 24 hours and time dependent changes in the expression of established marker of cardiomyocyte dedifferentiation ANP was assessed by RT-qPCR. Transmission electron microscopy was used for dedifferentiated cardiomyocytes detecting in endomyocardial biopsies (EMB) patients with CHF and DCM. ANP expression level was detected in EMB (15) patients with HF and DCM. RT-qPCR was used to assess PPARa expression level in the same samples.
mRNA levels of ANP increased following treatment with TNF-a. Induction ANP was gradual (peaking at 24 hours). Significant ANP expression level increase was detected in EMB in CHF in comparison with the myocardial samples without cardiovascular pathology. Expression levels of PPAR-alpha decreased in CHF.
Elevated ANP expression levels are associated with cardiomyocyte dedifferentiation. Our results demonstrate that TNF-a directly induces cardiomyocyte dedifferentiation. Cardiomyocytes with hallmarks of dedifferentiation as evaluated by electron microscopy have been found in our study in EMB in CHF. Revealed cardiomyocytes have main features of dedifferentiated cardiomyocytes - changes in size and shape of cardiomyocytes, sarcomere disorganization, enhanced glycogen content and mitochondria disposition. PPAR-alpha expression level decrease shows shift from oxidative phosphorylation to glycolysis, a transition to dedifferentiated state of cardiomyocytes. Identifying the specific metabolic pathways involved in dedifferentiation and differentiation is critical for further progress in the field of regenerative medicine without the requirement of genetic manipulation.

P1982

Cardioprotective and immunomodulatory effects of endomyocardial biopsy- and atrial appendage-derived stromal cells in an acute model of Coxsackievirus B3-induced myocarditis

M El Shafeey[1]; K Pappritz[1]; F Diedrichs[1]; M Seifert[1]; C Stamm[1]; M Haag[1]; M Sittinger[1]; C Tschoepe[1]; S Sophie Van Linthout[1]
[1]*Berlin-Brandenburg Center for Regenerative Therapies, Berlin, Germany*

Background: The atrial appendage (AA) has recently been shown to be a suitable source to generate cardiac-derived adherent proliferating (CardAP) cells for regenerative cell-based therapies. CardAP cells have cardioprotective and immunomodulatory properties and have originally been isolated from endomyocardial biopsies (EMB). The amount of CardAP cells derived from EMB is often limited due to the small EMB size, whereas one AA allows sufficient cells for the treatment of more than 250 patients.
Aim: The aim of the present study was to evaluate the cardioprotective and immunomodulatory potential of EMB- and AA-derived CardAP cells in experimental Coxsackievirus B3 (CVB3)-induced myocarditis.
Methods and Results: Before evaluation of the different CardAP cells in CVB3 mice, we demonstrated in vitro by immune cell co-cultures that EMB- and AA-CardAPs have similar immunogenic and immunomodulatory properties. Intravenous application of 10e6 EMB- and AA-CardAP cells, one day after CVB3 infection at a dose of 10e5 p.f.u. improved left ventricular function in CVB3-infected C57BL/6J mice as shown by a 1.3-fold ($p < 0.005$) and 1.4-fold ($p < 0.0005$) increase of the contractility parameter dP/dtmax, respectively, and a 1.5-fold ($p < 0.005$) and 1.5-fold ($p < 0.0005$) improvement of dP/dtmin, respectively. In parallel, both EMB- and AA-CardAP cells decreased cardiac collagen I expression by 1.6-fold ($p < 0.05$) and 1.7-fold ($p < 0.005$), respectively, leading to a 1.5-fold ($p < 0.05$) and 1.6-fold ($p < 0.005$) drop in collagen I / III ratio versus CVB3 mice. EMB- and AA-CardAP cells reduced the % of splenic TGF-ß-expressing CD68 cells in CVB3 mice by 2.2-fold ($p < 0.0001$) and 2.6-fold ($p < 0.0001$), respectively. Concomitantly, both EMB- and AA-CardAP cells reduced the % of T regulatory cells, defined as CD4CD25FoxP3 cells, to percentages of control mice, a finding which was also seen for CD4-IL10- and CD8-IL10-expressing cells.
Conclusion: The recently defined AA-CardAP cells exert cardioprotective and immunomodulatory effects comparable to EMB-CardAP cells in CVB3 myocarditis mice.

P1983

Influence of candesartan cilexetil and resveratrol on changes in the number of stem cells, cytogenetic and cytokinetic parameters of bone marrow of mice

A Aliaksandra Beliayeva[1]
[1]*National Academy of Science, Institute of Bioorganic Chemistry, Minsk, Belarus*

Introduction: The constant growth of incidence of cardiovascular diseases and increased mortality rate provoked by this pathology urges the need to formulate new drugs, to reassess potential of available medicines and their combinations.
Purpose: To investigate the effect of candesartan cilexetil (angiotensin-II receptor blocker) and resveratrol on the number of stem cells, cytogenetic and cytokinetic parameters of bone marrow of C57Bl/6 mice.
Methods: Male C57Bl/6 mice (n = 80) were chosen for study. Animals were divided into 8 groups (10 mice each). Animals of 7 groups received intragastrically daily for 7 weeks candesartan cilexetil and resveratrol, dissolved/suspended in 1% starch solution. Candesartan cilexetil at 1.5 mg/kg dose was administered to mice of group 1, whereas resveratrol at 1 mg/kg, 10 mg/kg and 50 mg/kg doses was supplied to groups 2, 3, 4, respectively. Animals of groups 5 - 7 were treated by combination of candesartan cilexetil at 1.5 mg/kg dose and resveratrol at 1 mg/kg, 10 mg/kg and 50 mg/kg doses, respectively. Control mice received daily 1% starch solution. Flow cytometry method was used to evaluate the number of CD117+ stem cells (endothelial progenitor cells), apoptotic and micronucleated cells, cell distribution at stages of cell cycle in bone marrow of C57Bl/6 mice.
Results: Candesartan cilexetil at 1.5 mg/kg dose caused no effect on the number of CD117+ stem cells in bone marrow of C57Bl/6 mice. Resveratrol raised the ratio of CD117+ stem cells in bone marrow of C57Bl/6 mice in comparison with the control ($p < 0.05$). It was originally established that combination of candesartan cilexetil at 1.5 mg/kg dose and resveratrol at 1 mg/kg, 10 mg/kg and 50 mg/kg doses stimulated generation of CD117+ stem cells in bone marrow of C57Bl/6 mice as compared to the control ($p < 0.05$). The obtained data were also significantly higher than those recorded for individual compounds. Candesartan cilexetil at 1.5 mg/kg dose increased the number of apoptotic and micronucleated cells in comparison with the control ($p < 0.05$), whereas the combined use of candesartan cilexetil at 1.5 mg/kg dose and resveratrol at 1 mg/kg and 10 mg/kg doses significantly reduced the number of genetically impaired cells induced by exposure to candesartan cilexetil and enhanced proliferation in bone marrow of C57Bl/6 mice.
Conclusion. This study is the first demonstration that concerted use of candesartan cilexetil and resveratrol stimulates the formation of CD117+ stem cells in bone marrow of C57Bl/6 mice. It was originally found that resveratrol reduced cytotoxic effects of candesartan cilexetil in bone marrow of mice. The experimental data might be used to develop new complex drug for treatment of cardiovascular diseases capable to mobilize endothelial progenitor cells and facilitate reparative processes in cardiovascular system.

P1984

Cardiac metabolic remodeling in chronic heart failure due to dilative cardiomyopathy and ischemic heart disease

AD Voronova[1]; TG Kulikova[1]; OV Stepanova[1]; MP Valikhov[1]; VP Masenko[1]; RS Akchurin[1]
[1]*Cardiology Research and Production Center, Moscow, Russian Federation*

Funding Acknowledgements: RFBR:?18-015-00198 "Studying of energy cardiac metabolism and cardiomyocyte dedifferentiation in chronic hert failure

The main causes of chronic heart failure (CHF) are dilatative cardiomyopathy (DCM) and ischemic heart disease (IHD). The CHF progression is accompanied with a pathological changes in cardiac energy metabolism - metabolic remodeling characterized by shifting from cardiac fatty acid oxidation as a primary energy source to glucose oxidation. ?ardiac ischemia is the result of hypoxia. What leads to cardiac energy metabolism changes in DCM is unknown. Cardiac energy metabolism is under the transcriptional control of nuclear receptors, such as peroxisome proliferator activated receptors (PPARs) and transcriptional coactivator of PPARs - PPAR gamma coactivator-1-alpha (PGC-1 alpha), PGC-1 alpha plays a critical role in controlling cardiac energy. These factors act as molecular sensors in response to extracellular and intracellular changes, regulating the expression of the target genes. The downregulation of PPAR alpha has been shown in the studies in mice model of ischemic cardiomyopathy. The purpose of our work is to study cardiac energy metabolism alterations in IHD and DCM.
RT-qPCR was used to measure mRNA expression of the nuclear receptor PPAR alpha - a key regulator of fatty acid beta-oxidation, its target genes LCAD, CPT-1, CD36, HFABP and PGC-1alpha, in surgical specimens of auricle from patients with IHD (n = 10), in human endomyocardial biobsy specimens from patients with DCM (n = 37) and in human non-diseased myocardium autopsy specimens (n = 5).
Gene expression levels of PPAR-alpha and LCAD, CPT-1, CD36 decrease in IHD and DCM relative human non-diseased myocardium autopsy specimens. The gene HFABP is upregulated in IHD and DCM. The level of expression of PGC-1 alpha significantly increases in IHD, whereas it decreases in DCM. Significant changes in the levels of expression of PPAR-alpha and its target genes in IHD and DCM may mean that these genes are involved in of cardiac energy metabolism alterations and there is a shift from the use of fatty acids to the use of glucose. The expression levels of the PGC-1 alpha were much higher in IHD than in the normal heart, there is downregulation of this gene in DCM, these data may indicate different coactivator activities in DCM and IHD. It can be assumed that the regulation of the cardiac energy metabolism is possible by acting on PPAR-alpha and its target genes, and apparently the mechanisms of action on PGC-1 alpha should differ. These results of our study are very interesting as the transcriptional coactivator of the PPARs PGC-1 alpha has emerged as a key player in the control of myocardial metabolism and perturbations in the PGC-1 alpha system could predispose to cardiomyopathic remodeling. The importance of the PPARs and PGC-1 alpha in the control of cardiac energy metabolism makes these regulatory pathways attractive for metabolic therapy. Much needs to be learned concerning the intricacies of modulating their activity for optimal therapeutic benefit.

P1985

Inotropes: bioenergetic consequences of omecamtiv mecarbil and levosimendan

A Dietl[1]; M Kohlhaas[1]; D Puetz[2]; E Bertero[3]; AG Nickel[1]; L Prates Roma[4]; C Maack[1]
[1]*Comprehensive Heart Failure Center, University Hospital and University of Wuerzburg, Wuerzburg, Germany*; [2]*Saarland University Hospital, Department of Internal Medicine III, Homburg, Germany*; [3]*IRCCS Policlinic Hospital San Martino & Department of Internal Medicine, University of Genova, Cardiology Unit, Genova, Italy*; [4]*Saarland University, CIPMM - Biophysics Department, Homburg, Germany*

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Purpose: Mitochondrial steady-state Ca2+ balances energy production and antioxidative capacity. We hypothesised that increased workload without concomitant Ca2+-elevation impairs mitochondrial redox state, increases ROS-emission and explains side effects of Ca2+-sensitizers. We used EMD-57033 (EMD), levosimendan (levo) and the myosin activator omecamtiv mecarbil (OM).

Methods: Isolated cardiac myocytes (guinea pigs, mice) were field stimulated, while sarcomere length and fluorescence (NAD(P)H/FAD, indo-1) were determined. To pinpoint mitochondrial H2O2, transgenic mice expressing mitochondrially targeted roGFP2-Orp1 were used. For the first time, NAD(P)H and specifically mitochondrial H2O2 were measured live and simultaneously in twitching cardiac myocytes. A statistical model was developed employing regression analyses to estimate the dependency of NAD(P)H on the absolute degree of orp1-sensor oxidation.
Results: EMD (3μM) increased fractional sarcomere shortening, but impaired relaxation (RT50%), without affecting [Ca2+]c. Mitochondrial redox states of NADH, FADH2 and NADPH were oxidized, impairing the electron supply for the respiratory chain (NADH, FADH2) and the antioxidative capacity (NADPH). Accordingly, EMD increased the mitochondrial H2O2 emission, while the compound had no direct effects on isolated mitochondria. Levo had minor effects on sarcomere shortening at micromolar concentrations, while minimal prestimulation of beta-adrenergic receptors increased the efficiency and potency of levo, related to the previously observed inhibitory effect on phosphodiesterase 3. In fact, the increase in cell shortening was related to an increase in [Ca2+]c. Accordingly, the redox state of NAD(P)H and FAD remained stable with Levo, while the occurrence of spontaneous extra beats was increased. OM (0.2-10μM) increased active and passive work (integral over sarcomere length). Mitochondrial redox state was slightly oxidized at therapeutic plasma concentrations (0.2 μM), but provoked only a weak increase in H2O2 emission that was less pronounced compared to EMD at equi-effective concentrations. At therapeutic concentrations, OM did not provoke spontaneous extra-beats, while at supra-therapeutic concentrations (1 μM), it induced substantial diastolic dysfunction, depleted the antioxidative capacity and caused cell death.
Conclusions: "Pure" Ca2+-sensitization (EMD) induces a mismatch between energy supply and demand and depletes NADPH, provoking excess mitochondrial H2O2-emission and cell death. Levo predominantly inhibits PDE, and through elevating [Ca2+]c avoids mitochondrial oxidation, albeit at the cost of arrhythmias. Compared to EMD, OM provokes less oxidation and ROS emission at therapeutic concentrations. At higher OM concentrations, diastolic dysfunction and mitochondrial oxidation induce cell death that may underlie the increase of plasma troponin T in early clinical trials through a mechanism independent of compromised coronary perfusion.

P1986

Downregulation of the mitochondrial calcium uniporter hinders cardiac energy supply-and-demand matching in Barth syndrome

E Bertero[1]; A Nickel[1]; M Kohlhaas[1]; M Hohl[2]; C Krug[2]; A Mueller[3]; M Lafontaine[4]; R Lancaster[4]; R Kappl[5]; K Von Der Malsburg[6]; M Van Der Laan[6]; J Dudek[7]; P Rehling[7]; C Maack[1]
[1]Comprehensive Heart Failure Center (CHFC), Würzburg, Germany; *[2]Saarland University Hospital, Clinic for Internal Medicine III, Homburg, Germany*; *[3]Saarland University Hospital, Clinic for Radiology, Homburg, Germany*; *[4]Saarland University Hospital, Department of Structural Biology, Homburg, Germany*; *[5]Saarland University Hospital, Department of Biophysics, CIPMM, Homburg, Germany*; *[6]Saarland University Hospital, Medical Biochemistry and Molecular Biology, Homburg, Germany*; *[7]Georg-August University, Department of Cellular Biochemistry, Göttingen, Germany*

Background: Barth syndrome (BTHS) is an X-linked disorder caused by mutations in the tafazzin (Taz) gene and characterized by cardiomyopathy, skeletal myopathy and neutropenia. Taz is involved in the remodeling of cardiolipin, a phospholipid of the inner mitochondrial membrane playing a key role in the organization of the electron transport chain complexes. Destabilization of respiratory chain super-complexes and subsequent increase in ROS production may underlie the pathogenesis of the disease. We investigated the consequences of global genetic deletion of Taz in a mouse model of BTHS.
Methods and Results: Left ventricular (LV) function (cardiac MRI) was not impaired in 10 weeks old (wo) mice, but 20 and 50 wo Taz-KD mice displayed a reduction in cardiac output compared with wild type (WT) littermates due to a combination of diastolic and slight systolic dysfunction (LVEF: $55 \pm 6\%$ vs $76 \pm 5\%$, $p < 0.05$) in the absence of cardiac enlargement. Cardiac dysfunction was associated with a 15-fold increase in ANP and 4-fold increase in CTGF mRNA expression. In isolated, field-stimulated Taz-KD ventricular myocytes, myofilament Ca2+ sensitivity was increased, possibly contributing to the diastolic dysfunction observed at a whole-heart level. In isolated cardiac mitochondria, maximal respiration was slightly reduced compared to WT in 10 wo mice, but was unchanged in 20 and 50 wo mice. ROS emission was unchanged at 10 and 20 weeks and even decreased in 50 wo Taz-KD mice. Strikingly, uptake of Ca2+ was virtually absent in isolated cardiac, but not skeletal muscle mitochondria at all time points. This was caused by downregulation of the mitochondrial Ca2+ uniporter (MCU) pore-forming subunit (MCUa) associated with structural rearrangement of the MCU complex (blue native gel), whereas regulatory components of the MCU were unchanged. The mechanism underlying MCU downregulation is not fully resolved, but microRNA-mediated downregulation and defective protein import can be ruled out. In isolated contracting cardiac myocytes, the lack of mitochondrial Ca2+ uptake hampered the Krebs cycle-mediated regeneration of NADH (for ATP production) and NADPH (for H2O2 detoxification) during physiological workload transitions (beta-adrenergic stimulation and 5 Hz stimulation). In 10 wo Taz-KD myocytes, excessive H2O2 emission was prevented by compensatory protein upregulation of H2O2-eliminating enzymes (catalase, glutathione peroxidase), but this upregulation vanished at 50 weeks. Accordingly, at 20 and 50 weeks, the baseline redox state of isolated cardiac myocytes was more oxidized in Taz-KD compared to WT, which remained aggravated during workload transitions.
Conclusions: Redox mismatch due to defective mitochondrial Ca2+ uptake precedes respiratory chain defects in BTHS and may represent a major driver of oxidative stress and thereby, disease progression. Because this defect is heart-specific, this may explain why cardiomyopathy is a dominant feature of the disease.

P1987

The ubiquitin ligase TRIM35 is a novel restriction factor for cardiomyocyte proliferation

H Hashim Ali[1]; L Braga[1]; S De Monte[1]; M Vu Deim[1]; S Vodret[1]; P Lesizza[2]; L Zentilin[1]; M Giacca[1]
[1]International Centre for Genetic Engineering and Biotechnology (ICGEB), Trieste, Italy; *[2]University of Trieste, Department of Medical, Surgical and Health Sciences, Trieste, Italy*

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Purpose: The majority of adult mammals are unable to regenerate their hearts after cardiac injury, largely due to the limited replicative potential of cardiomyocytes after birth. However, some adult vertebrates and newborn mammals are able to repair the lost myocardium through pre-existing cardiomyocyte proliferation. This occurs after partial de-differentiation of these cells, an event that requires disassembly of the contractile sarcomere and remodeling of the actin cytoskeleton. We hypothesized that controlled protein degradation by the ubiquitin-proteasome pathway might play a key role in this process.
Methods: High-througput siRNA screening, Edu incorporation assay, Crispr/cas9-mediated gene silencing, AAV-transduction, qPCR, echocardiography, histology and Co-immunoprecipitation.
Results: To identify the critical regulators in the process of cardiomyocyte de-differentiation that parallels cell proliferation, we performed a targeted RNAi screen based on high-content fluorescence microscopy, using a library of ~600 siRNAs against factors in the ubiquitin-conjugation and proteasome-mediated degradation pathway; screening endpoint was the incorporation of EdU in neonatal mouse cardiomyocytes; validation of hits was later performed testing phospho-histone 3 positivity and Aurora B kinase localization in midbodies during cytokinesis. Using a 2 fold-standard deviation threshold over control for EdU incorporation, we identified 6 siRNAs that stimulate cardiomyocyte proliferation and 10 siRNAs that inhibit it. Most of these siRNAs target cellular E3-ubiquitin ligases with still unidentified targets in cardiac biology. In particular, we found that depletion of the TRIM family member TRIM35 was able to markedly induce proliferation of both mouse and rat cardiomyocytes. Cardiac-specific deletion of the TRIM35 gene in vivo using the Crispr/Cas9 technology delivered through AAV vectors induced remarkable proliferation in the hearts of neonatal mice. Gene knock out in adult mice improved heart function and decreased fibrosis after myocardial infarction.
In conclusion: TRIM35 is a novel ubiquitin-conjugation component restricting cardiac regeneration both in vitro and in vivo.

P1988

The characterization of cardiac molecular defects in an in vitro disease model of Vici syndrome and identification of potential therapeutic target

EA Ezzaldin Ahmed Alfar[1]; J Qi[2]; J Gommlich[1]; M Gautel[3]; K Guan[1]
[1]Dresden University of Technology, Pharmacology and Toxicology, Dresden, Germany; *[2]University Medical Center of Göttingen, Cardiology and Pneumology, Göttingen, Germany*; *[3]King's College London, Cardiovascular Division, London, United Kingdom*

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Purpose: Vici syndrome is a rare disorder characterized by defective autophagy due to mutations in Epg5. As the disease progresses, development of dilated and hypertrophic forms of cardiomyopathies are observed. However, the mechanisms of cardiomyopathies development and possible therapeutic targets remain to be elucidated. Interestingly, previous work in c. elegans showed that targeting the O-GlcNAc transferase (OGT) in Epg5 deficient nematodes restored a functional autophagy. However, the effect of targeting OGT in a human Vici disease model is unknown. The unknown mechanisms of Vici cardiomyopathies and the unknown effect of targeting OGT in a Vici disease model intrigued us to establish a human Vici

disease model. This model allowed us to provide further insight into the mechanisms of cardiomyopathies development and to test the effect of OGT inhibitors in attenuating the Vici cardiomyopathies.
Methods: We obtained Vici patient-specific fibroblasts which we used to generate induced pluripotent stem cells (iPSCs). The iPSC-derived cardiomyocytes served as a human in vitro disease model allowing the characterization of cardiac defects, mechanisms of cardiac defects and testing the effects of potential therapeutic targets.
Results: First, we successfully generated patient-specific iPSC lines, which retained the Epg5 mutation. Then we derived cardiomyocytes from the Vici patient-specific iPSCs, which exhibited defective autophagy as predicted for the Epg5 mutation. In addition, we observed some of the known Vici associated cardiomyopathies including hypertrophy and sarcomere disarray in our in vitro disease model. Given that both oxidative stress and mitochondrial dysfunction are known contributing factors to cardiomyopathies and at the same time potential outcomes of a defective autophagy process, we investigated possible disease mechanisms including mitochondrial dysfunction and cellular oxidative stress. We showed that Vici derived cardiomyocytes accumulates fragmented and dysfunctional mitochondria and exhibit oxidative stress. Next, we tested the effect of several OGT inhibitors on oxidative stress in our disease model. We observed a reduction in cellular oxidative stress in OGT inhibitor treated cells, a result which indicates possible attenuation of the disease phenotype and improvement of mitochondrial function.
Conclusion: In this work, we established an in vitro human Vici syndrome cardiomyopathy model. We observed some of the known disease phenotypes in our disease model, and at the same time, provided further insight into the disease mechanisms. Additionally, we have preliminary results of a possible therapeutic target for Vici syndrome associated cardiomyopathies. Currently, we are characterizing further cellular defects including defective calcium handling, ER stress and reliance on glycolysis. In addition, we are further validating the therapeutic target we identified in attenuating the disease phenotype.

Basic Science – Vascular Biology and Physiology

P1989
Evaluation of cardiovascular biomarkers transcriptional levels in cardiac tissue of rats as function of age

C Salvadori[1]; M Cabiati[1]; AL Sapio[1]; S Burchielli[2]; C Caselli[1]; L Carlucci[3]; L Mattii[4]; S Del Ry[1]
[1]Institute of Clinical Physiology of CNR, Pisa, Italy; *[2]Gabriele Monasterio Foundation, Pisa, Italy*; *[3]Sant'Anna School of Advanced Studies, Institute of Life Sciences, Scuola Superiore Sant'Anna, Pisa, Italy*; *[4]University of Pisa, Pisa, Italy*

Background: Chronological age is considered to be one of the major risk factors for cardiovascular disease and mortality in developed countries. During this process cardiovascular system undergoes substantial functional and structural changes altering the levels of some cardiac function biomarkers as natriuretic peptides (PN) and endothelin-1 (ET-1). Recently the adrenomedullin (ADM) system and long non-coding (lnc) RNA have been identified as new biomarkers associated with aging but their role in this process is not yet defined.
Purpose: To evaluate the expression of the PN, ET-1 and ADM system, as well as the analysis of lncRNA MIAT, MALAT-1, CARMEN and XIST in cardiac tissue of rats of different ages.
Materials & **Methods:** Three groups of Wistar male rats were studied: A (n = 6; age = 248+0.00 days-young), B (n = 13; age = 413.8+8.20 days-adult), C (n = 10; age = 597.6+10.3 days-old). Total RNA was extracted from cardiac tissue samples and analyzed by Real-Time PCR. Echocardiographic and biochemical evaluation was performed and histological analyses completed the study.
Results: A significant increase of ANP and BNP mRNA levels was observed only in C and CNP remained in a steady-state in B and C groups, while ET-1mRNA levels increased gradually and significantly as a function of age (A = 0.46+0.15; B = 1.50+0.33; C = 2.01+0.98; p = 0.013 A vs. B; p = 0.018 A vs. C). The three NP receptor subtypes did not show statistically significant differences between the groups studied. Regarding ET-1 receptors, ET-A expression levels were statistically lower in Group B than A (p = 0.04) while ET-B were similar in all the three groups studied. The ADM showed a trend opposite to that of the other peptides studied, decreasing significantly as a function of age (A = 1.46+0.36; B = 0.64+0.17; C = 0.61+0.10; p = 0.04 A vs. B; p = 0.05 A vs. C) and presenting a counter-regulation of its main receptor complex CALR and RAMP-2. The analyzed lncRNAs showed decreased expression levels as a function of age reaching levels of significance in most cases (CARMEN: p = 0.036 B vs. C; MIAT: p = 0.005 B vs. C; MALAT-1: p = 0.0004A vs. B and C) except for XIST. ADM and lncRNA trend suggests that the animals are subjected a "healthy aging" as also confirmed by histological analysis that highlights a slight hypertrophy of cardiomyocytes and an increase in the expression of collagen fibers, a direct and non-pathological consequence of aging. Several significant correlations were observed between the analyzed genes and applying a multivariate logistic regression analysis, only LnANP (p = 0.003) and LnADM (p = 0.023) resulted significantly associated with aging. **Conclusions:** The results obtained identify, for the first time, ADM and ANP as independent aging markers. The study of transcriptional levels of both coding and non-coding RNAs plays a key role in better understanding the molecular mechanisms at the basis of the process, underlining the importance of a multi-label biomolecular approach in the evaluation of aging.

P1990
Reciprocal regulation of GRK2 and bradykinin receptor stimulation modulate Ca2+ intracellular level and permeability in endothelial cells: Role in RAAS antagonist induced angioedema.

M Ciccarelli[1]; J Gambardella[1]; D Sorriento[2]; M Bova[2]; S Loffredo[2]; A Fiordelisi[2]; G Iaccarino[1]
[1]University of Salerno, Salerno, Italy; *[2]"Federico II" University of Naples - Dept of Advanced Biomedical Sciences, Naples, Italy*

Background: Bradykinin (BK) accumulation represents the most frequent cause of reduced compliance to ACE inhibitors in Heart Failure, due to the multiple effects on the endothelium mediators through the Gq protein-coupled receptors B1 and B2,. The G protein-coupled receptor kinase GRK2 can modulate B1 and B2 receptors through desensitization.
Purpose: To evaluate level of GRK2 in peripheral blood mononuclear cells (PBMC) from patients with known history of ACE inhibitors adverse events and to verify the role of GRK2 in regulating endothelial functions in response to BK.
Methods: GRK2 expression levels were assessed in PBMC from patients with or without clinical history of angioedema. The regulation of GRK2 expression and subcellular localization to BK (3nM) was assessed in bovine aortic endothelial cells (BAEC). GRK2 degradation pattern in response to BK, were evaluated by interaction with mdm2 and GRK2 ubiquitination. In the same cells, a specific HJ-loop derived peptide inhibitor of GRK2, we evaluated: BK induced Ca2+ accumulation (Fluo4 AM), NO production (DAF-FM Diacetate), and cell permeability (Millipore).
Results: Patients with history of angioedema show reduced protein level of GRK2 but increased mRNA levels respect to controls. In BAEC. 5 min BK stimulation increases GRK2 levels, in several cellular compartments (Membrane, Mitochondria, and cytosol); at 15 minutes GRK2 returns to baseline levels. BK-induced GRK2 accumulation is dependent upon reduced GRK2 ubiquitination by interaction between GRK2 and mdm2. BK causes Ca2+ cytosolic accumulation which is enhanced by inhibition of the GRK2 by KRXC7 (CTRL: 50,4% vs KRXC7: 72% of fluorescence intensity over basal). Similarly, GRK2 inhibition by pre-treatment for 1 hour with KRX-C7, enhances BKA –dependent in vitro production of NO (BKA+KRX: 20 vs BKA: 10; fold of increase over basal) and permeability of endothelial cells (BKA+KRX: 40% vs BKA: 24%; increase over basal).
Conclusions: BK induces GRK2 intracellular accumulation, which in turn desensitizes BK receptors. Proteasome plays a key role in this negative feedback loop, by acutely regulating GRK2 cellular levels. Inhibition of GRK2 affects endothelial response to BKA, enhancing calcium accumulation, NO production, and cell permeability. Moreover in the context of a personalized medicine, we propose that evaluation of GRK2 levels (protein or mRNA) is a potential tool to identify patients at risk of angioedema with RAAS antagonists.

P1991
Aging and biomarkers: evaluation of opn/mirna-181a transcriptional levels in rats of different age ranges

C Salvadori[1]; M Cabiati[1]; AL Sapio[1]; S Burchielli[2]; C Caselli[1]; L Carlucci[3]; L Mattii[4]; L Sabatino[1]; S Del Ry[1]
[1]Institute of Clinical Physiology of CNR, Pisa, Italy; *[2]Gabriele Monasterio Foundation, Pisa, Italy*; *[3]Sant'Anna School of Advanced Studies, Institute of Life Sciences, Scuola Superiore Sant'Anna, Pisa, Italy*; *[4]University of Pisa, Pisa, Italy*

Background: It is well-known that human aging is attended by a low-grade systemic in?ammation and the Osteopontin (OPN), an extracellular matrix glycoprotein that plays an important role as cytokine during inflammation, has recently identified as a hepatic damage marker but which is its role in aging is not yet defined. Moreover, the aging process seems to be associated with several non-coding RNA (miRNA and lncRNA).
Purpose: To evaluate, in liver tissue of rats of different age ranges, the expression variations of OPN and miRNA-181a, the transcriptional profiling of the lncRNA GAS-5/miRNA-222 axis and the lncRNA NEAT-1. In addition, to monitoring the senescence process, the telomere shortening and the expression of TERT and TERC mRNA were also measured.
Materials & Methods: Three groups of Wistar male rats were studied: A (n = 6; age = 248+0.00 days-young), B (n = 13; age = 413.8+8.20 days-adult), C (n = 10; age = 597.6+10.3 days-old). Total RNA and miRNA were simultaneously extracted from liver tissue samples and analyzed by Real-Time PCR. Ultrasound and biochemical evaluation were performed in all rats as well as the histological analysis of the hepatic tissues.

Results: The OPN mRNA resulted lower in C (0.65+0.12) with respect to A (1.07+0.12) and B (1.32+0.26; p = 0.03 B vs. C) while the miRNA-181a expression resulted significantly increased as a function of age (A = 0.72+0.29; B = 1.09+0.08; C = 1.33+0.24; p = 0.03 A vs. B; p = 0.02 A vs. C). An increasing of miRNA-222 expression as a function of age (A = 0.9+2+0.22; B = 1.54+0.16; C = 1.94+0.21; p = 0.02 A vs. B; p = 0.003 A vs. C) in parallel with a decreasing of lncRNA GAS-5 expression in young and old rats but not in the adult ones (A = 0.01+0.003; B = 1.89+0.19; C = 0.07+0.01; p <0.001) was also observed while NEAT-1resulted: A = 0.22+0.04; B = 0.24+0.05; C = 0.49+0.09; p = 0.02 B vs. C. A positive correlation was observed between miRNA-181a and miRNA-222 (r = 0.73; p <0.0001). The hepatic ultrasound analysis revealed areas of hyperechogenicity distributed as a function of age. The study of telomeres highlighted a significant shortening of the telomeres as a function of age while the two subunits TERT and TERC expressions showing an opposite trend.
Conclusions: The results showed an indirect back regulation of the OPN miRNA-181a mediated, underlying their role as potential successful markers of inflamm-aging. The different trend observed for lncGAS-5 and miRNA-222 underlying a mutual regulatory feedback between the two targets. The balance between lncGAS-5 and NEAT-1 expression levels indicates the absence of neoplastic formations as also confirmed by the echographic and histological analysis. Although further studies are needed to understand the OPN and non-coding RNA role in the molecular process at the base of aging, this work provides a valid starting point to better understand the physiopathological changes occurring during aging process pinpointing in the OPN/miRNA-181a axis a potential marker of inflammation during aging.

P1992

Association of GSTM1, GSTP1 and GSTT1 polymorphisms with risk of chronic heart failure

N Natasa Jankovic[1]; D Simic[1]; V Coric[2]; S Suvakov[2]
[1]Clinical Center of Serbia, Clinic for Cardiology, Belgrade, Serbia; *[2]Institute for Medical Biochemistry, Belgrade, Serbia*

Background : Oxidative stress, due to an excess of reactive oxygen species (ROS), plays a role in the development and progression of heart failure (HF). 8-hydroxy-2'-deoxyguanosine (8-OHdG) is a marker of oxidative DNA damage caused by ROS. Genes encoding for glutathione transferases (GST) contain several polymorphic variants that may affect their role in protecting cellular DNA against oxidative damage, through altered protein levels or function.
Aim: The aim of this study was to investigate the role of certain GST polymorphisms in the risk of HF development, as well as the association of different GST variants with the level of 8-OHdG among those patients.
Material and methods : GSTM1, GSTT1 and GSTP1 genotypes were determined in 116 patients (100 male, 16 female) with chronic heart failure. The criterion for admission was left ventricular ejection fraction (LVEF) <45%. 166 healthy controls served as a control group. GST genetic polymorphisms were determined by multiplex PCR or qPCR. Byproducts of DNA oxidative damage (8-OHdG) were determined by ELISA method.
Results: The frequency of GSTM1-null genotype was higher in patients with HF (58%) compared to controls (49%), with an adjusted OR of 0.73 (95% CI: 0.33-1.64). Moreover, the GSTT1-null genotype enhanced the risk of HF compared to the GSTT1-active genotype (OR:3.08; 95%CI: 1.23-7.73, p = 0.016).The association of GSTM1-null genotype and level of 8-OHdG was statistically significant (p = 0.013). HF patients with GSTT1-null genotype didn't have statistically higher level of 8-OHdG compared to the HF patients with GSTT1-active genotype (p>0.05). There was no difference in serum 8-OHdG levels with regard to different GSTP1 genotype. On the other hand, HF patients with combined GSTM1-active/GSTP1-referent genotype had statistically higher level of 8-OHdG compared to the carriers of GSTM1-null/GSTP1-variant genotype (p = 0.011).
Conclusion: Although GSTM1 and GSTP1 polymorphisms have not been statistically significant associated with HF risk, GSTT1 polymorphisms was associated with risk of chronic heart failure and GST genotype status was shown to influence the level of 8-OHdG.

P1993

Pharmacological inhibition of sphingosine 1-phosphate receptor 2 (S1pr2) enhances angiogenesis and improves cardiac function after myocardial infarction (MI)

L Zhang[1]; XL Li[1]; YS Kuang[1]; HM Fan[1]; YZ Zhang[1]
[1]Tongji University School of Medicine, 1. Research Center for Translational Medicine, Shanghai East Hospital, Shanghai, China People's Republic of

On behalf of: Research Center for Translational Medicine, Shanghai East Hospital, Shanghai, People's Republic of China

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Background and Purpose: Sphingosine 1-phosphate (S1P) is a lipid metabolite and a ligand of five G protein-coupled cell surface receptors S1pr1 to S1pr5. Our preliminary study showed that S1pr1 and S1pr2 were highly expressed in mouse hearts. We have shown that activation of S1pr1 enhanced arteriole formation and improved vascular remodeling after myocardial infarction. However, it is unknown whether S1P/S1pr2 signaling controls cardiac remodeling after myocardial infarction. We aimed to investigate the effect of pharmacological inhibition of S1pr2 by JTE013 in a mouse model of acute myocardial infarction.
Methods: We performed left anterior descending artery (LAD) ligation to induce acute myocardial infarction in mice. We treated operated mice with 5 mg/kg/day S1pr2 inhibitor, JTE013, or placebo (DMSO) i.p., respectively, for 4 weeks. We performed echocardiography to investigate cardiac function. We also carried out histological analysis to study vascular remodeling in MI model.
Results: Echocardiography showed that cardiac function was significantly reduced in MI mice (ejection fraction (EF): 76.15 ± 1.65 % Sham group vs. 50.78 ± 4.85 % MI-DMSO group. P < 0.05). S1pr2 inhibitor, JTE013, significantly improved cardiac function 4 weeks after myocardial infarction (EF: 50.78 ± 4.85 % MI-DMSO group vs. 64.67 ± 2.64 % MI-JTE013 group. P < 0.05). Mason's trichrome staining showed that JTE013 treatment significantly reduced the infarct size: 21.25 ± 1.02 (%) MI-DMSO group vs. 18.31 ± 1.70 (%) MI-JTE013 group. P < 0.05). Our further isolectin B4 (iB4) antibody staining showed that capillary density in peri-infarct myocardium was remarkably more in MI-JTE013 group compared to MI-DMSO group. Moreover, co-staining of iB4 antibody and alpha smooth muscle actin (alpha-SMA) antibody showed that arteriole density in peri-infarct myocardium was significantly increased in MI-JTE013 group compared to MI-DMSO group.
Conclusions: Our results demonstrated that inhibition of S1pr2 boosted post-MI angiogenesis and vascular maturation, and thus improved vascular remodeling after myocardial infarction, suggesting that S1P/S1pr2 signaling aggravates post-MI cardiac remodeling, which is contrary to the beneficial effect of S1P/S1pr1 signaling on post-MI cardiac remodeling. Our investigations indicate that pharmacological modulation of S1P/S1PR1 and S1P/S1PR2 signaling might improve cardiac recovery after myocardial infarction.

P1994

Hypotension after coronary artery bypass grafting can be associated with endogenous ACE inhibition caused by cell free haemoglobin

A Csongradi[1]; IM Siket[1]; T Csipo[1]; A Toth[1]; T Szerafin[2]; Z Csanadi[3]; I Edes[3]; Z Papp[1]; M Fagyas[1]
[1]University of Debrecen, Faculty of Medicine, Department of Cardiology, Division of Clinical Physiology, Debrecen, Hungary; *[2]University of Debrecen, Faculty of Medicine, Department of Cardiology, Division of Cardiac Surgery, Debrecen, Hungary*; *[3]University of Debrecen, Faculty of Medicine, Department of Cardiology, Debrecen, Hungary*

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Background: A common intra-, and postoperative complication in patients undergoing coronary artery bypass graft (CABG) surgery is hypotension. During prolonged cardiopulmonary bypass (CPB) red blood cells are often damaged causing intravascular haemolysis therefore increasing the level of circulating plasma haemoglobin. We hypothesized that cell free haemoglobin can decrease the activity of the angiotensin converting enzyme (ACE) thereby contributing to the reduction of systemic blood pressure during and after CPB.
Purpose: In this study, we examined the effects of free haemoglobin on ACE-activities of sera and recombinant ACE, as well as on tissue bound ACE using saphenous vein rings.
Methods: Serum derived and recombinant ACE-activities were measured by a fluorescent kinetic assay. The inhibition of tissue ACE-activity was tested in unused saphenous vein rings (n = 20) that remained after CABG surgeries (n = 14) using an isometric myograph system.
Results: We found that free haemoglobin decreases ACE-activities in the serum and of recombinant ACE (IC50= 1.7 nM; 1.3 nM, respectively) in vitro. The mechanism of haemoglobin dependent inhibition was identified by Lineweaver-Burk double reciprocal plot as a non-competitive inhibition (common X-axis intersection point). During saphenous vein experiments where contractile responses elicited by angiotensin I in the presence (n = 10 rings) and absence of 0.5 g/L haemoglobin (n = 10 rings) were followed, contractile force was significantly decreased in the haemoglobin treated group in contrast to the control group (relative strength compared to norephinephrine: 39.49 ± 7.14%, 79.25 ± 5.70%; P = 0.0004, respectively). Significant differences between the kinetics of the contractions (control: 0.17 ± 0.04 mN/sec; 0.15 ± .04 mN/sec, P = 0.6849) and desensitizations (control: 5.10 ± 1.04 μN/sec; 6.48 ± 0.96 μN/sec, P = 0.3445) were not found.

Conclusions: : Our findings illustrate haemoglobin as non-competitive inhibitor of the ACE enzyme. In addition, we propose that free haemoglobin can suppress tissue ACE-activity thereby contributing to the development of hypotension during and after CABG in association with haemolysis.

P1995

Influence of age and cardiovascular risk factors on digital vascular function in Asians: a community-based study

S L Shir Lynn Lim[1]; SP Chan[2]; TP Ng[3]; CSP Lam[4]; AM Richards[5]; LH Ling[1]
[1]National University Heart Centre, Department of Cardiology, Singapore, Singapore; *[2]National University of Singapore, Department of Medicine, Singapore, Singapore*; *[3]National University Health System, Singapore, Singapore*; *[4]National Heart Centre Singapore, Department of Cardiology, Singapore, Singapore*; *[5]National University Heart Centre, Cardiovascular Research Institute, Singapore, Singapore*

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Background: The digital reactive hyperemia index (RHI) reflects endothelial function. Studies in Western populations have shown a counter-intuitive positive association of RHI with age.
Purpose: We assessed the clinical correlates of RHI in a multi-ethnic Asian population.
Method: We prospectively studied 988 adult Singaporeans in the community without overt cardiac disease. RHI was measured with the EndoPAT device. A generalized structural equation model was used to assess the association between RHI, age and cardiovascular risk factors (CVRF).
Results (see Table)
Mean RHI was 2.19 ± 0.56; 158 subjects had an "abnormal" RHI (<1.67). Age, Indian ethnicity and growth differentiation factor (GDF) 15 were univariately associated with RHI, but only age (p = 0.008) and Indian ethnicity (p = 0.011) were independently associated. While RHI increased with age, it declined after age 70. This inflection point was absent in those without hypertension, diabetes or = stage 3 chronic kidney disease. Age interacted significantly with CVRF - subjects older than 70 with = 1 of these 3 CVRF had lower RHI compared to those without (coefficient: -0.41, p = 0.001) and non-significantly higher GDF-15 (1396 vs. 1092 ng/L, p = 0.16). The interaction was observed in men (p = 0.001) but not women (p = 0.16).
Conclusion: Age was positively associated with RHI in an Asian population. The interaction between CVRF and age suggests an exhaustion of digital vasodilatory reserve to ischemic stress in older individuals, primarily men, with these comorbidities.

Clinical characteristics of subjects

	Mean±SD / n (%)	Univariate Regression Analysis Coefficient (p-value)
Age (years)	57.92±10.31	0.01 (0.001*)
Male sex	479 (48.5%)	0.03 (0.454)
Ethnicity -Chinese -Malays -Indians -Other	725 (73.4%) 180 (18.2%) 76 (7.7%) 7 (0.7%)	Reference -0.07 (0.114) -0.22 (<0.001*) -0.30 (0.150)
BMI (kg/m^2)	24.8±4.04	-0.01 (0.166)
Hypertension (%)	284 (28.7%)	0.02 (0.571)
Diabetes mellitus (%)	85 (8.6)	0.05 (0.449)
Smoking (%)	159 (16.1%)	0.05 (0.252)
LDL-cholesterol level (mg/dL)	125.06±34.38	0.00 (0.098)
Renal function (%) -eGFR≥60 ml/min/1.73m^2 -eGFR < 60ml/min/1.73m^2	933 (94.4%) 27 (2.7%)	Reference -0.04 (0.688)
GDF 15 (pg/ml)	734.55±498.09	0.11 (0.002) ?

*Significant at 5% in multiple regression model Abbreviations: BMI, body mass index; LDL, low-density lipoprotein; eGFR, estimated glomerular filtration rate; GDF-15, growth differentiation factor 15

P1996

Association between NT-proBNP and arterial stiffness in young healthy adults.

E Evgeniy Borisov[1]; A Alexandrova[1]; Y Orlova[1]; I Strazhesko[1]
[1]M.V. Lomonosov Moscow State University, Moscow, Russian Federation

Introduction:
Elevated serum levels of N-terminal fragment of B-type natriuretic peptide (NT-proBNP) and increased arterial stiffness, measured with pulse wave velocity (PWV), are well-known risk factors for future cardiovascular events.
The association between N-terminal pro-B type natriuretic peptide (NT-proBNP) and arterial stiffness is still unclear, especially in young healthy people without hypertension. The aim of this study was to investigate the association between NT-proBNP and arterial stiffness in young apparently healthy adults.
Material and Methods: We investigated 282 healthy young adults, mean age 18,5 ± 1,7 years, 47% male. NT-proBNP, waist circumference, body mass index (BMI), fasting plasma glucose, insulin resistance (HOMA-IR) and lipid profile were measured. PWV was measured with ambulatory blood pressure monitoring device BPLab Vasotens (BPLab, Russia) results. PWV was 9,4 ± 1,4 m/s (M+ SD), NT-proBNP level was 58, 61+2,39 pg/ml (M+m). Multivariate regression analysis showed positive association between PWV and NT-proBNP, BMI, total cholesterol and HOMA-IR (see table 1).
Conclusions: Arterial stiffness appeared to be associated with serum NT-proBNP level even in the young people with normal blood pressure.

Table 1.

Predictor	β	Standart error	p
BMI	0,097	0,040	0,017
Total cholesterol	0,508	0,228	0,029
HOMA-IR	0,371	0,108	0,001
NT-proBNP	0,008	0,005	0,097

P1997

Calmodulin-myosin interaction: a novel interaction regulating muscle function

V Vasco Sequeira[1]; S Conijn[1]; C Ottenheijm[1]; J Van Der Velden[1]; C Johnson[2]
[1]VU University Medical Center, Department of Physiology, Amsterdam, Netherlands; *[2]Vanderbilt University, Clinical Pharmacology, Nashville, United States of America*

Purpose: Calmodulin (CaM) is a Ca2+-binding protein that is essential for Ca2+-dependent regulation of cardiac rythm. Consequently, CaM-associated interacting partners include Ca2+-, Na+- and K+-channels, and ryanodine receptors. Perhaps the most surprising, no direct interacting-partner of CaM has been identified at the myofilaments, considering that myofilament volume occupies ¯70% of human myocardium. Here we demonstrate the novel interaction of CaM to cardiac myosin and how their interaction affects myofilament function.
Methods: In silico recognition of apo- (no Ca2+) and Ca2+-CaM binding to a specific sequence of human cardiac myosin was conducted and validated by Nuclear Magnetic Resonance (NMR) spectroscopy (1 μM CaM:5 μM myosin peptide). To assess the functional effects mediated by apo- and Ca2+-CaM in myofilament regulation of myosin, exogenous 1 μM CaM was added to human membrane-permeabilized cardiomyocytes, either in the presence of ADP (but no Ca2+) or Ca2+ (but no ADP), respectively. Furthermore, X-ray fiber diffraction of membrane-permeabilized rat skeletal soleous muscle (mostly cardiac myosin) was used to detect conformational changes to myosin (at the thick-filament region) mediated by addition of 1 μM CaM. Lastly, mass spectrometry of human myocardium was performed to assess CaM:myosin stoichiometry in vivo.
Results: The first IQ-motif region of myosin, localized to the myosin neck (where myosin light chains interact), was recognized as a potential binding region for CaM. NMR demonstrated that apo-CaM promoted conformational changes to the myosin peptide, which were much larger when Ca2+ was present. Human membrane-permeabilized cardiomyocytes showed increased myofilament force production in the presence of apo-CaM, which were exacerbated in the presence of Ca2+-CaM. The latter was shown to coincide with increased structural changes of myosin to the thick-filament, mediated by apo- and Ca2+-CaM, with increased myosin approximation towards actin, as evidence by X-ray fiber diffraction. Mass spectrometry revealed a 1 μM:22 μM ratio of CaM to myosin, consistent with a total 6 μM CaM to 150 μM myosin pool in human myocardium.
Conclusions: Here we provide structural evidence that supports CaM interaction to cardiac myosin. Notably, this interaction mediates conformational changes in myosin that re-positions its head closer to actin with accompanied increased force generation of human cardiomyocytes. Based on stoichiometry levels found in human

myocardium, cardiomyocte pool of CaM is sufficient to regulate cardiomyocte function in vivo.

Basic Science - Vascular Diseases

P1998

A novel intronic mutation in the fibrillin 1 gene causes pseudoexon inclusion and premature termination in Marfan syndrome with aortic dilatation

M Torrado[1]; E Maneiro[2]; JP Trujillo-Quintero[2]; A Evangelista[3]; AT Mikhailov[1]; L Monserrat[2]
[1]University of A Coruña, Institute of Health Sciences, A Coruña, Spain; [2]Health in Code, A Coruña, Spain; [3]University Hospital Vall d'Hebron, Cardiology Department, Barcelona, Spain

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Background: Mutations in the fibrillin 1 (FBN1) gene are typically associated with Marfan syndrome (MFS), suggesting that genetic testing would be useful for timely diagnosis to prevent life-threatening cardiovascular complications such as aortic dilation/dissection. However, for a proportion of patients, mutation analysis restricted to FBN1 exons fails to identify the genetic cause of MFS.
Purpose: To specifically assess the presence of pathogenic intronic variants of the FBN1 gene in a MFS patient with aortic dilatation.
Methods: DNA from patient saliva was used for target enriched next generation sequencing (NGS) for 34000 bases of FBN1 encompassing 66 exons along with their flanking (200 bp) intron regions. In addition, other 34 genes related to aortic diseases were NGS analyzed. Five independent algorithms for splice signal detection were used to annotate the variants for functionality. Predicted aberrant splicing variants were functionally characterized by minigene splicing assays coupled with RT-PCR and Western blot analyses of the splicing patterns of mutant versus consensus FBN1 constructs after transfection into HeLa and COS-7 cells.
Results: The NGS screening allowed identification of eight variants of FBN1 including seven variants localized in intronic non-coding regions and one synonymous exonic variant which does not influence the amino acid structure of the protein. The identified variants, with the exception of the heterozygous c.2678-15C?A, have been previously described and classified as benign or of uncertain significance. The novel c.2678-15C>A variant was not identified in either healthy relatives or individuals with phenotypes other than MFS who referred to our laboratory for NGS analysis. The computational predictions showed that the heterozygous c.2678-15C?A intronic variant might influence the splicing process by differentially affecting canonical versus cryptic slice site utilization within intron 22 of the FBN1 gene. RT-PCR and Western blot analyses, using FBN1 minigenes transfected into HeLa and COS-7 cells, revealed that the c.2678-15C?A variant disrupts normal splicing of intron 22 leading to aberrant pseudoexon inclusion, frameshift and premature termination codon. The aberrantly spliced transcripts are resistant to nonsense-mediated decay and express unstable truncated proteins, which could only be detected upon proteasome inhibition. Our NGS analysis did not reveal any relevant change in a panel of 34 additional genes related to aortic diseases, supporting the assumption that the c.2678-15C>A variant identified in the FBN1 gene of the investigated MFS patient is the likely cause of the clinical manifestations.
Conclusions: We report a novel variant in the FBN1 gene as pathogenic variant for MFS complicated by aorta dilation - a finding that further expands on the genetic basis of aortic pathology.

P1999

The molecular regulation of RIP3 in necroptosis of vascular smooth muscle cells by cyclic stretch

WP Wen Pin Cheng[1]
[1]Shin Kong Wu Ho-Su Memorial Hospital, Department of Medical Education and Research, Taipei, Taiwan ROC

Funding Acknowledgements: This study was supported, in part, by the Ministry of Science and Technology, Taipei, Taiwan.

Background: Programmed necrosis also termed necroptosis has been reported was responsible for atherosclerosis. In the process of necroptosis, receptor-interacting protein 3 (RIP3) appears to play a major role to regulate the necroptosis.
Purpose: How cyclic stretch affects the regulation of RIP3 in vascular smooth muscle cells (VSMCs) during necroptosis is not fully understood. This study is aim to clarify the molecular regulation of RIP3 under cyclic stretch in VSMCs necroptosis.
Methods: Rat VSMCs grown on a flexible membrane base were stretched by vacuum to 20% of maximum elongation, at 60 cycles/min.
Results: Cyclic stretch markedly enhanced RIP3 protein and mRNA expression. Addition of c-jun N-terminal kinase (JNK) inhibitor SP600125 and JNK siRNA before cyclic stretch inhibited the protein expression of RIP3. Cyclic stretch induced the DNA-binding activity of signal transducer and activator of transcription 1 (STAT1) by electrophoretic mobility shift assay. SP600125, JNK siRNA and interferon-gamma (IFN-gamma) antibody abolished the binding activity induced by stretch. RIP3 promoter activity was induced by cyclic stretch and RIP3-mut plasmid, SP600125 and IFN-gamma antibody attenuated the RIP3 promoter activity induced by stretch. Exogenous administration of IFN-gamma recombinant protein to the non-stretched VSMCs increased RIP3 protein expression similar to that seen after stretch. Addition of RIP3 siRNA reversed the VSMCs necroptosis induced by cyclic stretch.
Conclusion: Our results indicated that cyclic stretch induced RIP3 expression in VSMCs necroptosis. The stretch-induced RIP3 is through by IFN-gamma, JNK and STAT1 pathway.

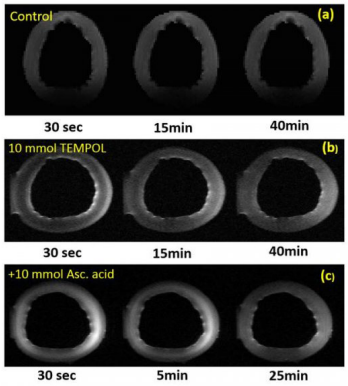
P2000

High-Resolution and Semidynamic Vessel Wall Imaging Kinetics obtained from Stable Radical MRI in ex-vivo Porcine Aorta

M Pali[1]; M Terekhov[1]; C Wittke[1]; N Wagner[2]; A Schroeder[3]; H Walles[3]; S Erguen[2]; A Zernecke-Madsen[4]; LM Schreiber[1]
[1]University Hospital , Chair of Cellular and Molecular Imaging, Comprehensive Heart Failure Center (CHFC), Wuerzburg, Germany; [2]University Wuerzburg, Institute of Anatomy and Cell Biology, Wuerzburg, Germany; [3]Fraunhofer Institute for Silicate Research, Translational Center 'Regenerative Therapies' (TLC-RT), Wuerzburg, Germany; [4]University Hospital, Institute for Experimental Biomedicine II, Wuerzburg, Germany

Funding Acknowledgements: Financial support was obtained from the German Ministry of Education and Research (BMBF) under grant#01E1O1504.

Introduction: Excessive production of Reactive Oxygen Species (ROS) leads to homeostatic breakdown followed by inflammation and cell injury. Increased local ROS level is considered a marker of early stage of atherosclerosis. Nitroxides can react with ROS with conversion from paramagnetic to diamagnetic species and, thus, changing local T1-contrast accessible by MR-imaging. The redox-sensitive properties were explored in organs mostly in spectroscopic based studies due to relatively short time frame available before its reduction by endogenous ROS. MRI of vessel wall using nitroxide radicals might offer a non-invasive method of analyzing both underlying anatomical structure and pathophysiological changes caused by ROS-production in vasculature.
Purpose: We established a protocol for high spatial and temporal resolution dynamic MRI of porcine aorta ex-vivo to visualize: 1) The distribution and diffusion of TEMPOL inside the vessel wall; 2) Kinetics of generated T1-contrast due to the conversion of TEMPOL to hydroxyamide stimulated by exogenously applied ascorbic acid to model of ROS overproduction.
Methods: MRI measurements of porcine aorta were performed on a 7T Bruker preclinical MRI system using a TX/RX 1H-cryoprobe. Excised aortic tissue was kept in isotonic saline solution and MRI scans were performed at 2, 24, 48 and 72 hours post excision. 5mm thick rings of aorta were prepared just before the treatment with low (10 or 30mM) dose of TEMPOL. Subsequent treatment of TEMPOL-perfused probes by 5 to 20mM ascorbic acid demonstrated the possibility of visualizing change of the redox of TEMPOL inside the vascular wall. The incubation times were 180 sec and 30 sec at 37°C for TEMPOL and ascorbic acid, respectively. The subsequent measurements were performed at ambient temperature. Protocols for maximizing spatial and temporal resolution were optimized by adjustment parameters of T1-weighted gradient (GRE) and spin-echo (RARE) sequences depending on time passed after excision and tissue treatment.
Results: Fig. 1a shows an untreated aortic ring with native T1 tissue contrast and with 100μm in-plane spatial resolution. Exposure to TEMPOL initially results in rapid accumulation on the intima and adventitia (Fig. 1b) and concentration-gradient driven diffusion through all aortic layers. Subsequent treatment with ascorbic acid results in conversion of TEMPOL to diamagnetic hydroxyamide clearly observed dynamically by significant T1-contrast reduction in images as ascorbic acid diffuses through the vascular tissue layers (Fig 1c).
Conclusion: High-resolution imaging protocol with 100μm spatial and 30 sec per image temporal resolution was established in ex-vivo porcine aorta using GRE and RARE pulse sequences. Successful proof-of-principle imaging of stable nitroxides as a T1 redox-sensitive contrast agent in porcine aorta provides the method for future in-vivo ROS imaging in vascular tissue.
Organizational support by David Lohr is appreciated.



Basic Science - Other

P2001

Increased adipocyte formation in STAT3-knockout hearts can be prevented by EPO administration

E Elisabeth Stelling[1]; M Ricke-Hoch[1]; M Scherr[2]; B Stapel[1]; J-L Balligand[3]; S Erschow[1]; D Hilfiker-Kleiner[1]

[1]Hannover Medical School, Department of Cardiology and Angiology, Hannover, Germany; *[2]Hannover Medical School, Department of Hematology, Oncology and Stem Cell Transplantation, Hannover, Germany*; *[3]Universite Catholique de Louvain, Institut de Recherche Experimentale et Clinique (IREC), Pole of Pharmacology and Therapeutics (FATH), Brussels, Belgium*

Funding Acknowledgements: DFG, Rebirth

Purpose: STAT3-dependent secreted factors like erythropoietin (EPO) have an influence on the differentiation potential of the endogenous Sca-1+-cardiac progenitor cell (CPC) population. Male mice with a cardiomyocyte-restricted knockout of STAT3 (aMHC-Cretg/+; STAT3flox/flox, CKO) develop spontaneous age-related heart failure in association with reduced cardiac EPO expression and subsequent impaired endothelial differentiation of CPCs and cardiac capillary density. Here, we evaluated whether reduced cardiac EPO levels in CKO mice promote differentiation of CPCs into adipocytes as increased cardiac fat deposition is frequently observed in failing hearts.

Methods and Results: HL-1 cardiomyocytes with a lentiviral STAT3-knockdown (STAT3-KD) showed reduced EPO expression. Cultivation of the preadipocyte cell line 3T3-L1 with conditioned media from STAT3-KD HL-1 cells significantly enhanced adipocyte formation compared to 3T3-L1 cells cultivated with conditioned media from control cells as measured by oil red absorbance, increased mRNA levels of adipocyte markers FABP4 and AdipoR1 and decreased mRNA levels of the preadipocyte marker Pref-1. The enhanced adipocyte differentiation could be prevented by recombinant mouse EPO (rmEPO) administration (10ng/ml).

CPC clones expanded from single cells were able to differentiate into adipocytes confirming that CPCs have the adipocyte differentiation potential. CPCs from WT (WT-CPC) and from CKO mice (CKO-CPC) were immunomagnetically isolated. After 4 weeks of cultivation a 2-fold increase in adipocytes formation was observed in CPC cultures isolated from CKO hearts (oil red staining, compared to WT-CPCs, *P <0.05). This was associated with increased mRNA levels of adipocyte markers FABP4 (+32%, *P <0.05) and OLR1 (+126%, *P <0.05) in CKO-CPCs.

EPO receptor expression was similar in freshly isolated CPCs from WT and CKO hearts. Addition of rmEPO during cultivation of CKO-CPCs prevented their enhanced adipocyte formation.

Hearts of 6 months old CKO mice displayed increased numbers of adipocytes as determined by adipogenesis assay (2.5-fold compared to WT, *P <0.01). Treatment of CKO mice with the EPO derivative CERA (Roche) in a non-hematocrit influencing dosage (3mg/kgBW) starting at 3 months of age and continued for 3 months completely prevented adipocyte formation in CKO hearts. CERA treatment delayed heart failure in CKO mice but could not prevent it (FS in NaCl-CKO mice at 4 months: 22 ± 9%, FS in CERA-CKO mice: 35 ± 5%, *P <0.05; FS in NaCl-CKO mice at 6 months: 17 ± 5%; FS in CERA-CKO mice: 13 ± 7%, n.s.).

Conclusion: Age related heart failure in CKO mice is associated with enhanced adipocyte differentiation from CPCs. This is in part caused by reduced EPO secretion by STAT3-deficient cardiomyocytes into the cardiac microenvironment. Longterm EPO treatment could prevent enhanced adipocyte formation in hearts of CKO mice and was able to delay but not prevent age-related heart failure in these mice.

Valvular Heart Disease - Pathophysiology and Mechanisms

P2002

Changes in extracellular matrix composition and cell populations parallel aortic valve stenosis progression

A Panzenboeck[1]; J Jakowitsch[1]; R Seitelberger[2]; R Rosenhek[1]; H Baumgartner[1]; IM Lang[1]

[1]Medical University of Vienna, Department of Internal Medicine II, Division of Cardiology, Vienna, Austria; *[2]University Clinics Salzburg, Department of Cardiac Surgery, Salzburg, Austria*

Background: Aortic valve disease is the most frequent valve disease in Western countries, and the third most frequent cause of cardiovascular death. Although aortic valve degeneration, which ultimately results in calcific aortic stenosis, shows similarities to atherosclerotic processes the underlying biological mechanisms are still unclear. In our study we investigated extracellular matrix (ECM) molecules and cellular markers as important components of atherosclerosis in aortic stenosis.

Methods: Aortic valves were collected at aortic valve replacement surgeries and heart transplantations. For sample stratification echocardiographically obtained mean valve gradients (mvg) at the time of surgery were used. RNA expression profiles of healthy (control), as well as sclerotic (mvg = 6 ± 2mmHg, mean ± SD), mildly (mvg = 22 ± 12mmHg), moderately (mvg = 49 ± 16mmHg) and severely stenotic (mvg = 63 ± 15mmHg) aortic valve leaflets (n = 5 per group) were analyzed using an Affymetrix Human Gene 1.0 ST Array. Array results were validated by Real-time PCR utilizing TaqMan probes.

Results: Collagen types I, III, V, XIV, XV and XXI as well as cathepsin S, B, D and K and perlecan showed a valve gradient-dependent increase of expression. Expressions of collagens type Ia1, Ia2, IIIa1 and Va1 and cathepsins S and D showed a significant correlation with stenosis progression (14,5 (9-17) m/sec/year, median(range), p < 0,05). The antiangiogenic ECM molecule chondromodulin was at a low level across the spectrum of mvgs, while VEGF decreased in parallel to increasing mvg. In addition we observed a valve gradient-dependent increase of osteoblast specific genes like CDH11, POSTN, SPARC and SPP1.

Conclusion: Our data demonstrates a shift in ECM production and composition in parallel with aortic valve degeneration. In addition we could show that while angiogenesis is suppressed, genes enhancing ossification and thereby aortic stenosis progression are increased.

Valvular Heart Disease - Epidemiology, Prognosis, Outcome

P2003

Traditional and biomolecular methods in ethiological diagnostics of infective endocarditis

EO Kotova[1]; MA Sorokina[2]; AS Pisaryuk[1]; EA Domonova[3]; JL Karaulova[1]; AS Milto[4]; V S Moiseev[1]

[1]Peoples Friendship University of Russia (PFUR), Moscow, Russian Federation; *[2]M.V. Lomonosov Moscow State University, Moscow, Russian Federation*; *[3]Central Research Institute of Epidemiology, Moscow, Russian Federation*; *[4]City Clinical Hospital No 64, Moscow, Russian Federation*

Background: Identification of etiological agent in blood is an important criterion for diagnostics and successful treatment of infective endocarditis (IE). We suggest using biomolecular methods, such as polymerase chain reaction (PCR) and cycle sequencing reaction.

Objective: Comparison of bacteriological and biomolecular methods in IE diagnostics.

Material: 67 patients with verified IE (DUKE 2009, 2015), hospitalized and treated in city clinical hospital ?64 in Moscow from September 2012 to January 2017. The biological and biomolecular tests were taken simultaneously for all patients. The DNA of S.aureus, Staphylococcus spp. (MRCoNS), Enterobacteriaceae, E.coli, Klebsiella spp., Proteus spp. and others., Streptococcus spp., A.baumanii, K.pneumoniae, P.aeruginosa, E.coli, S.agalactiae, S.pyogenes, Candida (C.albicans, C.glabrata, C.krusei, C.parapsilosis and C.tropicalis), enterococci (including E.faecium, E.faecalis, etc.) was determinted using PCR method.

Results: We studied 67 patients with IE, age median 62 [34-73], 41 (61,2%) male and 36 (38,8%) female. Etiological agents were detected in venous blood of 35 (52,2%) patients via bacteriological method. Types of agent were: Staphylococcus spp. (n = 20, 57,1%), Enterococcus spp. (n = 6, 17,1%), Streptococcus spp. (n = 2, 5,7%), K.pneumoniae (n = 1, 2,9%) and E.coli (n = 1, 2,9%). 32 (47,8%) cases showed no bacteria growth, and polyflora was detected in 5 (14,3%) cases. 45 (67,2%) had positive results of PCR, in 25 out of 35 (71,4%) cases the results of PCR were concordant with bacteriological study, and in 10 out of 35 (28,6%) - discordant. Full discordance of the results was shown in 4 cases: Enterococcus spp. growth was detected by bacteriological method, but PCR method showed DNA of

MRCoNS, Streptococcus spp. (1), Staphylococcus spp. (1), E.coli, Streptococcus spp. (1), S.gallolyticus (1). In two cases there was a wider specter of agents found by PCR method than by traditional method. In 4 cases, traditional method succeed in the detection of growth of S.aureus MSSA (3), E.faecium, K.pneumoniae (1), but PCR did not manage to identify any DNA. Also, we've received positive results of PCR in 14/32 (43,8%) cases with culture negative IE [S.epidermidis, S.haemolyticus (1); Aspergillus spp. (1); S.aureus MSSA (2); P.multocida (1); S.?galactiae, MRCoNS (1); Enterococcus spp. (2); S.constellatus (1); E.coli (1); Staphylococcus spp. (1); C.albicans, S.epidermidis (1); Staphylococcus spp., A.baumanii, E.coli (1); Enterococcus spp., Staphylococcus spp. (1)]. In 18 (26,9%) patients both methods failed to identify the etiological agent.

Conclusion: Via using traditional bacteriological methods, it was possible to verify etiological agent in venous blood for 52,2% of the patients, via biomolecular - for 67,2%, and with the help of both methods - for 73,1% of patients. Currently we've received both concordant and discordant results, which represents the main challenge in etiological diagnostics of IE.

P2004

Incidence and predictors of tricuspid regurgitation determined by 2D and 3D echocardiography after permanent pacemaker insertion

JP Rangel[1]; VB Flores[1]
[1]*Philippine Heart Center, Adult Cardiology, Manila, Philippines*

Funding Acknowledgements: Philippine Heart Center

Background: Tricuspid regurgitation related to permanent pacemaker insertion (PPI) can occur in 25-29% of patients compared to normal controls, with symptoms of right heart failure developing from one day to ten years after PPI. Proposed mechanisms for this include scar formation or thrombus on the leads impairing TV leaflet closure, neoendocardium formation leading to fibroses and adhesions, thrombosis or edema of TV leaftlets, and perforation or laceration of TV leaflets.

Methods: This is a prospective cohort study on 60 patients admitted for PPI from June to December 2017. Baseline clinical, electrocardiographic and echocardiographic parameters were collected. Patients underwent follow-up 2D and 3D echocardiogram with three days and within one to three months after permanent pacemaker insertion to determine any tricuspid regurgitation (TR) or increase in its severity from baseline.

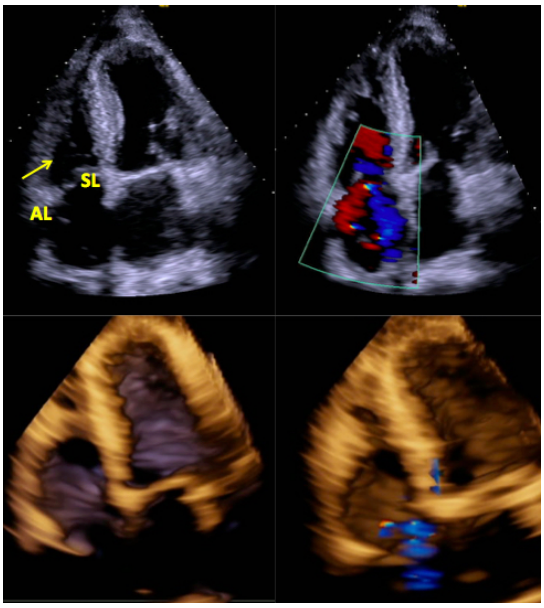
Results: The mean age is 65.2 ± 13.5 years, majority were females (58%) and majority had PPI due to Complete heart block (75%). Three patients developed mild TR and one patient developed moderate TR within three days postoperatively. On follow-up within one to three months postoperatively, thirteen patients (22%) developed moderate TR and one patient developed severe TR due to lead adherence to the tricuspid leaflet. There was no significant difference in the preoperative and postoperative echocardiographic parameters of the right ventricle and right atrium.

Conclusion: The presence of pacemaker-related tricuspid regurgitation is often under diagnosed as the cause of right-sided heart failure. Pacemaker insertion can produce tricuspid regurgitation and may increase the severity of underlying tricuspid regurgitation. Two-dimensional and 3D dimensional echocardiogram can be utilized to determine any postoperative tricuspid regurgitation and determine its mechanism.

Incidence of Tricuspid Regurgitation

Characteristics	Preoperative Frequency (%) (n = 60)	Postoperative - within three days Frequency (%) (n = 60)	Postoperative - within one to three months Frequency (%) (n = 60)
None	15 (25%)	12 (20%)	5 (8%)
Trivial	22 (37%)	22 (37%)	20 (33%)
Mild	23 (38%)	26 (43%)	21 (35%)
Moderate	0	1 (2%)	13 (22%)
Severe	0	0	1 (2%)

Characrteristics: grading of TR severity



2D and 3D Echo with TR

Myocardial Disease - Clinical

P2005

Increased expression toll-like receptor type 2 and type 9 in the myocardium as a marker of chronic active myocarditis

O V Olga Blagova[1]; EA Kogan[1]; N Faisulina[1]; AV Nedostup[1]
[1]*I.M.Sechenov I Moscow State Medical University, Moscow, Russian Federation*

Purpose: to study the expression of some structural proteins, cell proliferation and innate immunity markers in the myocardium to evaluate their diagnostic and possible pathogenetic role in patients with chronic myocarditis.

Methods: in 23 patients (16 males, 52.0 ± 12.4 years) with dilated cardiomyopathy and suspected myocarditis (group 1, n = 10) and other noncoronary diseases (valvular heart disease, hypertrophic cardiomyopathy, chronic pulmonary embolism and atrial myxoma), presumably without myocarditis (group 2, n = 13), were performed endomyocardial biopsy of right ventricle (n = 4), intraoperative biopsy of left ventricle (n = 17), and autopsy (n = 2) with histological, immunohistochemical investigation of vimentin, desmin, c-kit, Ki-67 and toll-like receptors (TLR) 2 and 9 types expression. It was also performed investigation of the viral genome and anti-heart antibodies.

Results: Active / borderline lymphocytic myocarditis diagnosed in all patients of group 1 and 6 patients of group 2 (totally in 9 / 7 patients). Viral genome detected in the blood in 4 patients and in the myocardium in 15 patients, including 5 patients without morphological signs of myocarditis (parvovirus B19 in 11 patients, 6 herpes virus type in 4 patients, herpes simplex virus type 1, 2 in 1 patient, Ebstein-Barr virus in 2 patients, and cytomegalovirus in 1 patient).

There was a strong correlation expression of TLR2 and TLR9 with the presence of morphological signs of active myocarditis in the absence of such correlation with expression of the other studied markers. The expression of TLR2 in borderline myocarditis or without him was 0 [0; 0.75] points versus 1.5 [1; 1.5] points in active myocarditis, the expression of TLR9 was 2 [2; 2] and 4 [3; 4] points respectively ($p < 0,001$). In borderline myocarditis the expression of TLR2 and TLR9 was lower than in patients without myocarditis. It may reflect the death / depletion of cardiomyocytes in the later stages of the disease. It is also found a strong correlation the expression of TLR2 and TLR9 between themselves ($r = 0.824$, $p < 0.001$) and with Ki-67 ($r = -0,531$ and $r = -0,702$, $p < 0.01$). TLR2 expression was significantly correlated with the effectiveness of immunosuppressive therapy of myocarditis in the patients of the group 1 ($r = 0.66$, $p < 0.05$). The patients of group 2 did not receive immunosuppressive therapy. There was no correlation with persistence of virus, titers of anti-heart antibodies, and degree of myocardial dysfunction. Conclusion. Detection of the expression of TLR2 and TLR9 in the myocardium may use as a marker of the presence of myocarditis and its activity. Increased expression of innate immunity markers may reflect one of the mechanisms of genetic predisposition to the development of myocarditis and its severe course and may be a potential target for therapy. Increased expression of TLR2 in patients with

inflammatory cardiomyopathy associated with a better effect of immunosuppressive therapy.

P2006

Correlation of genotypes of genetic polymorphisms of angiotensin converter enzyme and aldosterone synthase with echocardiographic subtypes in hypertrophic cardiomyopathy

A Freitas Pereira Gondar[1]; TCP Gil[1]; ALF Sales[1]; MI Bittencourt[1]; R Pozzan[1]; DC Albuquerque[1]; MB Castier[1]; DA Silva[2]; R Mourilhe-Rocha[1]
[1]State University of Rio de Janeiro, Cardiology , Rio de Janeiro, Brazil; *[2]State University of Rio de Janeiro, Laboratório de Diagnósticos por DNA do Instituto de Biologia Roberto Alcântara Gomes, Rio De Janeiro, Brazil*

Funding Acknowledgements: Fundação de Amparo á Pesquisa do Estado do Rio de Janeiro (FAPERJ)

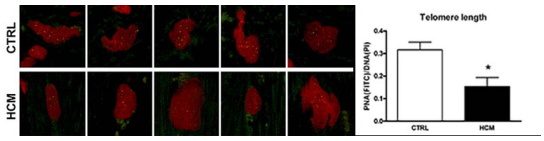
Background: The factors that determine the morphological characteristics and clinical evolution of patients with hypertrophic cardiomyopathy (HCM) are not clarified. It is believed that the genetic polymorphisms of angiotensin converting enzyme (ACE) and aldosterone synthase (CYP11B2) may influence phenotypic expression in individuals with HCM. The aim of this study is to evaluate the frequency of genetic polymorphisms variants ACE and CYP11B2 and to correlate them with echocardiographic subtypes according to the classification proposed by Maron (Am J Cardiol. 1981) in patients with HCM.
Methods: blood samples were collected and transthoracic echocardiography was performed in patients with HCM followed at an outpatient clinic specialized in a university hospital.
Results: Sixty-one patients with a diagnosis of HCM were included. It was observed that the sample was homogeneously composed of individuals of both genders, mean age of 48.41 ± 14.59 years, mostly caucasian (52.5%). The frequency of ACE variants genotypes were DD (24.59%), ID (60.65%), II (14.75%) and CYP11B2 variants genotypes were TT (39.34%), TC (54.09%), CC (6.55%). The most frequent echocardiographic subtypes were type II (31.1%) and III (29.5%). Type I was more frequent in ACE variant genotype II and in CYP11B2 variant genotype TT. Type II was more frequent in the ID genotype and TT. Type III was most observed in DD and CC. Type IV was most observed in II and CC. There was no statistical significance when the correlation of any echocardiographic subtype with the ACE and aldosterone synthase polymorphisms was verified.
Conclusion: the most common ACE variant genotype in our population was ID, while aldosterone polymorphism was TC. There was no correlation of any echocardiographic subtype with the ACE and aldosterone synthase polymorphisms variants. There was a tendency of the CC genotype to be more related to subtype III, the more obstructive subtype.

P2007

Telomere shortening in human hypertrophic cardiomyopathy

C Cristina Chimenti[1]; K Urbanek[2]; R Verardo[3]; C Grande[1]; F Rossi[2]; A Frustaci[1]
[1]Sapienza University of Rome, Rome, Italy; *[2]University of Campania "Luigi Vanvitelli", Department of Experimental Medicine, Section of Pharmacology, Naples, Italy*; *[3]INMI L Spallanzani IRCCS, Rome, Italy*

Background: Telomeres consist of repetitive sequences of DNA at chromosomal ends responsible for maintaining genomic integrity and are considered a marker of biologic aging. Recently, telomere shortening has been associated to different cardiovascular diseases and heart failure.
Purpose: To investigate the role of telomere shortening in patients with hypertrophic cardiomyopathy (HCM).
Methods: Endomyocardial biopsies from 10 patients with HCM (53 ± 5 ys) were analyzed and compared with 10 control hearts (55 ± 7 ys). Telomere length was assessed using fluorescence in-situ hybridization with peptide nucleic acid probe. Senescent cells were identified by the expression of the cell cycle inhibitor p16INK4a and cell death by hairpin 1 and 2. Replication of cardiomyocytes were assessed by Ki67 and MCM5 labeling. Cardiomyocyte cross-sectional area and myocardial fibrosis were also evaluated.
Results: HCM heart showed a reduction in telomere length and an increase in cell death rate compared to control hearts. This was associated with an increased number of p16INK4a positive cardiomyocytes. Cardiomyocyte proliferation was reduced compared to controls. The distribution of myocyte cross-sectional area in HCM patients showed that only a small fraction of cells was less than 150 μm2, while the majority of cells were more than 400 μm2. Myocardial fibrosis was significantly increase compared to controls.
Conclusions: Human HCM is characterized by telomere shortening and premature senescence of cardiomyocytes. Anticipated myocardial aging can contribute to the cardiac dysfunction occurring in the end stage of the disease. Although telomere dysfunction may also affect the regenerative potential of the myocardium, cardiomyocyte proliferation does not play a major role in determining the HCM cardiac phenotype.



Telomere shortening In HCM and controls.

P2008

Development and characterization of patient specific iPSC derived cardiomyocyte model systems

A Anna Janz[1]; Y Ueda[1]; N Nose[2]; CK Kwok[2]; P Woersdoerfer[2]; N Knoetgen[3]; F Edenhofer[2]; S Erguen[2]; E Klopocki[3]; B Gerull[1]
[1]Comprehensive Heart Failure Center, Cardiovascular Genetics, Wuerzburg, Germany; *[2]Medical faculty of the University of Wuerzburg, Institute of Anatomy and Cell Biology, Wuerzburg, Germany*; *[3]University of Wuerzburg, Institute of Human Genetics, Wuerzburg, Germany*

Funding Acknowledgements: Bundesministerium für Bildung und Forschung (01EO1504)

Background: Recent advances in genetic technology unraveled novel disease genes for inherited cardiomyopathies (CMPs), in this project for two different forms of dilated cardiomyopathy (DCM):
1.) DCM with ataxia syndrome (DCMA, OMIM #610198) is caused by a homozygous splice site mutation in the gene DNAJC19 (IVS3-1G>C) encoding for a mitochondrial inner membrane import protein.
2.) DCM with juvenile cataract is caused by a homozygous mutation in the LEMD2 gene (c.38C>T, p.L13R) encoding an inner nuclear membrane protein.
For both forms of DCM, the cellular and molecular mechanisms leading to the disease remain widely unknown.
Purpose: The goal of the study is to generate patient specific model system by using human induced pluripotent stem cells (hiPSCs) and their in-vitro derived individual cardiomyocytes (CMs) to discover the complex molecular events leading to the disease. Furthermore, isogenic controls will be generated by CRISPR/Cas9 technology.
Methods and Results: Dermal fibroblasts from patients carrying mutations for two forms of recessive CMPs (DNAJC19 and LEMD2) were obtained and reprogrammed into hiPSCs using Sendai virus. The identity and high purity of the generated hiPSC lines were confirmed by FACS analysis of pluripotency markers (SSEA-4>80%, Tra-1-60 > 94%) and by human G-banding karyotyping. The individual optimal conditions to differentiate patient derived hiPSCs to the cardiogenic path were successfully established to generate a network of contracting CMs in a monolayer as well as in three-dimensional Cardiospheres (CSs). Lactate based metabolic enrichment and verification experiments of CMs including IF, FACS analysis and qPCR for cardiac markers (c-TnT and a-actinin) are currently performed. The patient-derived contracting individual CMs indicate first beating abnormalities kept over prolonged cultivation time. Preliminary data show differences in mitochondrial uptake/storage of radioactive isotopes (18F-FDG, 99mTc-MIBI) between patient and healthy CMs. Next, the effects of the specific mutations within the remaining patient specific genetic background are currently generated by using CRISPR/Cas9 technology via homology directed repair. As an initial approach we successfully knocked-out the cell-junction protein plakophilin-2 - a disease gene for arrhythmogenic cardiomyopathy - in hiPSCs and showed proof of concept technology.
Perspectives: Patient specific CM models will be further developed into more mature/ organotypic model systems and characterized for structural, electrophysiological and molecular changes for the individual diseases. In particular, loss of DNAJC19 will be investigated towards mitochondrial dysfunction, whereas in mutant LEMD2 chromatin remodeling and cell senescence will be examined. The advantage of in vitro hiPSC derived CMs are not only to display clinical aspects of the disease, but also to determine its suitability for drug compound testing.

P2009

Prognostic impact of hypertrabeculation and noncompaction phenotype in nonischemic dilated cardiomyopathy

AR Ana Rita Pereira[1]; AR Almeida[1]; I Cruz[1]; A Marques[1]; S Alegria[1]; AC Gomes[1]; D Sebaiti[1]; A Briosa[1]; O Simoes[1]; LR Lopes[2]; M Ramalho[3]; H Pereira[1]
[1]Hospital Garcia de Orta, Cardiology, Almada, Portugal; *[2]Barts Health NHS Trust, Cardiology, London, United Kingdom*; *[3]Hospital Garcia de Orta, Radiology, Almada, Portugal*

Introduction: To date, it remains uncertain whether left ventricular noncompaction (LVNC) is a distinct type with different pathophysiology and outcome from other types of dilated cardiomyopathies. Probably due to the improvement of cardiac imaging modalities, myocardial trabeculations and noncompaction are now increasingly reported in adult patients (pts) with dilated cardiomyopathy (DCM). Nevertheless, their prognostic impact remains unknown.
Purpose: To evaluate the impact of hypertrabeculation and LVNC phenotype by cardiac magnetic resonance (CMR) on outcomes of pts with DCM.
Methods: Retrospective unicenter study that included the pts followed for nonischemic DCM with left ventricular (LV) ejection fraction (LVEF) < 40% at the time of diagnosis and submitted to CMR. The DCM diagnosis was established by the presence of LV dilation in the absence of uncontrolled arterial hypertension, hypertrophic or restrictive cardiomyopathy, significant valvular or coronary disease. LV trabeculations were identified by CMR as any endocardial wall contour irregularities present in the end-diastolic phase, distinct from papillary muscles and chordae. LVNC phenotype was established by an noncompacted to compacted (NC/C) length ratio = 2,3 or NC/C mass = 20%, measured on long-axis images. The primary endpoint (PE) was a composite endpoint of all-cause mortality, ventricular arrhythmias (VA) with hemodynamic instability and unplanned heart failure (HF) admission. Secondary endpoint (SE) was LVEF recovery (= 50%). Two groups are compared (group 1 - pts with DCM and LV trabeculations or LVNC phenotype; group 2 - pts with DCM without LV trabeculations or LVNC phenotype).
Results: 49 pts were included: 30 (61,2%) male; mean age 54 ± 12 years. At the time of diagnosis, 30 (61,2%) pts were in NYHA functional class = III with a median NT-proBNP value of 2451 pg/mL [interquartile range (IQR) 2233 pg/mL]. Initial LVEF, measured by transthoracic echocardiogram (TTE), was 25 ± 8%. In CMR, 13 (26,5%) pts presented hypertrabeculation phenotype and 10 (20,4%) LVNC diagnostic criteria. Age was the only baseline characteristic with significant difference between the two groups, being group 1 pts significantly younger than group 2 pts (47 ± 12 years vs 54 ± 12 years, p = 0,04). At a median follow-up (FU) of 26 months (IQR 51 months), there were 22 primary events (5 deaths; 3 AV with hemodynamic instability and 14 unplanned HF admissions). 17 (34,7%) pts recovered LVEF. Mean FU LVEF was 42 ± 15%. No significant difference, between the two groups, was also found in FU time (p = 0,58), PE (p = 0,79), SE (p = 0,23), time until PE (log rank 0,24; p = 0,63) and SE (log rank 1,95; p = 0,16) occurrence.
Conclusions: Cardiovascular outcomes of adult pts with nonischemic DCM do not appear to be influenced by the degree of trabeculation. This argues against a hypertrabeculation/LVNC phenotype designating a more severe form of nonischemic DCM.

P2010
Long-term prognostic value of late gadolinium enhancement in a cohort of patients with nonischemic dilated cardiomyopathy

AR Ana Rita Pereira[1]; AR Almeida[1]; I Cruz[1]; A Marques[1]; S Alegria[1]; AC Gomes[1]; D Sebaiti[1]; A Briosa[1]; LR Lopes[2]; M Ramalho[3]; H Pereira[1]
[1]Hospital Garcia de Orta, Cardiology, Almada, Portugal; *[2]Barts Health NHS Trust, Cardiology, London, United Kingdom*; *[3]Hospital Garcia de Orta, Radiology, Almada, Portugal*

Introduction: The presence of late gadolinium enhancement (LGE) in cardiac magnetic resonance (CMR), which enables quantification of myocardial fibrosis, is common in patients (pts) with dilated cardiomyopathy (DCM). The presence of LGE has been related with medium to long-term adverse events. However, limited data exist about the role of LGE extension and location.
Purpose: To evaluate prognostic value of the presence, extension and location of LGE in pts with DCM.
Methods: Retrospective unicenter study that included the pts followed for DCM with left ventricular (LV) ejection fraction (LVEF) < 40% at the time of diagnosis and which were submitted to CMR. The DCM diagnosis was established by the presence of LV dilation in the absence of uncontrolled arterial hypertension, hypertrophic or restrictive cardiomyopathy, significant valvular or coronary disease. The primary endpoint (PE) was a composite endpoint of all-cause mortality, ventricular arrhythmias (VA) with hemodynamic instability and unplanned heart failure (HF) admission. Secondary endpoint (SE) was LVEF recovery (= 50%).
Results: Forty-nine pts were included: 30 (61,2%) male; mean age 54 ± 12 years. At the time of diagnosis, 30 (61,2%) pts were in NYHA functional class = III with a median NT-proBNP value of 2451 pg/mL [interquartile range (IQR) 2233 pg/mL]. Initial LVEF, measured by transthoracic echocardiogram, was 25 ± 8%. LGE was present in 26 (53,1%) pts with a median involvement of 1,5 segments (IQR 4 segments). The most frequent distribution pattern of LGE was mid-wall [14 dts (20,4%)] and the basal anteroseptal segment was the most involved [9 dts (18,4%)]. In univariate analysis, baseline characteristics did not significantly differ between the pts with and without LGE. At a median follow-up (FU) of 26 months (IQR 51 months), there were 22 primary events: 5 deaths, 3 VA with hemodynamic instability and 14 unplanned HF admissions. Seventeen (34,7%) pts recovered LVEF. No significant difference was observed in FU time (p = 0,23), PE (p = 0,63) and time until PE (log rank 1,69; p = 0,19) occurrence between the pts with and without LGE. We also found no significant difference between LGE extension and PE occurrence (p = 0,13). Relatively to location, a higher number of PE events was significantly associated with the presence of LGE in the mid anteroseptal (p = 0,02) and inferoseptal segments (p = 0,02) and in the basal segments with the same location (p = 0,01 and p = 0,02, respectively). No significant difference was observed between SE occurrence and the presence (p = 0,71), extension (p = 0,61) and location of LGE.
Conclusions: In this study, the existence of myocardial fibrosis in the mid-basal segments of the interventricular septum was associated with medium to long-term adverse events. These results support a potential role of CMR in the risk stratification of DCM pts but not as a predictor of LVEF recovery.

P2011
Predictors of heart failure in left ventricular noncompaction

P Von Hafe Leite[1]; H Antunes[2]; N Marques[3]; N Craveiro[4]; L Reis[5]; R Guerreiro[6]; R Santos[7]; O Azevedo[1]
[1]Hospital Senhora da Oliveira, Cardiology, Guimarães, Portugal; *[2]Hospital Sao Teotonio, Cardiology, Viseu, Portugal*; *[3]Faro Hospital, Cardiology, Faro, Portugal*; *[4]Hospital of Santarem, Cardiology, Santarem, Portugal*; *[5]University Hospitals of Coimbra, Cardiology, Coimbra, Portugal*; *[6]Hospital Espirito Santo de Evora, Cardiology, Evora, Portugal*; *[7]Hospital Centre do Tamega e Sousa, Cardiology, Penafiel, Portugal*

Background: Left ventricular noncompaction (LVNC) is a rare cardiomyopathy. Heart failure (HF), arrhythmias and thromboembolic events (TE) are the main complications of LVNC.
Purpose: To identify predictors of HF development in LVNC patients.
Methods: Multicentric, retrospective study with 120 patients diagnosed with LVNC. Clinical, genetic, imaging and electrocardiographic parameters were collected. It was evaluated which are associated with the development of HF during the follow-up.
Results: In this study, the patients were predominantly male (58.3%) and had a mean age at diagnosis of 47 ± 18 years.
Patients had a follow-up lasting, on average, 3.7 ± 2.6 years.
About 46% of LVNC patients had HF during follow-up, more frequently in Class II of New York Heart Association (55.4%), and 10.7% presented in class IV.
Patients with LVNC and HF were predominantly males (67.3% vs 32.7%, p = 0.041), complained more frequently of dyspnea at clinical presentation (88.9% vs 7.5%, p < 0.001). On echocardiography, had significantly higher values of end-diastolic volume (EDV) of the left ventricle (LV) (60.4 ± 8.8 vs 50.8 ± 7.1ml/mm^2; t(111)= 6.4, p < 0.001), LV mass (138.4 ± 92.9 vs 100.0 ± 47.8 g/m^2; t(77)= 2.2, p= 0.024), and left atrial volume (LA) (36.1 ± 14.8 vs 27.1 ± 8.1 ml/mm^2; t(55)= 2.8, p= 0.007). As well this patients have higher frequency of diastolic dysfunction (DD) (75.0% vs 28.8%; p < 0.001), mitral valve disease (73.1% vs 31.6%, p < 0.001), aortic valve disease (26.5% vs 10.9%, p = 0.040), and disease of the tricuspid valve (27.3% vs 0%, p = 0.027).
On MRI, patients with HF had a higher LV mass (126.3 ± 76.6 vs 77.9 ± 33.4 g/m^2, t (45) = 2.8, p < 0.001), higher LV end-systolic volume (86.4 ± 50.8 vs. 51.0 ± 30.5 (43.3) = 2.8, p = 0.008) and higher frequency of late septal enhancement (14.3% vs 0%, p = 0.015).
On electrocardiography, patients with LVNC and HF presented more frequently atrial fibrillation (AF) (19.1% vs 0%, p = 0.001), complete left bundle branch block (LBBB) (23.3 vs 8.0%, p = 0.040) and non-sustained ventricular tachycardia (nsVT) (34.1% vs 13.7%, p = 0.020).
Multivariate regression identified, as statistically significant predictors of HF development during follow-up, the presence of dyspnea at clinical presentation (p < 0.001), DD (p = 0.048) and presence of AF (p = 0.013).
Conclusions: Dyspnea at clinical presentation, DD, and AF were independent predictors of HF development in patients with LVNC.

Pulmonary Circulation, Pulmonary Embolism, Right Heart Failure - Clinical

P2012
Correlation between right ventricular function assessed by echocardiography and by right heart catheterization among patients with pulmonary hypertension.

COM Christian Oscar Musante[1]; AJL Adrian Jose Lescano[1]; EB Ezequiel Besmalinovich[1]; DC Diego Crippa[1]
[1]Sanatorio Urquiza. Sanatorio Finochetto., Cardiologia., Buenos Aires, Argentina

Correlation between right ventricular function assessed by echocardiography and by right heart catheterization among patients with pulmonary hypertension.

Right ventricular (RV) dysfunction aggravates prognosis in pulmonary hypertension (PH) patients. Cardiac index (CI) assessed by right heart catheterization (RHC) is a robust indicator of RV function and prognosis. The utilization of noninvasive estimation of RV function by Doppler echocardiography (DE) methods such as tricuspid annular plane systolic excursion (TAPSE) or DTIderived tricuspid lateral annular systolic velocity wave (S') are currently supported by the DE practice guidelines. However, in PH patients, there is limited information regarding the precision and accuracy of those noninvasive methods.
To estimate the concordance between RV function assessed by two DE methods (TAPSE, S') and CI assessed by RHC. We included consecutive patients with confirmed PH diagnosis that underwent RHC between March 2012 and July 2017. TAPSE and S' values were obtained using two ultrasound systems and CI value was obtained by RHC. RHC and DE were performed with less than 24 hours of difference between them and the physicians were blind to the other method
Results: We analyzed the numeric variables (TAPSE, S', CI) with bivariate Pearson's correlation to visualize their relationship, reported as correlation coefficient and significance.
A total of 92 patients were included. Mean age was 56 years (SD 18) and 67% were women. PH group (G) distribution was GI 67%; GII 11%; GIII 12%; GIV 7% and GV 3%. Mean values were: TAPSE 17.8 mm (SD 4.0), S' 10.3 cm/s (SD 3.7) and CI 2.73 l/m/m2 (SD 0.76). The concordance correlation coefficient resulted in: r 0.32 ($p < 0.01$) for TAPSE and CI and r 0.29 ($p = 0.01$) for S' and CI. We found a poor relationship between two noninvasive methods (TAPSE, S') and invasive determination of RV function by RHC. These results supports the idea that TAPSE and S' must be used with caution in PH populations. Further investigations are needed to find noninvasive methods to estimate RV dysfunction with better precision in PH patients.

P2013
The process of increasing hematocrit in pulmonary hypertension depends on gender and degree of hypoxia

N Nadezda Pankova[1]; A Popova[1]; M Artemieva[1]; A Andreev-Andreevskiy[1]; E Volynnikova[1]; N Medvedeva[1]
[1]*M.V. Lomonosov Moscow State University, Biological, Moscow, Russian Federation*

Introduction: Hypoxic pulmonary hypertension (hPH) is characterized by an increase in vascular resistance of the lungs and systolic right ventricle pressure (RVSP). It is the body's response to chronic hypoxia. ?ne of the adaptation way to hypoxia is increasing hematocrit (HCT). The purpose of this work was to study the effect of sex on number of red blood cell (RBC) and its volume (MCV), depending on the degree of exposure to intermittent chronic hypoxia (13%,10% and 8% O2).
Method. Female and male gonadectomized Wistar rats were used. The procedures followed the FELASA/ICLAS for use of the laboratory animals (National Academy Press, Washington, D.C.1996). 4 weeks after the gonadectomy, rats were exposed to chronic intermittent hypoxia (10h/day, 2wk) with 13% or 10% or 8% O2 in hypobaric chamber. Wistar rats were divided into 6 groups by parameters: sex and level of hypoxia (8%, 10%, 13% O2). Two weeks after the onset of hypoxia systolic right ventricle pressure (SRVP) was measured as indicator of hPH. Blood hematocrit (HCT), hemoglobin (HGB), RBC and MCV were measured using a blood analyser Gemalait 1280 (Diksion Russia). The statistical analysis of the data was made using the nonparametric criterion for independent variables from the Statistic8 program package. Results Two weeks after the onset of hypoxia all groups of rats developed hPH with different extent of the disease. RVSP was higher by 30% in female 10% O2 group and was not changed in male. Increasing degree of hypoxia from 10 to 8% O2 did not change RVSP of all groups, but enlarged mortality in all groups by 61%. Every increase in the degree of hypoxia was accompanied by increases in HCT. The change in the concentration of oxygen in hypoxic chamber from 13% to 10% increased RBC from $7,1 \pm 0,4$*10^12/L to $9,4 \pm 0,5$ *10^12/L in female rats and did not change ($7,9 \pm 0,5$*10^12/L and $7.9 \pm 0,1$*10^12/L) in male. In this case MCV was not changed in female, and have increased by 24% the male. The change in the concentration of oxygen from 10% to 8% increased RBC from $7.9 \pm 0,1$*10^12/L to $10.1 \pm 0,3$*10^12/L in male without changed it in female rats. ($9,4 \pm 0,5$*10^12/L and $9,4 \pm 0,6$*10^12/L). MCV was increased only in female rats (from $60,2 \pm 0,5$ to $69,7 \pm 1,7$ fL).
Conclusions: Increase the degree of hypoxia in the chamber (from 13% to 8% O2 is accompanied by increasing RVSP only up to certain values (about 60-70 mm Hg). There are gender differences in the mechanisms of adaptive increase in hematocrit in the case of hypoxic forms of pulmonary hypertension. The change degree of hypoxia from 13% to 10% increases female HCT due to the increase in the number of red blood cells, and from 10 to 8% due to the increase of their volume. In males it is the opposite.

Cardiovascular Surgery - Other

P2014
Pharmacological stimulation of the NO/SGC/cGMP pathway reduces ischemia-reperfusion injury and improves donor organ function in a rat model of heterotopic heart transplantation

B T Nemeth[1]; K Benke[1]; A A Sayour[1]; B K Agg[1]; A Olah[1]; M Ruppert[1]; K Stark[1]; M Polos[1]; I Hartyanszky[1]; B Merkely[1]; Z Szabolcs[1]; T Radovits[1]
[1]*Semmelweis University, Heart and Vascular Center, Budapest, Hungary*

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Introduction: Despite the fast evolution of mechanical circulatory support devices, heart transplantation (HTX) remains the definitive therapy of end-stage heart failure. Ischemia-reperfusion (I/R) injury occurring during transplantation is a primary determinant of long-term outcome of HTX and primary graft insufficiency. The most important pathobiochemical changes induced by reperfusion in the myocardium of the donor organ are increased production of reactive oxygen species (ROS), intracellular calcium overload, energy deficit and acidosis. Modification of the nitric oxide (NO)/soluble guanylate cyclase (sGC)/cyclic guanosine monophosphate (cGMP) signaling pathway appears to be the most promising among the pharmacological interventional options developed recently. The first clinically applicable member of this group is the sGC stimulator riociguat. We aimed at characterizing the cardio-protective effects of this drug in a rat model of heterotopic heart transplantation.
Methods: Donor Lewis rats were treated orally with either riociguat (10mg/BWkg) or placebo for two days. Hearts were stored for an hour in cold preservation solution (Custodiol) following explantation, then were transplanted heterotopically. One hour after initiation of reperfusion, left ventricular (LV) pressure-volume relations and coronary flow were recorded in order to assess post-transplant graft function. Molecular biological measurements and histological examination were also completed.
Results: LV contractility (LV systolic pressure at 120µl of LV volume: 117 ± 13 vs. 48 ± 5mmHg, $p < 0.001$; dP/dtmax: 2963 ± 221 vs. 1653 ± 159mmHg, $p < 0.001$) and active relaxation (dP/dtmin at 120µl of LV volume: -2014 ± 305 vs. -1063 ± 177mmHg, $p = 0.019$) improved significantly after an hour of reperfusion, while alteration of coronary flow standardized to heart weight (2.52 ± 0.34 vs. 1.67 ± 0.22ml/min/g, $p = 0.06$) showed a strong increasing trend following pretreatment with riociguat. Myocardial expression of antioxidant markers were significantly improved after heart transplantation.
Conclusions: Pharmacological preconditioning with riociguat decreases I/R injury and improves donor organ function in our small animal model of heart transplantation. The observed cardio-protective effect might be attributed to the stimulated sGC and increased myocardial cGMP-signaling. Riociguat therefore might be a potential cardio-protective agent in the inventory of heart transplantation surgery and during cardiac surgical procedures requiring sustained ischemia.

P2015
Comparison of efficacy between ramipril and carvedilol on limiting the expansion of abdominal aortic aneurysm in mouse model

SM Park[1]; D Choi[2]
[1]*Hallym University, Chuncheon Sacred Heart Hospital, Chuncheon, Korea Republic of*; [2]*Yonsei University College of Medicine, Cardiology Division, Seoul, Korea Republic of*

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Objective: Abdominal aortic aneurysm (AAA) is a common condition that may be life-threatening when it is unrecognized. The aim of this study is to evaluate and compare the efficacy of ramipril and carvedilol on limiting AAA expansion in mouse model.
Methods and Results: A total of thirty-six experimental AAA mouse model was induced with the continuous infusion of angiotensin II (Ang II) in 20 week-old male apolipoprotein E-deficient (apoE-/-) mice. They were randomly divided into three treatment groups and fed orally for 8 weeks; saline alone, ramipril (2.5 mg/30g/day), or carvedilol (3.125mg/30g/day) respectively. Aortic diameter (AD) was measured by micro-computed tomography (CT) and the level of biomarkers of aortic tissue such as monocyte chemoattractant protein-1 (MCP-1) and tissue inhibitor matrix metalloproteinase-1 (TIMP-1) were evaluated. After treatment, AD of both ramipril and carvedilol group was smaller than in the saline group. The percentage change of AD in both ramipril and carvedilol groups were significantly smaller than that of the saline group. Pathologic examination revealed relatively well-preserved aortic walls in the ramipril group compared to the carvedilol and saline groups. The level of MCP-1 was markedly decreased in both the ramipril and carvedilol groups

compared to the saline group. The level of TIMP-1 was higher in the carvedilol group when compared to either the saline or ramipril groups.
Conclusions: Ramipril and carvedilol treatment shows similar efficacy in limiting AAA expansion in mouse model. Future clinical research would be warranted to validate these results.

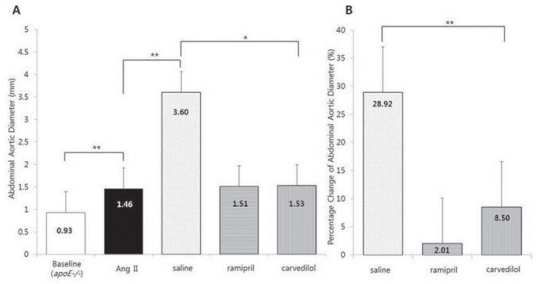


Fig 3. Changes of aortic diameter

Hypertension - Other

P2016
Neutrophil extracellular trap formation is enhanced in arterial hypertension via and AT1R and NADPH oxidase-dependent pathway

TM Hofbauer[1]; T Scherz[1]; A Ondracek[1]; J Mueller[1]; L Kascha[1]; C Feist[1]; A Frueh[1]; I Horvat Menih[1]; A Mangold[1]; IM Lang[1]
[1]Medical University of Vienna, Cardiology, Vienna, Austria

Background: Arterial hypertension is a major risk factor for coronary artery disease (CAD). By formation of neutrophil extracellular traps (NETs), neutrophils release their nuclear content into the extracellular space, fighting pathogens. NETs have been implicated in CAD. In preliminary studies of CAD patients, we observed a positive correlation between blood pressure and NETosis ex vivo, implicating blood pressure modulating NETosis. Angiotensin-II (Ang-II) mediates blood pressure via its potent vasoconstrictive properties, but also exerts pro-inflammatory functions via the angiotensin type 1 receptor (AT1R). AT1R is expressed on neutrophils. We thus hypothesized that Ang-II might influence NETosis.
Methods: We stimulated isolated neutrophils with ionomycin ex vivo. NETosis was measured using Sytox® Green, a dye that exclusively stains extracellular DNA, a hallmark feature of NETs. The detergent Triton served as positive control. To assess the role of the Ang-II pathway, we pre-incubated neutrophils with Ang-II, AT1R antagonist losartan or NADPH oxidase inhibitor diphenyleneiodonium (DPI).
Results: We observed a dose-dependent NET release by ionomycin. Irrespective of ionomycin concentration, pre-treatment with Ang-II significantly enhanced NETosis to 80-90% of positive control. Losartan abolished this effect, suggesting an AT1R-dependent pathway. NADPH oxidase is crucial for NETosis due to release of reactive oxygen species. DPI abolished the effect of Ang-II on NETosis.
Conclusion: Our results implicate that via Ang-II, arterial hypertension aids neutrophils to undergo NETosis by increasing intracellular ROS production, which makes neutrophils more susceptible to pro-NETotic stimuli. This provides new insight in how effective blood pressure lowering might lead to more favorable outcomes in CAD.

Obesity

P2017
Sex-related differences in influence of obesity on outcomes of patients with heart failure: results from the Polish cohort of the ESC Heart Failure Long-Term Registry

MI Marta Izabela Kaluzna-Oleksy[1]; JM Migaj[1]; J Nessler[2]; MG Crespo-Leiro[3]; AP Maggioni[4]; J Drozdz[5]; M Lesiak[1]; E Straburzynska-Migaj[1]
[1]Poznan University of Medical Sciences, Ist Department of Cardiology , Poznan, Poland; *[2]John Paul II Hospital, Krakow, Poland*; *[3]Instituto Universitario de Ciencias de la Salud, A Coruna, Spain*; *[4]ANMCO Foundation For Your Heart, Florence, Italy*; *[5]Medical University of Lodz, Lodz, Poland*

Introduction: Many investigators reported an "obesity paradox" presenting improved outcomes of obese patients with chronic diseases including, among others, kidney disease and heart failure (HF). Mechanisms underlying this phenomenon are not known and its existence remains controversial. Men and women differ in incidence and patterns of obesity, which gives strong reasons to suspect sex-related differences in influence of obesity on outcomes.
Aim: The aim of the hereby-presented study was to compare the influence of obesity on outcomes of men and women with HF with both reduced (HFrEF) and preserved (HFpEF) ejection fraction.
Methods: This study is a part of a large prospective European registry of HF patients followed for 12 months. It includes 1030 Polish in-patients and out-patients treated for HF, men (n = 724) and women (n = 304). The subjects have both HFrEF, n = 746, and HFpEF, n = 255. The endpoints were all-cause death (n = 113), hospitalization (n = 425) and both combined (n = 494). This study uses body mass index (BMI) to divide subjects into groups according to WHO 18.5-24.99 (n = 276), 25-29.99 (n = 430) and 30-39.99 (n = 278); there were too few patients with BMI < 18.5 (n = 16) and >40 (n = 28) for further analyzes. Survival analysis was adjusted for markers of poor prognosis - AF, NYHA class, hemoglobin, LVEF, BNP and heart rate. P value of 0.05 was considered significant in all analyzes.
Results: There were no differences in incidence of normal weight, overweight and obesity between men and women (26% vs. 32%, 45% vs. 40% and 29% vs. 28% respectively, NS) and between HFrEF and HFpEF (28% vs. 28%, 40% vs. 45% and 32% vs. 27% respectively, NS). Univariate regression model shows that higher BMI reduced risk of death (HR 0.94, p = 0.001; for men HR 0.94, p = 0.006; for women HR 0.95, NS), the same for obesity (HR 0.72, p = 0.002; for men HR 0.73, p = 0.015; for women HR 0.70, NS). Multivariate regression model showed that higher BMI reduced risk of death (HR 0.96, p = 0.023; for men HR 0.96, p = 0.06; for women HR 0.96, p = 0.23), the same for obesity (HR 0.79, p = 0.036; for men HR 0.83, NS; for women HR 0.76, NS). BMI and obesity do not influence risk of hospitalization (HR 1.00, NS and HR 0.97, NS respectively). Univariate regression model shows that higher BMI reduced risk of death in men with HFrEF (HR 0.92, p = 0.002) and women with HFpEF (HR 0.89, p = 0.029); the same for obesity (HR 0.66, p = 0.004 and HR 0.49, p = 0.011 respectively). BMI and obesity did not influence risk of death and hospitalization in patients with NYHA III and IV and in men with HFpEF and women with HFrEF, and there were no sex-related differences in this group.
Conclusions. Obese patients with HF show reduced risk of death in 12-month follow-up. This phenomenon may be observed mainly in men, particularly with HFrEF, and in women with HFpEF.

Exercise Testing

P2018
Association between oxygen uptake efficiency slope (OUES), an effort-independent measure of cardiorespiratory fitness (VO2max), and robust/pre-frail status in an elderly Chinese population

E Fung[1]; L T Lui[1]; F Yau[1]; J Leung[1]; J Woo[1]
[1]The Chinese University of Hong Kong, Hong Kong, Hong Kong SAR People's Republic of China

On behalf of: Laboratory for Heart Failure and Circulation Research, CUHK

Background/Introduction: Peak oxygen uptake or consumption (VO2max) is a measure of cardiorespiratory fitness that provides prognostic information in heart failure patients being considered for transplant, and is also widely used in exercise capacity testing. However, accurate determination of threshold capacity is effort-dependent, and poses challenges when assessing older adults. Previous studies have shown that calculating the oxygen uptake efficiency slope (OUES) through the use of multiple VO2 data points at different exercise levels in conjunction with minute ventilation (VE) can inform exercise capacity independent of effort and may be superior to VO2max. We hypothesise that OUES in this physiological context can distinguish robust versus pre-frail older adults.
Purpose: To compare VO2max with OUES in a community-dwelling older adult population able to freely ambulate.
Methods: This study included subjects in the Mr & Ms Os Cohort with a complete set of cardiopulmonary exercise testing (CPET) data. OUES ('a') was calculated using the following equation: $VO2 = a \cdot \log(VE) + b$. A 4-point frailty scale was used to classify robust/pre-frail status, and 1 point was assigned for each positive criterion: i) very little or no energy, ii) difficulty in climbing up 10 steps of stairs, iii) inability to walk 100 yards, and iv) presence of 3 or more predefined co-morbidities. A score of zero (0) was considered 'robust', and 1 to 2 points indicated pre-frailty. Four primary measures were used to assess cardiorespiratory fitness against robust/pre-frail status: VO2max, VO2max/kg (or VO2max indexed to body weight in kilograms), OUES, and OUES/kg. Student's t test was used for comparing means between two groups. The study was approved by the institutional ethics review committeee and adhered to the Declaration of Helsinki.
Results: The study included 550 subjects (457 males and 93 females) with a mean age of 76.7 y $\pm$ 5.34. The ratios (or relative proportions) of robust:pre-frail individuals in the male and female subject groups were 3.57 (78.12% vs. 21.88%) and 1.74 (63.44% vs. 36.56%), respectively. The robust group outperformed the pre-frail group in all four measures. Among these, VO2max/kg most strongly differentiated robust/pre-frail status in male (22.6 vs. 19.6, P = 7.32 x 10e−12) and female (20.4 vs. 17.4, P = 2.59 x 10e−5) subjects. OUES did not significantly differentiate robust/pre-frail status in male subjects (1769.9 vs. 1709.9, P = 0.11), and only

modestly in female subjects (1486.8 vs.1259.0, P = 0.001). VO2max and OUES/kg also differentiated robust/pre-frail status to varying extents in both sexes (range, P = 0.0067 to 7.85 x 10e−7).
Conclusion(s) In the manner in which older Chinese adults have been stratified by robust/pre-frail status as used in this study, VO2max/kg (or indexed VO2max) was the most strongly significant metric for differentiating robust versus pre-frail individuals compared with VO2max, OUES or OUES/kg.

Autoimmune/Chronic Inflammatory Disorders and Heart Disease

P2019
GRK2 is a novel early marker of cardiotoxicity in response to doxorubicin

A Antonella Fiordelisi[1]; J Gambardella[2]; M De Rosa[1]; M Ciccarelli[2]; B Trimarco[1]; G Iaccarino[2]; D Sorriento[1]
[1]Federico II University of Naples, Department of biomedical sciences advanced, Naples, Italy; [2]University of Salerno, Medicine and surgery, Salerno, Italy

Background: Doxorubicin (DOXO) is common anticancer drug, whose efficacy is limited by a cumulative dose-dependent cardiotoxicity which can lead to severe heart failure and death. The current goal of cardio-oncology research is the identification of early markers of cardiotoxicity to promptly start an effective therapy. In this context, the G protein coupled receptor kinases type 2 (GRK2) is an useful marker of cardiac injury since its levels and activity are elevated in damaged heart. Moreover, it has been shown that myocardial GRK2 expression and activity are mirrored by lymphocyte levels of this kinase and can predict late ventricular remodeling as early as 3 days after Myocardial Infarction proposing this kinase as early biomarker of cardiac injury.
Purpose: The aim of the study is to evaluate the role of GRK2 as early marker of cardiac dysfunction induced by DOXO.
Methods: In vitro, GRK2 and Cleaved Caspase 3 levels were analyzed in cardiomyoblasts (H9C2) after treatment with DOXO 5 uM, by western blot. In vivo, C57B WT mice were treated with a single intraperitoneal injection of DOXO (20 mg/ Kg). Heart and blood from mice were collected at 24, 48 and 72h after treatment. The levels of GRK2 were evaluated by western blot in whole heart lysate and in PBMCs isolated from mice blood. Cardiac gene expression of ANF and MCP1 was evaluated by Real time PCR.
Results: In cardio-myoblasts, GRK2 levels were reduced in response to DOXO at 1 hour from starting treatment while Cleaved caspase 3, marker of damage, increased in a time dependent manner only after 3 hours from starting treatment. Similarly, in vivo, GRK2 levels were decreased in whole heart lysates from mice treated with DOXO compared with controls, at 24, 48 and 72h, when the transcriptional levels of ANF and MCP-1, were not still increased by DOXO administration. Also in PBMCs from mice blood, the levels of GRK2 were reduced after 24, 48 and 72h from starting treatment, reflecting the GRK2 cardiac reduction.
Conclusion: DOXO induces an early decrease of GRK2 levels in cardiac cells. This reduction occurs in a pre-damage phase suggesting the potential role of GRK2 as early markers of cardiotoxicity. Moreover, the correlation between GRK2 levels in the heart and its expression in PBMCs, suggest that this protein could be easily detectable from peripheral blood to indirectly evaluate its expression levels in the heart. These data suggest that the reduction of GRK2 levels in PBMC could be an early marker of DOXO induced toxicity since it arises before the activation of DOXO-dependent damage.

Cardiovascular Nursing - Other

P2020
Can the acceptance of the illness increase compliance with non-pharmacological treatment recommendations in patients with heart failure?

B Beata Jankowska-Polanska[1]; B Kowalczyk[1]; K Lomper[1]; A Chudiak[1]; G Mazur[2]
[1]Medical University of Wroclaw, Health Science Faculty, Wroclaw, Poland; [2]Wroclaw Medical University, Department and Clinic of Internal and Occupational Diseases and Hypertension, Wroclaw, Poland

Patients, in particular elderly, affected by heart failure (HF) that are non-compliance to therapeutic treatment are exposed to frequent exacerbations of HF symptoms and consequently to high risk of re-hospitalizations. Non-compliance with non-pharmacological treatment is major problem for HF patients that need caring. Previous studies assessed the importance of pharmacological treatment but only few focused on lifestyle recommendations and depth on the importance of acceptance of illness on compliance with therapeutic treatments according by most recent guidelines of HF. Aim: To assess the effect of acceptance of disease in HF patients related to the compliance to therapeutic treatment.
Methods: 105 participants were enrolled in this study divided into 3 groups depending on the degree of acceptance of illness scale (AIS): I group (AIS 8-18), II group (AIS 19-29), III group (AIS 30-40). Elderly HF patients were recruited in a outpatient cardiovascular clinic in Poland. The acceptance of disease were assessed using Acceptance of Illness Scale (AIS) and the Revised Heart Failure Compliance Scale was used to assess the compliance to the non-pharmacological treatment in 6 domains: sodium restrictions, exercise, appointment keeping, fluid restriction, regular weighing and pharmacological treatment. SPSS software was used to data analysis.
Results: In comparative analysis of HF patients depending on AIS there were statistically significant differences in compliance level especially in sodium restrictions domain (I group 1.3 ± 1.2 vs II group 2.0 ± 1.5 vs III group 2.3 ± 1.3; $p = 0.047$) and exercise (I group 0.5 ± 0.9 vs II group 0.8 ± 1.2 vs III group 1.3 ± 1.2; $p = 0.045$). We no found statistically significant differences in other domains. Moreover AIS is a independent predictor of compliance with the reduction in sodium intake ($\beta = 0.061$; $p = 0.006$).
Conclusions: The acceptance of disease improves significantly the compliance with therapeutic recommendations, especially in the non-pharmacological treatment. Elderly patients with a high level of acceptance have better compliance to non-pharmacological treatment of HF. Assessment of acceptance and compliance level may be useful in planning tailored education in HF patients.

Poster Session 3 - Clinical Cases

Chronic Heart Failure - Pathophysiology and Mechanisms

P2021

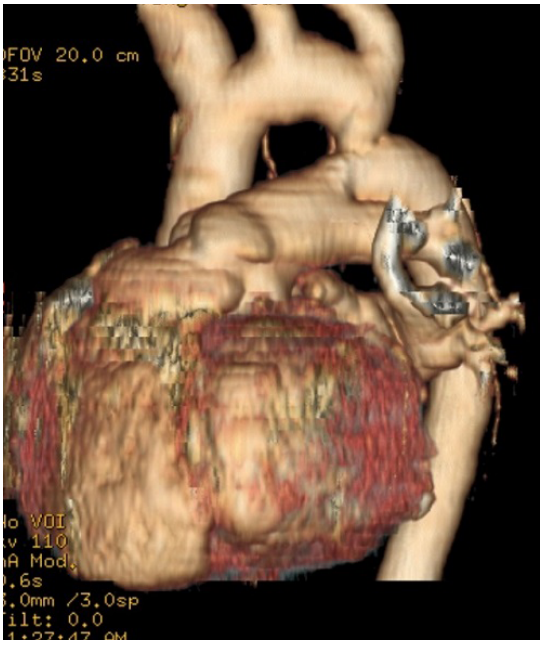
An unexpected cause of heart failure diagnosed in adulthood: the unfortunate poker of cardiac anomalies

M Maria Trepa[1]; I Sa[1]; M Fontes-Oliveira[1]; R Santos[1]; R Costa[1]; VA Dias[1]; S Torres[1]

[1]*Hospital Center of Porto, Cardiology, Porto, Portugal*

Congenital heart disease is particularly challenging due to a vast range of anatomic lesions with different adaptive mechanisms and presentations.

We present the case of a 35 year old female patient referred to cardiology due to dyspnea. Previous history included late-diagnosed phenylketonuria (PKU) resulting in mild cognitive impairment, hypertension and a history of a heart murmur in childhood. At initial consultation she was in class III NYHA. Physical exam revealed



CT_reconstruction

equalized hypertension in all 4 limbs and a grade III systolic murmur. EKG was in synus rhythm and had intraventricular conduction delay and hypertrophy criteria.

The echocardiogram showed several abnormalities: 2D showed a bicuspid aortic valve (BVA), right ventricular (RV) hypertrophy, dilatation of the pulmonary artery (PA) and abnormal septum movement. There was apical hypertrabeculation, moderate left ventricular (LV) dysfunction and RV impairment. Spectral Doppler revealed severe pulmonary hypertension (PH) (PA systolic pressure ~100 mmHg). A close look at the left PA revealed a diastolic retrograde flow from a large patent ductus arteriosus (PDA). Also, a small perimembranous ventricular septal defect (VSD) was seen and, in the supraesternal view, a post-isthmus significant narrowing of the descending aorta with a gradient of ~50mmHg made the diagnosis of coarctation of the aorta (COA).

The subsequent cardiac magnetic resonance confirmed the echocardiographic findings and the high suspicion for a small VSD. The hypertrabeculation was not significant and there was no late myocardial enhancement.

Cardiac catheterization showed severe COA (gradient through COA ~52 mmHg) and large PDA with bidirectional shunt but mainly right to left (Qp/Qs: 0.77) with severe PH (equal to systemic pressure). Ductal occlusion had no effect on PSAP.

Given the presence of Eisenmenger physiology at initial diagnosis, there was no indication for PDA closure. The patient was started on diuretics, b-blockers, angiotensin converter inhibitors, aldosterone antagonists and pulmonary vasodilators and is currently stable on class II NYHA, with mild cyanosis and eryhtrocytosis. She has also undergone tubal ligation.

Major chromosomal abnormalities were ruled out and she is currently under further genetic testing. The relation to PKU was considered but the only reports associating this metabolic disease with cardiac abnormalities refer to children born from mothers with PKU, which was not the case.

Although congenital cardiac lesions may occur in association, to our knowledge, this is the first report describing this particular combination of multiple anomalies, namely BAV, PDA, COA and VSD. This case is remarkable for its singularity and physiological complexity but also because it highlights the importance of screening cardiac murmurs in childhood to avoid late and irreversible presentations. Timely referral of these patients to an experienced Heart Team in essential.

P2022

Assessment and treatment strategy of heart failure due to combined cardiomyopathy (ischemic,toxic and valvular)

R Rok Stopar[1]

[1]*Izola General Hospital, Cardiology, Izola, Slovenia*

Assessment and treatment strategy of heart failure due to combined cardiomyopathy (ischemic,toxic and valvular)

70 year old male was admitted to cardiologic department of regional hospital with signs of new onset heart failure. In the past he had been diagnosed sarkoidosis without had been treated and arterial hypertension. He had a history of alcochol abuse as well. ECG registered sinus tachicardia without ST alteration. Lab exames showed BNP 2708 pg/ml (100), cTnI 108 ng/L (40), kreatinin 155 μmol/L, urea 11,1 μmol/L, ionogram and blood gas analysis unremarble. Transthoracic echocardiography revealed moderatly dilated left ventricle with severly depressed systolic function (EF 25%), hypokinetic right ventricle, calcified aortic valve with low transvalvular gradient and reduced (AVA 0,9 cm2) indicating possible low flow severe aortic stenosis. Elevated serum transaminase and abdominal ultrasound revealed hepatopathy due to congestion and past alcochol consumption. Kidney failure with GFR 38ml/min/P was also diagnosed. Coronarography showed severe LM, proximal LAD and LCX stenosis. Due to high risk for surgical intervention (ESC II 11,93 %), we decided for step by step approach. First stenting coronary lesions afterward refering to TARV . PCI of LM, LAD and LCX was performed . In mean time patient was treated with high doses of diuretics. Before PCI levosimendan was administerd as well. Therapy with ACE, eplerenon, bisoprolol, atorvastatin, ASA and ticagrelor was prescribed according to ESC guidelines. At discharged our patient was in NYHA class III . CMR was consistent with ishemic cardiomyopathy . 2 months later patient had been recovered to NYHA class II, TTE showed increased both (EF 35%) and (AVA 1 cm2) with only slightly increase of transvalvular gradient. So far TAVR was postponed .

Heart failure may be caused by combined cardiomyopathy that need holistic approach in order to select right treatment strategy for a given clinical situation

P2023

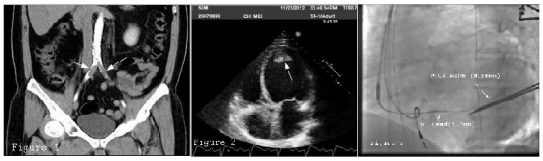
A case of dilated cardiomyopathy suffered attack of cardiac arrest during left ventricular epicardial lead implantation

M-T Ming-Ting Chou[1]; CY Chiang[1]

[1]*Chi-Mei Medical Center, section of Cardiology, Tainan, Taiwan ROC*

A 50–year-old male was admitted through emergency department due to progressive dyspnea with orthopnea for days. He was diagnosed as dilated cardiomyopathy 5 years ago and received regular medical treatment in cardiovascular section. About 2 months ago, he was admitted to cardiovascular surgery section due to progressive bilateral lower leg weakness. Abdominal CT scan revealed occlusion of

bilateral iliac artery.(Fig 1) . Leriche syndrome was diagnosed. He received IV urokinase infusion and symptom improved and shift to oral wafarin treatment. At ER, Chest X ray showed cardiomegaly with pulmonary edema; ECG showed complete LBBB pattern with QRS width about 154msesc. Echocardiogram showed poor LV systolic performance with ejection fraction estimated about 15%. Also LV thrombus was found (fig 2). He received IV diuretic and dobutamine infusion first but without much symptom improvement. Cardiovascular surgery was consulted for possible heart transplant . Biventricular pacemaker implantation was performed 1 week after admission. During the procedure, the 0.36mm PTCA wire can go into the coronary sinus but the 1.3mm LV lead just stop at the coronary sinus ostial site after repeated trial. Coronary sinus ostial stenosis was highly suspected (fig 3). Finally, only RV and RA leads were implanted. So surgical LV epicardial lead implantation was arranged . Sudden cardiac arrest occurred during general anesthesia induction; After successful cardiac-pulmonary resuscitation, VA ECMO implantation was also done. LV epicardial leads was then successfully implanted with good test function. Successful endotracheal extubation and removal of ECMO was done 5 days later. He was later discharged in stable and improved condition. He lived uneventfulty with functional class II status one year later. Follow-up echocardiogram showed improved ejection fraction up to 44% with resolution of LV thrombus .



Bleeding during dabigatran treatment of a patient with acute renal injury induced by a combination of spironilactone and enalapril

P2024

ZK Salpagarova[1]; DA Andreev[1]; AA Bykova[1]; M Chashkina[1]; DA Sychev[2]; AL Syrkin[1]

[1]I.M. Sechenov First Moscow State Medical University, Moscow, Russian Federation; *[2]Russian Medical Academy of Postgraduate Education, Moscow, Russian Federation*

A 75-year-old man with hypertension, paroxysmal atrial fibrillation, aortic stenosis, type 2 diabetes, and chronic kidney disease stage 3a (glomerular filtration rate (GFR) by the CKD-EPI 52 ml/min/1.72 m2) presented with another episode of acute decompensated heart failure NYHA class 4. The patient also underwent hemicolectomy with colostomy 6 years ago for a colorectal cancer.

On admission in clinical blood analysis there were nothing abnormal detected. The patient was received metoprolol succinate 150 mg / day, digoxin 0.375 mg / day (but was withdrawn due to the frequent ventricular extrasystoles), enalapril 20 mg / day, amlodipine 2.5 mg / day, spironolactone 50 mg / day, furosemide 80 mg / day, atorvastatin 20 mg / day and gliclazid 30 mg / day. Dabigatran 220 mg / day was also prescribed (CHA2DS2-VASc 5 score). Patient status on the top of already administered therapy improved significantly. However, by the day 10 after discharge, severe weakness, shortness of breath and dizziness were occurred, so the patient was rehospitalized.

In blood tests, the following changes were observed: hemoglobin 69 g / l, creatinine 3.6 mg / dL (GFR by the CKD-EPI 18 ml/min/1.72 m2) and potassium 5.5 mEq / L. In the coagulogram: APTT - 2.51 (norm 0.75-1.25), PR - 50% (norm 85-110%), TT > 3 (min 27-33 sec). Fecal occult blood test was strongly positive. Microhematuria had not been detected. Also observed dabigatran concentration in the blood plasm - 980 ng / ml. There were no any pathological changes in the esophagogastroduodenoscopy. A colonoscopy was planned, but the patient refused the procedure. Spironolactone, dabigatran, enalapril were stopped. The patients had received intravenous iron therapy, as well as red blood cell mass and fresh-frozen plasma infusion until the state became stable. All parameters in coagulogram were in normal ranges within five days. The patient was discharged on a stable state without anticoagulant therapy. Three month later, when hemoglobin reached 110 g / l and creatinine decreased to 1.4 mg / dL (GFR by the CKD-EPI 49 ml/min/1.72 m2), warfarin had been started.

Conclusion: 1. Renal injury is a known adverse effect induced by the combined use of angiotensin-converting-enzyme inhibitor and spironolactone, however there is no increased risk of nephrotoxicity in clinical trials. When reduced kidney function, it should be noted the pharmacokinetics of concomitant drugs that have renal clearance. 2. The patient had increased TT, APTT and decreased PR, as well as dabigatran concentration in the blood plasm 980 ng / ml, that indicate an overdose of this drug. 3. Taking into account the inability to predict the safety of NOAK therapy, this patient was assigned warfarin. 4. This case emphasizes the importance of drug-drug interaction in polypharmacy, which is unavoidable in the treatment of chronic heart failure.

P2025

Early and delayed cardiac injuries as a consequence of blunt chest trauma

C Cristina Asla Ormaza[1]; A Elorriaga Madariaga[1]; PM Mendoza Cuartero[1]; A Arregui Lopez[1]; A Andres Morist[1]; RJ Saez Moreno[1]; R Martinez De Bourio Uriarte[1]; L Ruiz Gomez[1]; N Garcia Ibarrondo[1]; G Ramirez-Escudero Ugalde[1]; G Aurrekoetxea Bajeneta[1]; A Ullate De La Torre[1]; I Bravo Martinez[1]; JM Aguirre Salcedo[1]

[1]Hospital de Basurto, Bilbao, Spain

We report a case of a 72-year-old man in outpatient follow up because of nonischemic dilated cardiomyopathy with mild to moderately depressed left ventricular ejection fraction (LVEF) and atrial fibrillation (AF). On the last echocardiogram, one year before the event, he presented an end-diastolic diameter of 70 mm with a LVEF of 42%, but no wall motion abnormalities neither significant valvular disease, and a normal right ventricular systolic function. He used to ride a bicycle 50 kilometres three times per week, until he suffered a cycling accident with blunt chest trauma.

On admission to hospital, the patient was conscious and hemodynamically stable. Electrocardiogram showed AF and rapid ventricular response with incomplete right bundle branch block morphology. Thoracic computed tomography was performed to detect other complications of blunt chest trauma. Along with multiple rib fractures, left clavicle and scapula, mild pericardial effusion was visualized. The patient was transferred to the intensive care unit. Analytics then revealed elevation of cardiac biomarkers, with an initial troponin I of more than 50000, being diagnosed as a cardiac contusion.

Once the patient was stabilized, he was transferred to a hospital ward. Control echocardiogram displayed moderate LVEF with mid and basal inferoposterior akinesia and severe functional mitral regurgitation. Being hospitalized, he developed cardiac tamponade requiring pericardiocentesis with drainage of serohematic fluid. After one month and a half, he was finally discharged home.

Two months later, the patient returned to hospital with heart failure. He already presented a severely dilated left ventricle with an end-diastolic diameter of 80 mm and severely depressed LVEF (28%), with mid and basal inferoposterior scar, severe mitral regurgitation and moderate dilation and systolic disfunction of right ventricle, with moderate tricuspid regurgitation and moderate pulmonary hypertension. Cardiac magnetic resonance was not practiced because of the presence of splinters. A coronary angiogram would confirm absence of coronary lesions.

Although it uses to heal spontaneously, cardiac contusion can sometimes leave delayed sequelae, involving pericardium, atrioventricular and semilunar valves, coronary arteries and conduction system. Heart failure can be an early or relatively late sequel and it is sometimes progressive. Wall motion abnormalities are also rather frequent. Furthermore, trauma can originate or even impair a previous heart disease. In the case we present, cardiac contusion was early identified mainly due to associated chest wall lesions. However, low energy trauma can also cause cardiac contusion which probably goes unnoticed, being more difficult its diagnosis out of the acute phase. As heart injuries following trauma can progress gradually and leave delayed sequelae, considering the possibility of a previous trauma is of the utmost importance in cases of unexplained heart disease.

P2026

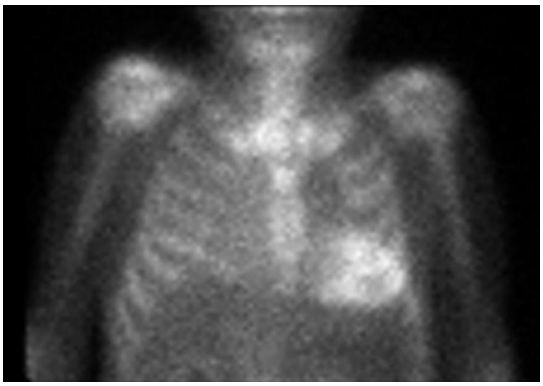
An unrecognized case of infiltrative heart disease

AC Baroncini[1]; A Pratesi[2]; A Lo Forte[1]; C Ghiara[1]; E Carrassi[1]; S Parlapiano[1]; A Herbst[1]; G Biagioni[1]; F Fedeli[1]; M Di Bari[2]; A Ungar[2]; F Orso[2]; S Baldasseroni[2]

[1]University of Florence, Florence, Italy; *[2]Careggi University Hospital (AOUC), Florence, Italy*

Presentation of case: Male, 90 years old, with a history of hypertension, dyslipidaemia, chronic kidney disease stage G2 KDIGO, bilateral carpal tunnel syndrome. Permanent atrial fibrillation (AF) since 2015: at that time main echocardiographic findings were left atrial enlargement, left ventricular hypertrophy (LVH) (interventricular septum (IVS) thickness 14 mm, posterior wall thickness 14 mm), small pericardial effusion. In 2016 appearance, and progressive deterioration, of signs and symptoms of heart failure (HF) and, in june 2017, the patient was sent to our HF clinic: electrocardiography (ECG) revealed AF with a slow ventricular response and low voltages in limb leads while echocardiography revealed left atrial enlargement, progression of LVH (IVS thickness 17 mm, posterior wall thickness 16 mm), diastolic dysfunction, mild pericardial effusion and moderate tricuspid regurgitation. We managed signs and symptoms of HF with optimisation of medical therapy and, considering the rapid progression of LVH, ECG and echocardiographic findings, we started a diagnostic workup in the suspicion of infiltrative disease. Cardiac Troponin I measurement and workup for a monoclonal protein process resulted at the upper

limit of normality; he also underwent 99mTcPYP scintigraphy that revealed a significant diffuse myocardial 99mTcPYP uptake. Furthermore, in july 2017, a pace maker was implanted due to the evidence on Holter ECG of AF with a slow ventricular response and several pauses. Finally, taking into account the history of the disease, the ECG and echocardiographic findings and the diffuse myocardial 99mTcPYP uptake, ATTR cardiac amyloidosis (ATTR-CA) was diagnosed. **Conclusions:** ATTR-CA is a progressive disorder that typically affects white older males leading to significantly reduced survival and quality of life. Acquired wild-type variant (ATTRwt-CA) is often an unrecognized cause of diastolic HF due to hypertrophic restrictive cardiomyopathy, frequently misdiagnosed as hypertensive heart disease or hypertrophic cardiomyopathy. ATTRwt-CA is associated with and increased rates of AF, bundle branch block and varying degrees of heart block, valves thickening, small pericardial effusions and angina with normal coronaries. Carpal tunnel syndrome often precede clinical HF by several years. New diagnosis of hypertrophic cardiomyopathy in an elderly patient may raise suspicion of ATTRwt-CA while the classic hallmark of CA is the combination of low voltage on ECG and increased left ventricular wall thickness on echocardiogram; subsequent laboratory tests or cardiac imaging, in particular 99mTcPYP scintigraphy, are used to confirm the diagnosis. Treatment includes management of cardiac symptoms and treating the underling amyloid disease; significant progress has been made and, given the fact that ATTRwt-CA is more common than previously recognized and even more treatable, early diagnosis and prompt initiation of therapy are important.



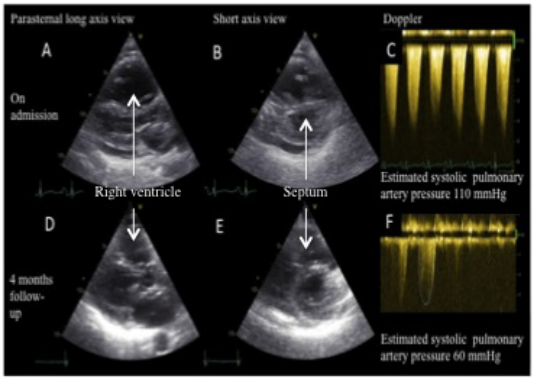
99mTcPYP scintigraphy

P2027

Cardio-oncology; more than left ventricular systolic dysfunction

G Gulati[1]; E Berge[1]; S Holmen[1]; TG Von Lueder[1]
[1]*Oslo University Hospital, Ullevål, Department of Cardiology, Oslo, Norway*

Introduction: A rare but severe complication of treatment for chronic myeloid leukaemia (CML) with dasatinib (a protein kinase inhibitor) is pulmonary hypertension. There is limited evidence on how these patients should be followed.
Case Report: A 29-year-old female with paroxysmal atrial fibrillation was referred to the cardiology department for shortness of breath. The symptoms had started two months previously and deteriorated so that she could barely walk without getting



breathless. The patient had been diagnosed with CML in 2008 and put on imatinib. Due to lack of optimal efficacy and side effects, her therapy had been changed to dasatinib in 2011. On clinical examination a holosystolic murmur was noted over the heart and diminished lung sounds in the base on the right side. Her vitals, including oxygen saturation was normal. Computed tomography excluded pulmonary embolism. Echocardiography revealed a pulmonary artery systolic pressure of 110 mmHg and markedly dilated right ventricle with paradoxical septal motion (Figure 1, panels A, B and C). There was no left ventricular or valvular dysfunction. Pulmonary function test revealed no significant pulmonary disease. Circulating biomarkers of connective tissue disease and HIV were negative. Invasive right heart catheterization confirmed severe precapillary pulmonary hypertension with mean pulmonary arterial pressure of 46 mmHg and pulmonary vascular resistance of 10 WU. On the six minutes walk test the patient achieved a distance of 395m. Dasatinib was discontinued, and the patient commenced therapy for pulmonic hypertension with tadalafil and macitentan. Bosutinib was given for her CML. On follow up four months later her symptoms had greatly improved. Echocardiography showed a marked drop in pulmonary artery systolic pressure at 60 mmHg (Figure 1, panels D, E and F). Repeat right heart catheterization confirmed improvements (mean pulmonary arterial pressure was 31 mmHg and pulmonary vascular resistance 11 WU). Her six minutes walk test showed a marked 25% improvement to 500m.
Problem and Discussion: Despite the abundance of novel effective agents constantly being introduced into oncology, little is known about their potential adverse effects on the cardiovascular system. While the field of cardio-oncology commonly focuses on left ventricular dysfunction, this case of extreme drug-induced precapillary pulmonary hypertension and imminent right ventricular failure illustrates the broad spectrum which cardio-oncology constitutes. High clinical vigilance and a close collaboration between cardiologists and oncologists are vital for optimal management of these patients.
Conclusion: This case of severe precapillary pulmonic hypertension and right ventricular dysfunction in a young female is an important reminder of the rare but severe complication of cancer treatment with dasatinib and the need for multidisciplinary management in cardio-oncology.

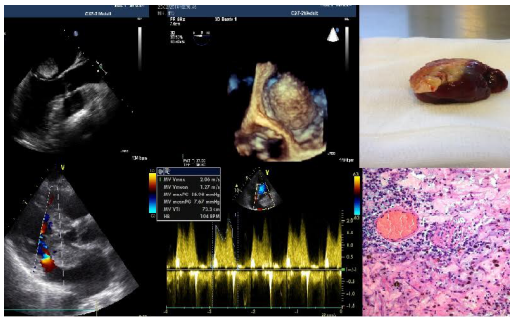
Chronic Heart Failure - Diagnostic Methods

P2028

Incidental atrial myxoma in two asymptomatic patients: a case report

G Muckiene[1]; A Kavoliuniene[1]; D Rimkeviciute[1]
[1]*Lithuanian University of Health Sciences, Department of Cardiology , Kaunas, Lithuania*

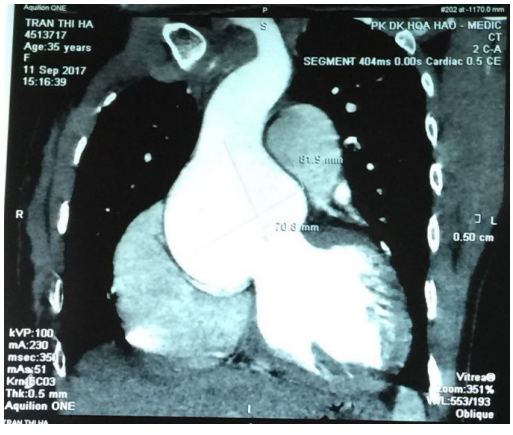
A 60 year-old driver was reffered to preventive examinations in order to prolong his driver's licence. Electrocardiogram showed atrial fibrillation which was asymptomatic, duration and origin unknown. Elective cardioversion and oral anticoagulations were recommended, as where was no previous chonic heart disease. However, termination of cardiac rhythm disturbance with direct current cardioversion and pharmacological therapy failed. Then 2D echocardiography was performed in order to reveal any structural heart disease that could be associated with resistant arrythmia, and the mass of 2,96 x 2,7 cm was revealed, with a stalk attached to the atrial septum in enlarged left atrial (47 mm), no other abnormalities were detected.
Physical examination did not reveale any clinics signs of left atrial enlargement just normorythmic atrial fibrillation.
On trasthoracic echocardiography oval mass of 35 x 27 mm attached to the inferior part of atrial septum in short distance from the aortic and mitral valve annulus. The mass was fixed to the atrial septum.
Preoperative coronarography detected unusual vascularisation of the mass supplying blood from the circumflex coronary artery without significant coronary artery stenosis at age of 60.
Transesophageal echocardiography (TEE) was performed in order to clarify relation with left atrial walls.
The patient was referred to open heart surgery. A large, 3 cm × 3 cm × 4 cm solid encapsulated mass, attached to atrial septum and posterial left atrial wall, was successfully removed, and histopathological examination showed typical morphologic features of myxoma.
Case II. Woman with hypertensive heart disease and incidentaloma
A 58 year-old asymptomatic woman was referred to cardiologist consultation due to hypertension.
Physical examination revealed a loud first heart sound and additional a diastolic rumble.
Echocardiography was performed in order to clarify structural abnormalities characteristic to hypertensive heart disease but revealed incidentaloma - large (30 × 49 mm) and mobile mass with a stalk attached to the interatrial septum. The tumor from the left atrium prolapsed into the left ventricle through the mitral valve during diastole causing obstruction of atrioventricular orifice, thus typical signs of pseudomitral valve stenotic lession was clarified.
Nor coronary artery stenotic lesions neigher vascularisation of the left atrium mass was detected on preoperative coronarography. Open heart surgery was performed resulting in successful removal of the large (3,5 × 4,0 × 3,5 cm) tumor in the left atrium.



Histopathological examination showed typical features of myxoma.
In summary, both case reports illustrate uncommon course of primary cardiac tumors that may remain almost asymptomatic or present with non-specific cardiac conditions.

P2029
A case of aneurysms of the sinus of valsalva
H Thai Hao Phan[1]
[1]*Pham Ngoc Thach University of Medicine, Cardiology, Ho Chi Minh, Vietnam*

Introduction: Aneurysms of the sinus of Valsalva are very uncommon, with an incidence ranging from 0.1 to 3.5% of all congenital heart defects. Such aneurysms account for only 0.14% of all open heart surgical procedures. Aneurysms of the sinus of Valsalva are usually diagnosed as an incidental finding or after an acute rupture into an adjacent cardiac structure. Before rupture, aneurysms of the sinus of Valsalva may present with conduction-system abnormalities attributable to erosion into the interventricular septum, thromboembolism originating in the aneurysm sac, and myocardial ischemia attributable to coronary compression. We report a case of aneurysms of the sinus of Valsalva associated with severe aortic valve regurgitation.
Case: A 35-year–old female with no past medical history was admitted for exertional dyspnea during 2 weeks. There was no relevant family history. Her cardiovascular physical examination was significant for a 4/4 diastolic murmur at at third left intercostal space and other peripheral signs: Corrigan pulse, Hill's sign, Duroziez's murmur. Her admission ECG showed sinus rhythm with a heart rate of 91 bpm, left ventricular hypertrophy. Her portable chest x-ray was significant for cardiomegaly. Because of these abnormal findings the patient underwent a transthoracic echocardiogram, which revealed a massively enlarged aortic root with large sinuses of Valsalva aneurysms measuring 7.5 cm in diameter. Severe aortic regurgitation was present, and left ventricular function was normal. The patient was further evaluated by computerized tomography of the ascending aorta. This imaging modality further confirmed the findings in the echocardiogram. These findings were not previously known by the patient. The patient denied any signs or symptoms of cardiac ischemia or embolic complications such as stroke. Subsequently, the patient will undergo modified Bentall surgical repair of her sinus of Valsalva associated with severe aortic valve regurgitation.



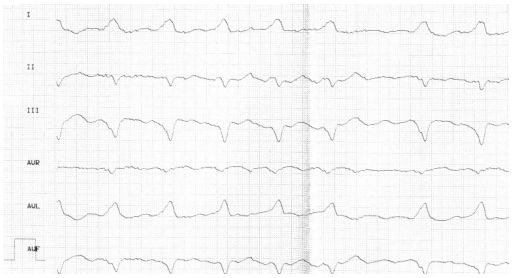
cardiac MSCT

Discussion: Sawyers et al demonstrated a mean survival period of 4 years in patients with untreated ruptured sinuses of Valsalva aneurysms, a finding that favors the need for early surgical intervention in this group. The optimal management of an asymptomatic, nonruptured aneurysm is less clear because of the absence of a precise natural history. Improvements in surgical technique in the past 15 years have resulted in low complication rates with no early mortality (0%) and low morbidity (4%).
Conclusion: Sinus of Valsalva Aneurysms are rare congenital or acquired cardiac defects that have been increasingly diagnosed as a result of improved imaging techniques. This is a case of aneurysms of all 3 coronary sinuses presenting with no clinical signs or symptoms. Despite being asymptomatic and having a favorable course thus far, we recommended that our patient have surgery performed as soon as possible to minimize the risk of future cardiovascular events.

Chronic Heart Failure - Treatment

P2030
CRT and the fight for sinus rhythm to survive
V Lebedeva[1]; T Lubimceva[1]; A Kamenev[1]; K Malikov[1]; S Gureev[1]; D Lebedev[1]
[1]*Almazov National Medical Research Centre, Saint Petersburg, Russian Federation*

A 46-year-old man with a short history (2 months) of persistent left atrial flutter (AF) had progressive fatigue, dyspnea, edema and other symptoms of heart failure (HF) since arrhythmia manifestation. Initial tests revealed raised levels of brain natriuretic peptide (617 pg/mL) and a left bundle branch block (LBBB). An echocardiogram showed left ventricle (LV) diffuse hypokinesia, severe systolic dysfunction (Simpson ejection fraction - EF 23%), left atrium size 55 mm, severe mitral regurgitation, moderate tricuspid regurgitation (TR) and interventricular dyssynchrony. The HF etiology was tachycardia-induced cardiomyopathy.
His congestive symptoms improved with optimal HF therapy only for 1 month and then the patient was urgently hospitalized to hospital with decompensated HF. Coronary angiography showed no signs of atherosclerotic lesions. After 2 months with a target anticoagulant therapy and amiodarone background cardioversion was carried to restore sinus rhythm, but it was failed thrice. CRT-D was implanted with LV electrode in the basal segment of the LV lateral wall. Then radiofrequency (RF) isolation of the pulmonary veins has been made. Sinus rhythm was restored. Patient felt better. However, 2 weeks later recurrence of AF occurred followed by fast HF decompensation. Second RF ablation of AF urgently carried. During the ablation procedure it has been revealed large LV electrode loop in the right ventricle with tricuspid regurgitation increasing from moderate to severe. So, LV electrode reposition was done with the elimination of tricuspid regurgitation. Because of the AF continuing, large left atrial size and HF decompensation patient was a candidate to the atrioventricular (AV) nodal ablation for decreasing the heart rate and proper CRT working. However, it was decided to hold third attempt of left atrial flutter RF ablation. 3 months after the last procedure the patient had stable sinus rhythm, LVEF 46%, no LV dyssynchrony. 5 months later LVEF was 61%, no LBBB, left atrium size became 41 mm and NYHA class I. Eventually patient was operated 5 times during 6 months to keep the sinus rhythm and to reduce heart failure symptoms.
Conclusions: and implications for clinical practice. The tachycardia-induced cardiomyopathy leads to rapid disability and HF progression. AV nodal ablation should not be the first choice for tachycardia-induced cardiomyopathy treatment. Preservation of native AV conduction seems better then artificial AV blockade. Interventional treatment of tachyarrhythmias makes a significant contribution to the HF treatment in spite of the low LVEF and disease severity.



Baseline: left atrial flutter with LBBB

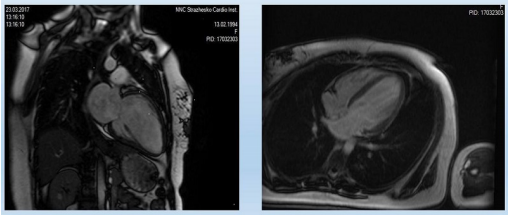
P2031

Use of bromocriptine in a patient with peripartum cardiomyopathy

I Igor Katsytadze[1]
[1]*O. Bogomolet's National Medical University, Kyiv, Ukraine*

Female, 28 y. o., on the 18th day after childbirth (the first pregnancy, the first birth) applied for medical help with complaints of dyspnea at rest, which was intensified during the conversation, expressed swelling of the legs, puffiness of the face, general weakness, cough, palpitation.
Symptoms appeared a week before the childbirth (earlier, according to the words, the patient felt well throughout the pregnancy period),
On a scheduled visit to a gynecologist, the patient's condition was regarded as satisfactory, and the symptoms as a manifestation of functional dystonia.
The patient was hospitalized on a routine basis in the clinic a day before the delivery. The birth took place physiologically.
On the second day of stay in the hospital, the patient felt worse (increasing in the above symptoms, especially dyspnea and tachycardia).
Status objectivus:
•During hospitalization, she is severe dyspnea. Ortopnoe. Acrocyanosis. Generalized edema
•The body mass index is 27.2 kg / m2.
•Blood pressure 100/50 mm Hg . Wet rales less than 50%.
•Heart sounds are arrhythmic (extrasystole beats) , tachycardia with heart rate = 118 beats per minute. Systolic murmur at all points of auscultation, with a maximum of expression at the apex.
•The liver protrudes 3.5 cm below the edge of the right rib, slightly painful. The spleen is not palpable
MRI is attached
ECG, ECHO - will be posted
Treatment :
•Bromocriptine 2,5mg Od, enoxaparin 40mg x2, Levosimendan, Torasemid, ASA 75mg, Eplerenon 25mg, Enalapril 5mg, Carvedilol 2,5mg, Ivabradin 5mg x2
Discharge on 10th day with positive dynamic.
BP- 105/75 mmHg, HR- 80' . Significant reduction of HF symptoms. GFR increased to 106 ml/min/1,73m2.
Further treatment: enalapril, carvedilol, eplerenon, diuretics, rivaroxaban, ivabradin
6 Mo later: No complaints, skin is pale pink, no edema, BP 108/72 mm Hg, HR at rest 63', rhythmic, Vesicular breathing, no crepitation, The border of the heart is not expanded. Positive dynamic on ECHO (LVOT- 22 mm, Ao- 25 m?, LA - 28 m? (V-50 ml), IVS – 9 mm, EF- 44%, EDV - 113 ml, ESV - 59 ml, RV- 39 mm, RA- 31 mm. PAP - 15 mmHg)

Contrast MRI (Tomovist-20 ml) – dilatation of all cavities, global hypokinesis. Absence of ischemic injury, fibrosis, edema is more evidence in favor of cardiomyopathy. Moderate pulmonary hypertension



MRI

Chronic Heart Failure - Clinical

P2032

Stroke and heart failure causing myocardial metastases - a frequent primary tumor with its rare cardiovascular consequences

M Rabai[1]; L Toth[2]; L Szapary[3]; V Sarosi[1]; E Kalman[4]; K Toth[1]; T Habon[1]
[1]*University of Pecs, Medical School, 1st Department of Medicine, Pecs, Hungary*;
[2]*University of Pecs, Medical School, Department of Radiology, Pecs, Hungary*;
[3]*University of Pecs, Medical School, Department of Neurology, Pecs, Hungary*;
[4]*University of Pecs, Medical School, Department of Pathology, Pecs, Hungary*

Introduction: Primary tumors of the myocardium are extremely rare. Metastatic lesions of the heart muscle occur in a few percentages and their diagnoses are usually made in late stages.

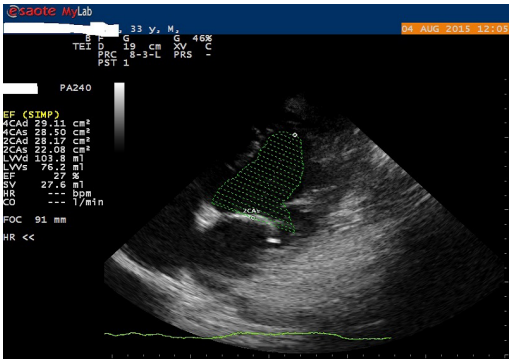
Case history: A hypertensive, formerly smoking 72 year old male patient was admitted to the Stroke Division of Neurology Department, with symptoms of stroke and heart failure. In the background, vascular and cardiogenic origins were also hypothesized. While CT angiography showed significant right carotid artery stenosis, ECG revealed newly diagnosed atrial fibrillation. Echocardiography demonstrated a massive, inhomogeneous and mobile infiltration with thrombotic surface in the heart muscle of the left ventricle and moderate amount of pericardial effusion was noticed, which did not cause cardiac tamponade. Due to the observed changes, a cardiac MRI scan was done showing preserved ejection fraction, nodular infiltration of the heart muscle resulting in myocardial disorganization and metastatic pericardial effusion. Besides the cardiac alterations, a 3x4 cm right sided, central lung cancer with numerous metastases was diagnosed by a chest CT scan. Further investigations were made for histological diagnosis in the Division of Pulmonology, but these diagnostic efforts failed. After that the clinical state of the patient progressively deteriorated and he died in heart failure within a short time. During the autopsy, a planocellular lung carcinoma showing fusocellular appearance with unusual muscle metastases (myocardial, skeletal and lingual) was verified. The massive myocardial infiltration resulted in a thrombogenic endocardial surface causing stroke and a progressive heart failure, which ended in the death of the patient.
Conclusion: Although atrial fibrillation can mostly be seen in the background of a cardiogenic stroke, the routinely performed echocardiography may reveal other rare etiology also.

P2033

Refractory heart failure and ischemic stroke as first symptoms signs undetected cryptogenic chronic endocarditis

N Zlatanovikj[1]
[1]*Private medical practice "Cor-Medico", Skopje, Macedonia The Former Yugoslav Republic of*

Newly diagnosed end stage heart failure in young patients causes numerous diagnostic, therapeutic, and ethical dilemmas. If combined with an ischemic stroke with no apparent reason, the dilemmas multiply.
33 y/o patient was referred to cardiologist office for examination due to persistent, non-productive cough and lying dyspnea. The symptoms occurred 5 days previously, and he was treated with antibiotics for suspected right lobar pneumonia. Patient denies any previous cardiac illnesses, but mentions that year before had a high fever and that the cough is present in lesser extent months ago.
At his physical examination he has tachycardia, few medium cracks in the right hemithorax, mild pretibial edema. The BP was 95/70. ECG registered heart beat 117/bpm with inverse T waves in all precordial leads. Echocardiography revealed dilatation of all heart chambers, thinned walls, severe hypokinesis, LVEDd of 71mm and decreased ejection fraction of 30% (Simpson bi plane). It also revealed mitral regurgitation, moderate aortic and tricuspid regurgitation and still no signs of pulmonary hypertension. Apart from thickened mitral valve leaves, no significant sign of vegetation was observed. Patient was classified in NYHA II-III class. Patient was placed on standard heart failure treatment with loop and Potassium sparring diuretic and beta blocker. He continued to receive medical treatment for his pulmonary ailment.



Ejection Fraction

After 7 days he was referred by his GP to the cardiology clinic for further evaluation. While at the clinic the suffered ischemic stroke which was treated with thrombolysis with good response. Five days later he was discharged in relatively good condition with moderate speech problems and no other neurogical consequences. He was placed on antiplatelet therapy (aspirin) An ACE inhibitor was added. However his echocardiogram has deteriorated with LVEDd now measuring 80mm and EF in 20's % .His physical finding did not reveal any significant changes. His unilateral

lung finding persisted unchanged even after multiple antibiotic therapy. Pulmonary assessment tests suggested partial chronic respiratory insufficiency .
7 days latter due to fall in the blood pressure 70/50mmHg and extreme fatigue he was readmitted to the cardiology clinic, put on i.v. diuretics, positive inotropes. Simultaneously he developed behavioral changes and aphasia suggestive of new cerebrovascular incident, although he is now on anticoagulation therapy. A hemoculture was done and turned positive on Klebsiela species. The patient's condition continues to deteriorate and he passed away of multiple organ failure.
Sudden onset of refractory heart failure accompanied with ischemic stroke with no evidence of septal defects, are highly suggestive of cryptogenic chronic endocarditis. It's diagnosis remains elusive and circumstantial, making the treatment delayed and often futile and prognosis poor.

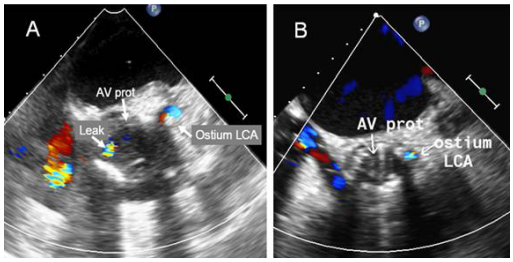
Acute Heart Failure - Diagnostic Methods

P2034

Diagnostics of left main coronary artery occlusion during aortic valve replacement

EV Elena Dzybinskaya[1]; EE Vlasova[1]; RS Akchurin[1]
[1]*National medical research center of cardiology, Cardiovascular Surgery, Moscow, Russian Federation*

Coronary ostial stenosis is a rare but potentially serious complication after aortic valve replacement, whereby the effective intraoperative imaging plays a key role in correct decision making.
A 63 years old man was scheduled for early repeated aortic valve replacement (AVR) because of paravalvular leak. He had fatigue, dyspnea, left ventricular (LV) ejection fraction (EF) 27%, and signs indicating low output state. Pretreatment with Levosimendan was performed one day before surgery.
Repeated AVR was performed under cardiopulmonary bypass (CPB, 137 min) as planned. The weaning from bypass was difficult - visually observable LV failure and arterial hypotension persisted despite the high doses of dopamine (6-12 mcg*kg-1*min-1) and norepinephrine (400 ng* kg-1*min-1). The preliminary version was myocardial failure as a consequence of the preoperatively lowered LVEF. The transoesophageal echocardiography (TOE) showed LV systolic failure (EF <20%) and acutely emerged mitral regurgitation. The partial occlusion of the ostium of the left main coronary artery with prosthetic valve sewing ring was detected to be the cause of these disturbances. The most important diagnostic criterion was the change of the left main flow characteristics from laminar (before CPB, Fig., A) to turbulent (Fig., B) by color flow Doppler. Because the valve function was satisfactory, decision to perform the coronary artery bypass grafting was made. Repeated CPB (151 min) was initiated, left anterior descending and left circumflex arteries were shunted by autovenous grafts. Echocardiographic control demonstrates the LVEF increasing up to 35%, and weaning from CPB was successful with small doses of dopamine. The postoperative course was uncomplicated, and the patient was discharged from hospital with LVEF 43%.
The most important problem, which was solved on time in this case, is the differential diagnostics of causes of severe acute heart failure.
The intraoperative TOE, as a method of anaesthesiological management, is a corner stone of early diagnostics of different types of myocardial dysfunction.

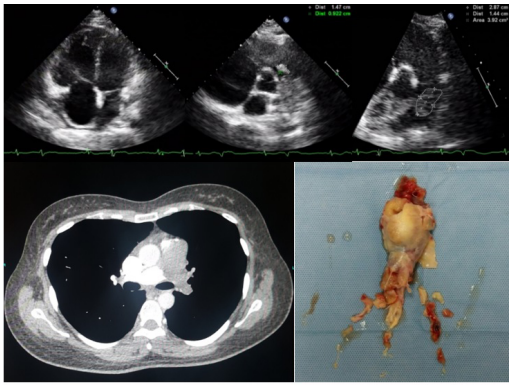


P2035

Right sided heart failure: a tumor or a thrombus?

M J Jhessica Pecson[1]
[1]*Philippine Heart Center, Adult Cardiology, Quezon City, Philippines*

This is a case of a 36-year old female without co-morbidities who presented with sign and symptoms of a right-sided heart failure. Physical examination showed an RV heave, a loud P2 and a holosystolic murmur at the left parasternal border. Sinus rhythm with RV hypertrophy was noted on ECG. Chest X-ray revealed cardiomegaly. Transthoracic echocardiography noted a fluttering echogenic density from the MPA protruding through the pulmonic valve, a dilated RV with signs of pressure and volume overload and severe pulmonary hypertension. Thrombolysis and anticoagulation were administered, however the patient remained symptomatic. Chest CT scan was then done, which showed a large pulmonary artery filling defect in the main and left pulmonary arteries suggestive of thromboembolism, however malignancy cannot be ruled out. Progression of the right heart failure despite medical therapy prompted surgical intervention. The patient underwent pulmonary endarterectomy. Intraoperatively, a pulmonary artery mass consistent with a myofibroblastic sarcoma with myxoid features was noted. Patient succumbed to death due to RV failure on the second post-operative day.



Pulmonary artery sarcoma

Acute Heart Failure - Treatment

P2036

A case of cardiogenic shock caused by anterolateral papillary muscle rupture: when imaging makes the difference.

I Figliuzzi[1]; A Romaniello[1]; G Gallo[1]; M Grimaldi[1]; A D'angelo[1]; M Volpe[1]
[1]*Sant' Andrea Hospital, Division of Cardiology, Department of Clinical and Molecular Medicine, Faculty of Medicine, Rome, Italy*

A previously healthy 55-year-old man, presented to the emergency department with chest pain and shortness of breath started after an intensive exertion. He denied fever and recent infective episodes. His blood pressure was 85/50 mmHg; heart rate was 120 beats per minute. Arterial blood gas analysis showed severe hypoxaemia. The electrocardiogram showed sinus tachycardia with a 3 mm ST depression in leads II, III, aVF, from V3 to V6, and ST elevation in leads I and aVR. Bedside transthoracic echocardiography showed preserved left ventricular ejection fraction without regional wall motion abnormalities, moderate mitral regurgitation posteriorly directed and absence of pericardial effusion. Since the clinical scenario suggested an acute myocardial infarction without ST elevation complicated by papillary muscle dysfunction, the patient underwent emergency cardiac angiography, which showed small intermediate and marginal branches occlusion but percutaneous coronary intervention was not feasible due to their small sizes. To better evaluate mitral regurgitation mechanism, transoesophageal echocardiogram was performed, detecting severe mitral regurgitation with anterolateral papillary muscle rupture. Due to the persistence of cardiogenic shock, orotracheal intubation was performed and noradrenalin infusion was started and progressively uptitrated. Intraortic balloon pump was positioned, obtaining only a mild increase in blood pressure without considerable improving of gas exchanges and lactate levels. Thus, the patient underwent emergency mitral valve replacement with mechanical prosthesis. Histological analysis of native valve and of papillary muscle showed aspecific fibroblastic endocarditis, whereas bacteriological examination assessed an infection by Staphylococcus aureus and Staphylococcus Warneri, treated with antibiotic therapy with Vancomycin. The patient was discharged eventually after about two weeks. The differential diagnosis was challenging and included endocarditis and myocardial infarction. On one hand there is the detection of bacterial infection of the valve, although blood cultures and inflammatory markers were negative, and there were no microscopic or macroscopic signs of bacterial colonisation in the histological analysis, suggesting a possible contamination of the sample. On the other hand the more likely ischemic mechanism, supported by the angiographic finding of small vessels occlusion and troponin I hs peak of 71338 pg/ml, compatible with an acute myocardial injury. Since cardiogenic shock is marked by high mortality rate, it is very important the prompt identification of cardiogenic shock as well as the careful research of the underlying causes, even throughout the use of invasive exams and

procedures. This case also illustrates the importance of early surgery intervention in patients with hemodynamic instability, since medical treatment is associated with poor short- and long-term survival.

Antero-lateral papillary muscle

Coronary Artery Disease - Treatment

P2037

Myocardial infarction with nonobstructive coronary arteries twice in one week

A Gomiscek[1]; M Bunc[2]; G Plevnik[1]
[1]*Izola General Hospital, Department of Internal Medicine, Izola, Slovenia*;
[2]*University Medical Centre of Ljubljana, Clinical Department of Cardiology, Ljubljana, Slovenia*

A 47-year-old female smoker without previous medical history presented to the emergency department (ED) with chest pain lasting for about twelve hours. She described the pain as a substernal pressure sensation (7/10 on VAS), the pain was radiating up to the shoulder and independent of movement or breathing.
Clinical examination was insignificant.
12-lead electrocardiogram (ECG) showed sinus rhythm, T-wave inversion in precordial leads V2 - V6, with poor R-wave progression (Fig. 1).
Troponin I was found as 482 ng/L (cut off 40 ng/L). Other lab work was within normal limits.
Bed-side echo showed akinesia of anteroseptal and apical left ventricular segments (Fig. 1).
The patient was administered 500 mg acetylsalicylic acid, 5000 I.U. heparin and 180 mg ticagrelor and referred to the catheterisation laboratory for coronary angiography.
Angiography was performed 30 minutes after drug administration, at that time the patient had no chest pain any more and was feeling much better. On coronary angiography, non-obstructive coronary artery disease was detected, all TIMI 3 flow, and no culprit lesion (Fig. 1).
After two days, the patient was dismissed home with the diagnosis of NSTEMI with no target lesion found, with most likely spontaneous reperfusion of LAD. As myocarditis could not be ruled out we referred the patient to out-patient cardiac MRI and a follow-up TTE in one month. She was discharged with DAPT, ACE inhibitor, betablocker and statin.
Five days later the patient presented to the ED in the middle of the night with chest pain radiating down the left arm. Clinical examination was unremarkable, ECG showed similar abnormalities as at the first admission, troponin levels were slightly elevated.
We believed that intravascular imaging (either intravascular ultrasound (IVUS) or intracoronary optical coherence tomography (OCT)) should be performed to determine the morphology of non-obstructive LM, LAD and LCX coronary artery disease. As intravascular imaging was not available at our institution we transferred the patient to the University Medical Centre. Coronary angiography was performed, no significant stenosis was visible, IVUS revealed significant thrombotic stenosis of the proximal LAD and one drug-eluting stent was successfully placed.
Conclusion: Myocardial infarction with non-obstructive coronary arteries (MINOCA) should be considered as a 'working diagnosis', and thus prompts further evaluation regarding its underlying mechanism(s). Plaque disruption (rupture or erosion), epicardial or microvascular spasm, coronary thrombembolism, coronary dissection, Takotsubo and myocarditis have to be ruled out. IVUS and OCT are more sensitive methods for presenting intracoronary morphology than angiography. As such they should be performed for the determination of the cause of MINOCA. Additional diagnostic tools as fractional flow reserve (FFR) or instant wave-free ratio (iFR) may also be considered in the acute setting.

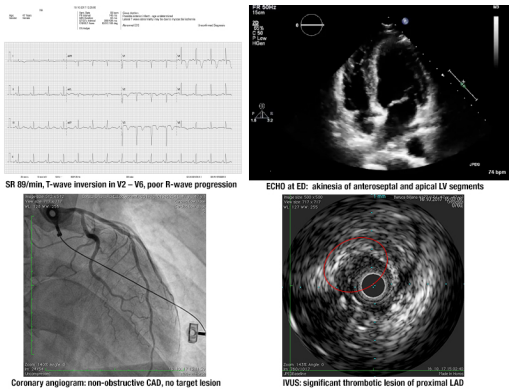


Figure 1

P2038

Polyarteritis nodosa coronary vasculitis leading to pericardial tamponade and severe ischaemic cardiomyopathy.

K Be[1]; H Rashid[1]; A Nasis[1]
[1]*Monash Health, MonashHEART, Melbourne, Australia*

We present a rare case of polyarteritis nodosa coronary vasculitis with pericardial tamponade and severe ischaemic cardiomyopathy.
A 34 year old lady presented with acute chest pain, dyspnoea and syncope. She had no previous medical conditions. She had a systolic blood pressure of 60mmhg on arrival. Examination revealed raised jugular venous pressure and pulsus paradoxus. Electrocardiogram revealed low voltage complexes. Urgent echocardiography showed moderate pericardial effusion (maximal 2 cm apically) with features of pericardial tamponade.
Pericardiocentesis drained 250ml which normalised of her vitals. Subsequent echocardiography revealed dilated left ventricle with moderately reduced left ventricular ejection fraction and non-left anterior descending coronary artery territory hypokinesis. Left heart catheterisation revealed all coronary arteries were severely aneurysmal with features of intra-aneurysmal thrombus in the right coronary artery aneurysms. The first obtuse marginal and first diagonal branch had aneurysmal segments followed by chronic total occlusions.
Laboratory analysis revealed that the pericardial fluid was exudative but had negative microbiology and cytology screen. Her erythrocyte sendiment rate was elevated at 50mm/hr but a c-reactive protein of 6mg/L and negative autoimmune screen. Subsequent computed tomography angiography confirmed liver and renal artery aneurysms, consistent with polyarteritis nodosa (ANCA-negative). She was treated with intravenous cyclophosphamide and high dose corticosteroids. Her erythrocyte sediment rate subsequently improved.
A subcutaneous implantable cardioverter-defibrillator was inserted for primary prevention. Follow-up computed tomography coronary angiogram at 5 months revealed persistence of coronary aneurysms and intra-aneurysmal thrombus. At 8 month review her immunosuppressants were successful weaned, her functional status improved with heart failure treatment and repeat echocardiography revealed mildly improved left ventricular ejection fraction.
The alternative diagnosis of Kawasaki disease rarely presents in adulthood, with the coronary sequalae typically resulting in proximal coronary aneurysm dilation with relatively normal distal segments. Other medium sized vessel may be affected, but very rarely the renal or hepatic vessels. Polyarteritis nodosa commonly affects the renal, hepatic, coronary and gastrointestinal tract with multiple microaneurysms suggestive of diagnosis.
Polyarteritis nodosa coronary vasculitis is a rare but serious cause of coronary artery aneuryms with treatment options available to improve outcomes. While diagnosis of polyarteritis nodosa is ideally made with histopathology, classic imaging findings of beading and aneurysms of medium vessel arteries (coronary, hepatic and renal arteries) strongly suggests diagnosis.

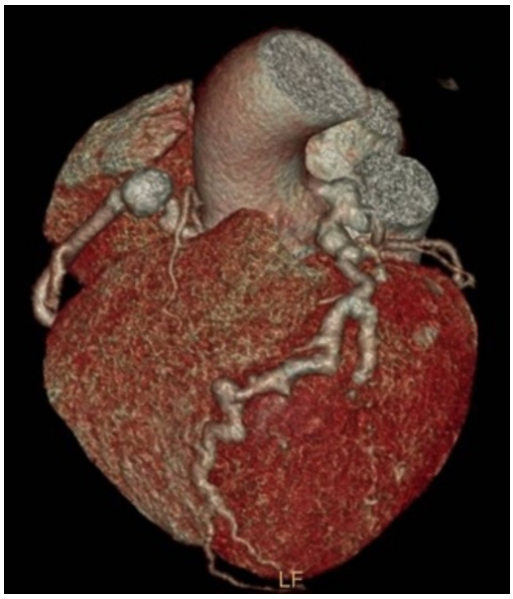


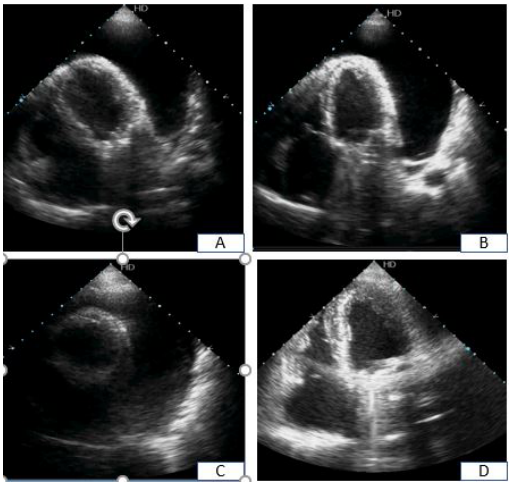
Fig 1

Myocardial Disease - Clinical

P2039
Rare post mitral valve replacement nightmare

A Ahmed Yehia[1]; M Dawood[1]; O Elgebaly[1]; M Hassan[1]; A El Maghraby[1]; F Mohamed[1]
[1]*Alexandria University, Department of Cardiology, Alexandria, Egypt*

The case is 30 years old female whom had mitral valve replacement with mechanical prothesis for correction of severe symptomatic mitral valve stenosis. Postoperatively the patient remained symptomatic with exertional dyspnea grade II that progressed over a course of 1 month to dyspnea grade IV associated with orthopnoea , bilateral lower limb swelling and low grade fever since 3 days.
The patient reports compliance on warfarin with regular check up having INR in the target zone. The patient denied any chest pain, syncope, abdominal pain or any neurological manifestation.
Examination showed blood pressure of 90/70 mmHg, thready pulse at 110 bpm , distant heart sounds , bilateral congested neck veins and bilateral lower limb odema.
Baseline laboratory investigations was unremarkable except for INR of 10 and mildly elevated white cell count 13,000. Chest X ray revealed increased cardiothoracic ratio with flask shaped heart.
Transthoracic echo (TTE) strikingly revealed massive pericardial effusion mainly lateral and apical measuring 5 cm in maximum dimensions as shown in panel (A,B,C) The right ventricle showed normal dimensions, markedly reduced contractility with no pericardial effusion related to the right side. The left ventricle showed severe global hypokinesia with reduced systolic function EF = 25%. Mitral prothesis was well functioning with no visible masses or vegetations. CT chest was done to help characterize the pericardial effusion. CT chest showed fusion of the right ventricle walls to the anterior chest wall explaining the localization of the pericardial effusion and absence of tamponade.
After correction of INR, Pericardiocentesis of 900 ml of straw coloured effusion was done through an apical approach. Analysis of the fluid showed exudate with negative microbiological culture. Pathology of the fluid showed inflammatory smear with abundant neutrophils.
According to characteristics of the aspirate and presence of low grade fever, Post cardiac Inflammatory Syndrome (PCIS). Accordingly treatment with high dose of aspirin 750 mg t.i.d, colchcine 0.5 od, Ramipril, spironolactone, furosemide, pantoprazole was intiated . Regular daily follow up showed absence of effusion recurrence.
2 weeks later, TTE strikingly revealed complete recovery of both left and right ventricular functions with no effusion noted (Panel D).Regular monthly follow up of the patient revealed no interval changes.
To conclude ,PCIS is a very important post operative complication and TTE plays essential rule in diagnosis of this complication. Pericardiocentesis of large post operative effusion is crucial to for symptomatic relief and analysis of pericardial fluid. Although that Post pericardiotomy myocarditis is a very rare condition but its an important cause of post operative LV failure and complete recovery can be anticipated. High dose of aspirin and colchince are the most accepted regimen for intial treatment of PCIS with high success rate.



P2040
Not ischemic, against all odds

AR Ana Raquel Barbosa[1]; P Teixeira[1]; AI Azevedo[1]; M Ponte[1]; N Dias Ferreira[1]; A Dias[1]; M Fonseca[1]; V Gama[1]
[1]*Hospital Center Vila Nova Gaia, Porto, Portugal*

A 75-year-old male patient was referred to our centre due to recent onset heart failure. He had a history of long-standing hypertension, type 2 diabetes mellitus, dyslipidaemia and overweight; he was a former smoker. The patient complained of dyspnoea for ordinary activities for the last 2 months and recent onset oedema. At physical examination an apical systolic murmur and bilateral leg oedema were noted. The electrocardiogram revealed sinus rhythm, first degree atrioventricular block, left anterior fascicular block and right complete bundle branch block. The transthoracic echocardiogram evidenced mild left ventricular dilation with mitral leaflet tethering, particularly of the posterior one, moderate functional mitral regurgitation and lateral, posterior and inferior walls hypokinesis with moderately depressed left ventricular systolic function. Given the clinical and echocardiographic picture, an ischemic aetiology was considered the most likely. However the patient went to a coronary angiogram which showed no epicardial coronary artery disease. He was submitted to cardiac magnetic resonance (CMR) that confirmed left-chambers dilation and depressed left ventricular function (ejection fraction 33%) and showed mural late gadolinium enhancement at basal and mid segments of inferior and inferosseptal walls, suggestive of prior myocarditis.
The patient was started on disease-modifying therapy and symptoms improved significantly. Echocardiogram and CMR were repeated 6 months later and, despite the maintained pattern and extent of late gadolinium enhancement, mitral regurgitation became mild and there was improvement in left ventricular volume and function (ejection fraction by CMR 45%). The aetiology of the myocarditis remained elusive. Myocarditis presents in many different ways, which requires a high degree of suspicion to make this sometimes challenging diagnosis.

P2041
Non-compaction cardiomyopathy: case report

H Hugo Rafael Corrales-Santander[1]
[1]*Corporación Universitaria Rafael Nuñez, GINUMED - Programa de Medicina, CARTAGENA, Colombia*

On behalf of: GINUMED - CORPORACIÓN UNIVERSITARIA RAFAEL NUÑEZ, CARTAGENA DE INDIAS, COLOMBIA
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Introduction: Left ventricular noncompaction (LVNC) is a rare disease with genetic origin, characterized by the presence of numerous myocardial trabeculations probably due to a detention of the normal process of the endomyocardial embryogenesis. **Clinical case:** 38 years-of-age man without pathological history, which had been presented progressive dyspnea, dyspnea at rest and orthopnea since two months

ago. At physical examination, the patient had tachypnea, tachycardia, S3 left ventricular gallop and crackles in the bases of the lungs. The electrocardiogram showed sinus tachycardia and unspecified diffuse changes of ST-T. The thoracic radiography displayed cardiomegaly and signs of pulmonary congestion. Color doppler echocardiography revealed left ventricle severely dilated with multiple trabeculations and intertrabecular spaces. Ambulatory electrocardiography for 24 hours reported sinus rhythm, frequent isolated monomorphic ventricular extrasystoles with episode of monomorphic no supported ventricular tachycardia.
Conclusion: the clinical manifestations, seriousness and the age of beginning of the symptoms of the LVNC are variable. The differential diagnosis must be done with other common pathologies, especially with hypertrophic cardiomyopathy and dilated cardiomyopathy.

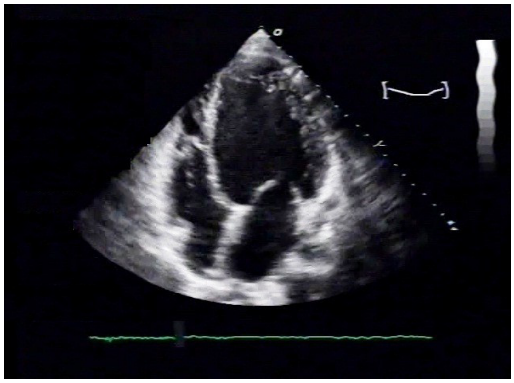


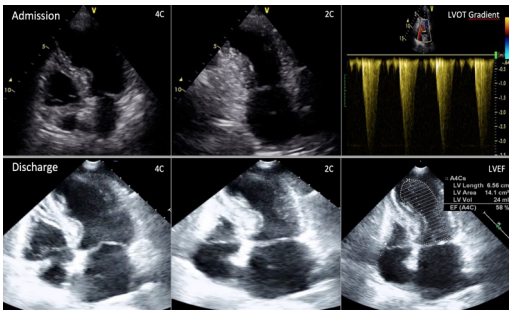
Imagen 1

P2042

A less common cause of dynamic left ventricular outflow tract obstruction

AR Ana Rita Pereira[1]; AR Almeida[1]; I Cruz[1]; A Marques[1]; S Alegria[1]; AC Gomes[1]; D Sebaiti[1]; A Briosa[1]; I Rangel[1]; F Ferreira[1]; O Simoes[1]; MJ Loureiro[1]; H Pereira[1]
[1]*Hospital Garcia de Orta, Cardiology, Almada, Portugal*

A 71-year-old woman, with clinical history of essential arterial hypertension and mixed dyslipidemia, was admitted in our Emergency Department due to a transient, self-limited loss of consciousness, following a familiar discussion, with loss of postural tone resulting in fall and head trauma. After recovering consciousness, the patient (pt) referred oppressive chest pain with dorsal radiation and dyspnea. At hospital admission, she was hypotensive but normocardic with no other relevant findings at clinical examination. Blood tests revealed high-sensitive cardiac troponin T 512 ng/L [normal range (NR) < 13 ng/L] and NT-proBNP 2952 pg/mL (NR < 153 pg/mL). A 12-lead ECG showed sinus rhythm, heart rate of 78 bpm, ST segment elevation in V3 to V5 leads and T wave inversion in V4 and V5. Transthoracic echocardiogram (TTE) demonstrated a normal sized left ventricle (LV), with mild septal hypertrophy, moderate systolic dysfunction and several segmental wall-motion abnormalities (apical segments akinesia, middle segments hypokinesia and basal segments hyperkinesia) conditioning a significant LV outflow tract (LVOT) gradient (peak gradient of 50 mmHg and mean gradient of 26 mmHg). After performing a head computerized tomography to exclude acute traumatic hemorrhagic complications, the pt was submitted to a coronariography that revealed non-significant epicardial coronary lesions. Thus, according clinical and imaging findings, Takotsubo cardiomyopathy (TC) was established as diagnosis. During hospitalization, no complications were observed and beta-blocker therapy was initiated and up-titrated. Pre-discharge TTE showed recovery of LV systolic function (ejection fraction 58%) with segmental contraction improvement (only remaining apical akinesia) and absence of significant intraventricular obstruction. She was discharge, six days after admission, in NYHA functional class II, kept under regular follow-up in Cardiology appointment.
This clinical case is an example of TC which brings together several less common features of this type of cardiomyopathy. On the one hand, the predominant symptom on admission was syncope, unlike most published data in literature that describe chest pain as the most common (75,9%) and syncope occurring only in 7,7% of patients as predominant symptom. On the other hand, dynamic LVOT obstruction has not been described as frequent in TC and lower severity of LV systolic dysfunction is usually observed. Early recognition of dynamic LVOT obstruction is clinically and therapeutically important. Conventional treatment for acute coronary syndrome, the main differential diagnosis of TC, such as nitrates and afterload vasodilators would likely increase the degree of LVOT obstruction, resulting in clinical worsening. Thus, the presenting case intends to highlight the heterogeneity of this clinical entity of increasing interest but there is still a lot to be known about it.

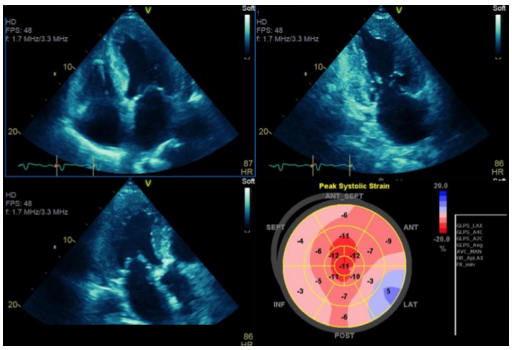


P2043

Left ventricular hypertrophy: the usual suspects, an unexpected culprit

AR Ana Rita Pereira[1]; I Cruz[1]; AR Almeida[1]; A Marques[1]; S Alegria[1]; AC Gomes[1]; D Sebaiti[1]; A Briosa[1]; I Joao[1]; H Pereira[1]
[1]*Hospital Garcia de Orta, Cardiology, Almada, Portugal*

We present the case of an 88-year-old man, with clinical history of essential arterial hypertension, referred to our Cardiology appointment owing to an asymptomatic moderate aortic stenosis evaluated by a transthoracic echocardiogram (TTE). At clinical examination, he was hemodynamically stable without any pulmonary or peripheral congestion sign. A grade III/VI, systolic heart murmur with neck radiation were best heard over the aortic area with preserved aortic second sound (A2). A 12-lead electrocardiogram (ECG) showed sinus rhythm, heart rate of 92 bpm, first-degree atrioventricular block (AVB), left axis deviation and complete right bundle branch block. TTE demonstrated a tricuspid aortic valve with thickened and calcified leaflets resulting in moderate aortic stenosis [peak velocity 3,4 m/s; mean gradient 30 mmHg; Doppler velocity index (DVI) 0,3] and moderate aortic regurgitation; a non-dilated left ventricle (LV) with moderate concentric hypertrophy (interventricular septum 16 mm, posterior wall 14 mm) and normal systolic function but diastolic dysfunction and reduced global longitudinal strain (GLS -7); and a normal-sized inferior vena cava with inspiratory collapse. Given the absence of clinical and imaging indications for valvular intervention, the patient was kept under regular outpatient follow-up (FU), remaining asymptomatic under a low-dose of beta-blocker and angiotensin-converting enzyme inhibitor therapy. After 30 months of FU, he was hospital admitted with complaints of progressive worsening exertional dyspnea (at admission, triggered by mild physical activity) and lower limbs oedema with 1 month of evolution. At admission, he was bradycardic and a third-degree AVB was showed by the 12-lead ECG. Due to symptomatic extreme bradycardia, isoprenaline infusion was initiated and a temporary followed by a definitive dual-chamber pacemaker was implanted. The TTE was similar but a "speckling" appearance of the myocardium and a reduced GLS with LV apical sparing pattern were noticed. Considering the LV findings and the cardiac conduction disease, a 99mTechnetium-3,3-diphosphono-1,2-propanodicarboxylic acid (DPD) was performed with a positive result. Thus, the considered final diagnosis was wild-type transthretin cardiac amyloidosis (wt-ATTR).
This clinical case illustrates an increasingly recognized cause of heart failure (HF) with preserved ejection fraction (HFpEF) and cardiac arrhythmias, especially in men over 60 years of age. Given the burden of HF in society and the economic implications for health-care delivery, emerging targeted therapies are currently being studied in multiple clinical trials. Consequently, the recognition of wt-ATTR will likely continue to be of increasing importance. Ultimately, this clinical case also intends to emphasize the importance of the differential diagnosis of LV hypertrophy and HFpEF.



P2044
This time it was a zebra

AR Ana Raquel Barbosa[1]; C Espada Guerreiro[1]; M Passos Silva[1]; A Mosalina[1]; M Ponte[1]; N Dias Ferreira[1]; R Pereira[1]; M Fonseca[1]; A Dias[1]; J Primo[1]; V Gama[1]
[1]*Hospital Center Vila Nova Gaia, Porto, Portugal*

A 55-year-old male went to the emergency department due to palpitations and a poorly defined chest discomfort during the last 5 hours. He had a history of dyslipidaemia, overweight and smoking habits; he had an intense level of usual physical activity, having been an high competition rower for years.
At admission the electrocardiogram revealed a regular wide complex tachycardia (ventricular frequency about 220/per minute), with left bundle-branch morphology and superior axis. The patient was haemodynamically stable with no signs of heart failure. Adenosine and then amiodarone were tried unsuccessfully; the patient became hypotensive and was electrically cardioverted. The eletrocardiogram post-cardioversion showed no significant alterations. The echocardiogram performed revealed normal left ventricular function but a dilated right ventricle, with free wall hypokinesis and depressed systolic function.
A coronary angiogram was performed to exclude coronary artery disease, however given the typical pattern of the ventricular tachycardia and the abnormalities of the right ventricle the most likely diagnosis at this point was a arrhythmogenic right ventricular cardiomyopathy. The angiogram showed an abnormal origin of the right coronary artery, not possible to be selectively catheterized. Therefore the patient went to an angio-computed tomography revealing a right coronary artery originating high in the aortic left coronary sinus and running between the aorta and the pulmonary trunk; a significant luminal stenosis was evident at the origin.
To better characterize the right ventricle a cardiac magnetic resonance was done, showing right ventricular dilation (index telediastolic volume 117 ml/m2) with regional dyskinesia and mild depression of systolic function (ejection fraction of 45%). Late gadolinium enhancement was evident at the basal inferior and mid-basal lateral segments.
Despite the presence of two major criteria for arrhythmogenic right ventricular cardiomyopathy, we assumed this clinical scenario was explained by arrhythmogenic scar tissue in the context of a right ventricular infarction caused by the abnormal right coronary artery with evidence of luminal stenosis.
The patient went to a surgical correction (unroofing) of the coronary anomaly and at the same time a biopsy of the right ventricle (with no evidence of arrhythmogenic right ventricular cardiomyopathy). Because of the presence of arrhythmogenic scar a catheter ablation was attempted, however, given the persistence of a ventricular tachycardia with hemodynamic repercussion a single chamber implantable cardioverter defibrillator was implanted.
At one year follow up the patient had no other episode of ventricular arrhythmia.
This case illustrates the diagnostic complexity of pathologies afflicting the right ventricle, particularly rare ones.

Pulmonary Circulation, Pulmonary Embolism, Right Heart Failure - Clinical

P2045
Pulmonary embolism at patient taking NOACs for atrial fibrillation: why anticoagulation therapy was not rather effective?

G Gulnoza Dussekeyeva[1]; AB Isakhanova[1]; GS Bimagambetova[1]
[1]*Scientific Research Institute of Cardiology and Internal Diseases, Almaty, Kazakhstan*

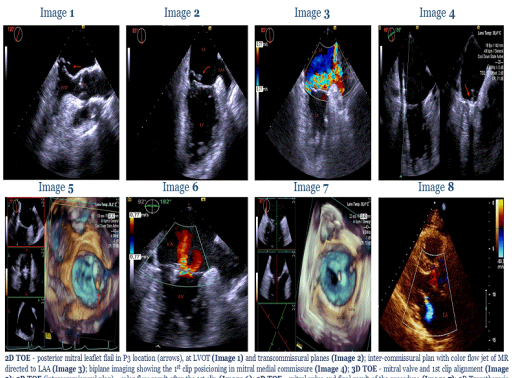
82-year-old male was consulted to the cardiology because of clinics of heart failure (severe symmetric edema on the legs, dyspnea). He had history of hypertension, permanent atrial fibrillation for more than 10 years. Coronary angiography 1 year ago showed no significant stenosis of coronary arteries. He was using rivaroxaban 20 mg daily for prevention of thromboembolism regularly for 6 months. On clinical examination, percussion sound was blunted on right lung upper lobe from third to fifth ribs, vesicular breathing on this side was weaken. He was admitted chest-X-ray. Chest-X-ray showed peripheral wedge of airspace opacity and right lung upper lobe infarction. Patient's hemodynamics was stable. Probability of pulmonary embolism was estimated by Wells criteria and Geneva score. It was moderate, that is why we analyzed D-dimer. The indicator was upgraded. After that we multidetector computed tomography (MDCT) was made. MDCT showed thromboembolism of sub segmental branch of right pulmonary artery with right lung upper lobe infarction. Pulmonary embolism was verified and patient was given rivaroxaban dosage regimen using in the case of pulmonary embolism (15 mg 2 times a day 3 weeks, then 20 mg for this patient permanently). We investigated is there any other factors predisposing pulmonary embolism in the case of this patient, expect of atrial fibrillation. We find that this patient has thrombocytopenia, higher level of lupus anticoagulant and positive antiphospholipid antibodies. Antiphospholipid syndrome was diagnosed and patient was admitted specific therapy (Hydroxychloroquine 200 mg per day).

Cardiovascular Surgery - Other

P2046
A challenging case of mitral regurgitation treatment with mitraclip: beyond scientific evidence

A Ana Manuel[1]; C Guerreiro[1]; J Ribeiro[1]; B Melica[1]; M Fonseca[1]; A Dias[1]; D Caeiro[1]; A Rodrigues[1]; P Braga[1]; V Gama[1]
[1]*Hospital Center Vila Nova Gaia, Cardiology, Porto, Portugal*

Introduction: Mitral valve (MV) percutaneous repair with the MitraClip (MC) benefits patients with severe MR and considered inoperable or at high-risk to open mitral valve surgery (oMVS). Some anatomic characteristics that predict better results after MC are: non-commissural primary regurgitant jet, MV area = 4cm2, minimal calcification in the grasping area, no leaflet cleft in the grasping area, flail width < 15mm and gap < 10mm, left ventricular ejection fraction (LVEF) >20% or LV end systolic diameter < 60mm. The absence of these characteristics in inoperable patients with severe degenerative MR is challenging.
Description: A 79-year-old male was referred for the treatment of MR. He had heart failure with preserved LVEF (NYHA class III), poor functional capacity and he was under optimal medical therapy.
Transthoracic echocardiography: severe left atrium dilation, slightly thickened MV with posterior leaflet prolapse due to chordal rupture, resulting in severe MR, moderate tricuspid regurgitation and signs of pulmonary hypertension. Transoesophageal echocardiography (TOE): MV posterior leaflet flail (P3 location) with no cooptation near the medial commissure, severe MR directed to the left auricular appendage and systolic inversion of pulmonary veins flow. Considering his frailty and a porcelain aorta on CT scan, the Heart Team referred him to a MC. One MC was implanted in A3–P3 (commissural) level. Intra-procedural TOE revealed persistence of moderate MR after the 1st MC and a transvalvular mean pressure gradient of 1.8mmHg. Based on this observation, a 2nd clip was implanted in a mid-medial location to improve results and stabilize the 1st clip. After the 2nd MC, TOE revealed optimal results with mild MR. There were no complications. At one-year of follow-up, the patient had a significant improvement on his life quality, NYHA class I and mild MR. Problems: 1) Given the high-risk to oMVS and an unfavorable anatomy to percutaneous intervention, what would be the alternative for the patient then? 2) What possible complications could happen with MC procedure?
Discussion: This case highlights the importance of a careful evaluation, case by case, when screening the optimal candidate for MC. Although, the lesions were located near the medial commissure, the team performed the procedure in a patient otherwise considered inoperable (P1). Clipping mitral leaflets near the commissures may cause severe damage to the MV apparatus which turns the procedure more complex (P2). TOE, with 3D image, was crucial to guide MC procedure, optimize the technique and its final results.
Conclusion: Interventional edge–to–edge repair with the MC in a patient with relatively unfavorable anatomy, showed feasible in this case, with clinical improvement and good results at one year. Patients with MR represent a heterogeneous group and candidates for MC should therefore be selected carefully.



2D TOE - posterior mitral leaflet flail in P3 location (arrows), at LVOT **(Image 1)** and transcommissural planes **(Image 2)**; inter-commissural plan with color flow jet of MR directed to LAA **(Image 3)**; biplane imaging showing the 1st clip posicioning in mitral medial commissure **(Image 4)**; **3D TOE** - mitral valve and 1st clip alignment **(Image 5)**; **2D TOE** (intercommissural plan) - color flow result after the 1st clip **(Image 6)**; **3D TOE** - mitral valve and final result of the procedure **(Image 7)**; 2D Transthoracic echocardiography (parasternal long axis) - color flow result at one year of follow-up **(Image 8)**.

P2047

Ruptured Valsalva aneurysm with patent ductus arteriosus - echocardiographic puzzle

M Magdalena Dudek[1]; M Kaluzna-Oleksy[1]; S Stefaniak[2]; J Migaj[1]; M Lesiak[1]; Z Oko-Sarnowska[1]; M Jemielity[2]; E Straburzynska-Migaj[1]
[1]Poznan University of Medical Sciences, 1st Cardiology Department, Poznan, Poland; *[2]Poznan University of Medical Sciences, Department of Cardiac and Transplantology Surgery, Chair of Cardio-Thoracic Surgery, Poznan, Poland*

A 39-year-old male patient without significant previous medical history was admitted to the hospital because of a 3-month-long dry cough and reduced exercise tolerance with cardiomegaly in chest X-ray. Auscultation revealed a loud systolic murmur over the whole heart, and quieter diastolic murmur between the scapulae. ECG showed sinus rhythm 62 bpm and left anterior hemiblock (LAH). In laboratory tests - elevated bilirubin (25.32 μmol/L) and brain natriuretic peptide type B (BNP) (835.3 ng/L).
Transthoracic echocardiography (TTE) showed enlargement of left-sided cardiac chambers and fistula between non-coronary sinus of Valsalva aneurysm (SVA) and right atrium with a small left-to-right shunt. Moreover, patent ductus arteriosus (PDA) between descending aorta and left pulmonary artery (flow velocity 4,5cm/s) was found. Cardiac magnetic resonance imaging (CMR) confirmed the diagnosis and showed the exact position of the connection between aorta and pulmonary artery. CMR pictures, both T1 and T2 related, and SE TSE GRE and cine-MR sequences before and after contrast phase, showed presence of PDA and rupture of the non-coronary sinus into the right atrium. Due to difficult evaluation of CMR because of artifacts, a 64-slice computed tomography angiography (CTA) was performed. CTA showed shunt between descending aorta and left pulmonary artery, 15 mm below the ostium of left subclavian artery. Coronary angiography revealed with no significant stenoses in coronary arteries and blood flow between the non-coronary SVA to the right chambers of the heart . The patient underwent surgical treatment, using the Bentall technique, and PDA ligation. He made a full recovery and was discharged 3 weeks later. Aneurysms of the sinuses of Valsalva are rare and mostly congenital anomalies with the highest incidence among young males. Rupture of a SVA can be caused by physical exertion, chest trauma or infective endocarditis, and usually is an indication for urgent surgical treatment. Main symptoms are dyspnea and reduced exercise tolerance with a sudden onset. Echocardiography plays a key role in initial diagnosis and developing a suspicion of a ruptured SVA, as it is easily accessible. It demonstrates the place and size of a rupture and can show comorbidities and other anomalies, as PDA in this case. Angio-CT or CMR confirm the diagnosis and can provide additional information. The treatment of choice is surgery.

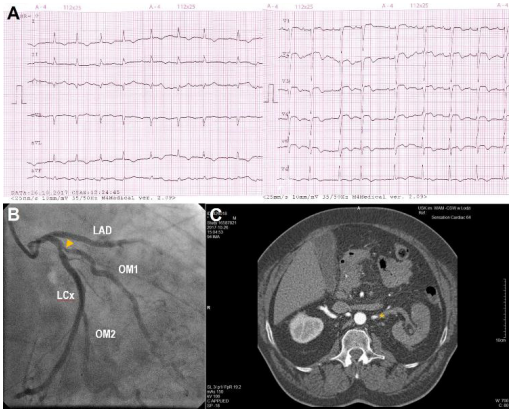
Atrial Fibrillation - Epidemiology, Prognosis, Outcome

P2048

Acute renal artery thromboembolism in the course of untreated atrial fibrillation manifested by Pickering-like syndrome

M Marcin Ksiazczyk[1]; A Debska-Kozlowska[1]; I Karcz-Socha[1]; E Pokrywka[1]; A Lubinski[1]
[1]University Clinical Hospital Military Memorial Academy - Central Veterans' Hospital, Department of Interventional Cardiology and Cardiac Arrhythmias, Lódz, Poland

A 72-year-old man with past medical history of well-controlled arterial hypertension, hypercholesterolaemia, ischaemic cerebral stroke and obesity was admitted to our department because of pulmonary oedema development with concomitant severe abdominal pain localised in the epigastric and umbilical region lasting for about 18 hours prior to admission. On physical examination blood pressure (BP) was 175/100 mmHg, heart rate - 100/min, blood oxygen saturation was 90% with signs of lung congestion and moderate bilateral lower extremities oedema.
The electrocardiogram (ECG) on admission revealed significant ST-segment elevations in precordial leads suggesting acute coronary syndrome (Panel A). Invasive coronary angiography demonstrated insignificant narrowings of the left anterior descending (LAD) and the 1st obtuse marginal (OM1) arteries (Panel B). Echocardiography showed enlarged both atria, left ventricular hypertrophy with global hypokinesis and depressed left ventricle ejection fraction (LVEF) of 30%. In lab tests elevated levels of cardiac troponin T (229 ng/l), D-Dimers (1,77 mg/l FEU) and NT-proBNP (24466 pg/ml) were observed. Because of the persistent abdominal pain, a computed tomography angiography of the aorta was performed - acute aortic syndrome was excluded, but left renal artery was occluded with an uncertain time of occlusion (Panel C).



Pickering-like Syndrome 800x600

On the next day, a patient reported the pain in the left lumbar-sacral area with positive left-side Goldflam's sign; constantly increased BP up to 180/110 mmHg, erythrocyturia and elevated inflammation markers were observed. We concluded that abdominal pain was the consequence of acute renal artery occlusion resulting in left-side renal ischaemia. Co-existing pulmonary pre-oedema condition was a clinical manifestation of Pickering syndrome occurring typically in patients with uni- or bilateral renal artery stenosis. The patient was consulted by vascular surgeon and urologist and both recommended conservational treatment.
It is known that one of the most common causes of renal ischaemia are cardiac diseases including atrial fibrillation (AF). In 24-hours Holter monitoring AF and atrial tachycardia episodes in our patient were recorded so we suggested that documented arrhythmia without previous anticoagulant treatment in combination with a high risk of thromboembolic complications (CHA2DS2-VASc 6 points) could be a potential mechanism of renal artery thromboembolism resulting in acute heart failure manifested by flash pulmonary oedema.
At discharge patient's condition was good: echocardiography showed mild improvement of LVEF up to 35%, lab tests revealed lower levels of NT-proBNP (3829 pg/ml), although a deterioration of renal function was observed (GFR CKD-EPI: 74 ml/min/1,73 m2 at admission; 44 on discharge).
Probably this is the first documented case of Pickering-like syndrome manifested by new-onset heart failure and pre-oedema condition due to acute renal artery thromboembolism.

P2049

Atrial fibrillation and atrial flutter ablation in patient with mitral valve replacement and severe heart failure: you never know what you can do till you try.

O Sapelnikov[1]; O Olga Nikolaeva[2]; D Cherkashin[1]; O Pidanov[3]; D Ardus[1]; T Uskach[2]; I Zhirov[2]; A Chapurnih[3]; I Grishin[1]; S Tereschenko[2]; R Akchurin[1]
[1]Russian Cardiology Research and Production Complex, Cardio-vascular surgery department, Moscow, Russian Federation; *[2]Russian Cardiology Research and Production Complex, Heart failure and myocardial disease department, Moscow, Russian Federation*; *[3]Federal Clinical Hospital under the Business Administration of the President of Russian Federation, cardio-vascular surgery department, Moscow, Russian Federation*

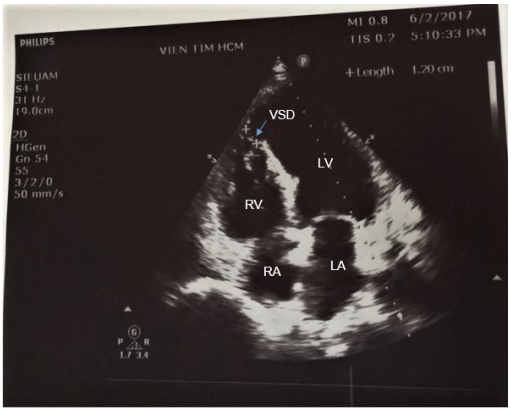
Nowadays endocardial catheter ablation is a 'gold standard' for AF/AFlutter treatment. In most cases the existence of a mechanical prosthesis is a reason for refusal in performing catheter treatment especially in patients with severe heart failure.
We present the patient with a mechanical mitral valve prosthesis and severe reduced left ventricle systolic function. This case demonstrates a possibility and usefulness of performing catheter treatment of AF which allowed to improve a condition and prognosis of the patient.
The 61 years old patient. In 2011 dilated cardiomyopathy was diagnosed. In 2012 a mitral valve chordae abruption occurred. This became a reason for a mitral valve replacement. The same year according to coronary angiography results arteries were intact. Since 2017 patient's condition worsened, including heartbeat, chest pain, dyspnea during small physical activity and leg edema. According to ECG AF/AFlutter with high ventricle rate were registered (average heartbeat was 100 per min.). LV EF was 27 % by echocardiography. Antiarrhytmic therapy was ineffective. The radio frequency anlation was performed. It should be noted that intraoperative INR was 3,2. During procedure AF and AFlutter episodes with 365 mc cycle and left activation front were registered. Under X-ray and intracardiac echocardiography control transseptal puncture was performed. Left atrial electroanatomic map was created. Circular 20-pole catheter Lasso was placed in pulmonary veins and

antral pulmonary vein isolation was performed. Left atrial and right atrial activation map was created. The earliest activation was registered in right atrial on the antero-lateral wall closer to superior vena cava, in place of supposed cannulation of superior vena cava. Intercaval line was performed with short-term sinus rhythm restoration and transformation to AFlutter with 380 mc cycle and right activation front. Cavo-tricuspid isthmus ablation was performed with restoration of sinus rhythm during ablation.In 3 months follow-up patient's condition was satisfying. Sinus rhythm was registered. LV EF was 38%.
Conclusion: Sinus rhythm restoration and maintenance in patients with severe heart failure can significantly improve the quality of life and condition of the patient. ?atheter ablation for AF/AFlutter treatment is possible and safe among patients with mitral valve replacement, so it should not be a contraindication, but such procedure should be performed in high-volume centers by qualified specialists where open heart surgery can be held.

Acute Heart Failure - Clinical

P2050
A case of ventricular septal rupture complicating acute myocardial infarction
H Thai Hao Phan[1]
[1]*Pham Ngoc Thach University of Medicine, Cardiology, Ho Chi Minh, Vietnam*

Introduction: Ventricular septal rupture (VSR) is a rare but lethal complication of acute myocardial infarction (AMI). As acute reperfusion strategies for AMI have evolved, VSR has become increasingly rare and is identified earlier in the post-MI course. Despite significant improvements over the last two decades in overall mortality for patients with AMI, the outcome of patients who develop VSR remains poor. We present a case of ventricular septal rupture complicating acute myocardial infarction.
Case Presentation: A 49-year-old Cambodian, smoker, alcoholic, non-diabetic, hypertensive farmer presented with acute dyspnea after ten days acute myocardial infraction on medical therapy at a hospital in Cambodia. His blood pressure was 109/77 mm Hg, Pulse 113bpm, spO2 99% (air room). Cardiac auscultation revealed a harsh holosystolic murmur, which was heard over the entire precordium. Bibasilar crackles of the lungs.



Results: high sensivity Troponin T 167.9ng/L (<14ng/L), NT-proBNP 3568pg/ml (<125pg/ml). Electrocardiogarphy showed rapid sinus rhythm with ST elevation and T wave inversion in inferior wall. Chest X-ray: PA views showed increase in pulmonary blood flow, cardiac shadow was within normal limits. Left larger than right pleural effusion.Transthoracic echocardiography revealed a left ventricle (LV) with overall preserved systolic function and inferior hypokinesis, a dilated right ventricle, pulmonary hypertension with PAPs 55mmHg and a large, sharply demarcated interventricular septal defect with a large, turbulent left-to-right transseptal flow.
Discussion: the diagnosis is made by a prompt transthoracic echocardiogram identifying drop-out of the ventricular septum in the 2D image and demonstration of flow across the septum using colour Doppler. Evidence of right-ventricular dilation and pulmonary hypertension are also important clues to the diagnosis. The remaining portions of the left ventricle are often hyperdynamic unless there is a large territory of infarction, or previous ischaemic insults have led to compromised function. Colour Doppler evaluation can also be useful to assess the anatomical size of the defect.
Conclusion: Rupture of the interventricular septum is an uncommon complication of MI. VSR occurs in a zone of necrotic myocardial tissue, usually within the first 10-14 days. A high index of suspicion is a loud systolic murmur is heard, usually within the first week after an acute myocardial infarction coincident with the onset of the murmur, the patient's clinical course undergoes a sudden deterioration, with the development of congestive heart failure and, often, cardiogenic shock. Diagnosis is confirmed with the aid of echocardiography and the presence of a left-to-right shunt.

P2051
Clinical case of heart failure due to neoplastic origin in women with uterus adenocarcinoma
I A Leonova[1]; O Chizhova[1]; S Boldueva[1]
[1]*North-Western Sate Medical University named I.I. Mechnikov, St-Petersburg, Russian Federation*

Pericarditis of neoplastic origin is often the first manifestation of the disease, when a cancer has not been established yet.
A clinical case of a patient with paraneoplastic pericarditis, hospitalized with a clinical picture of heart failure is presented.
A woman of 56 years was hospitalized to the therapeutic department with complaints of cough without sputum, inspiratory dyspnoe/orthopnea, edema of the lower extremities to the middle of the hips, the increase of the abdomen. Heart failure level was IV. Complaints appeared and intensified within 3 months prior to admission. Additional complaint was bleeding from genital tract during 1 month. Medical history: arterial hypertension II stage, mild chronic iron deficiency anemia. Based on X-ray examination of the chest ("spherical heart shadow "), ECG, Echo CG (divergence of pericardial leaflets for all the walls of 5-6 cm, the walls of the right ventricle and atrium were collapsed, vienna cava inferior didn't response to breathing) pericarditis was diagnosed. By pericardiocentesis more than 2 liters of turbid serous fluid was evacuated. Viral, tuberculosis, bacterial, autoimmune pericarditis were not confirmed. Based on gynecological examination, MRI of the pelvic organs, increase level of tumor markers (CA125, CA19-9), histological examination the diagnosis of endometrial carcinoma was done. After treatment of heart failure patient was referred to an oncologist. Follow-up 2 month after pericardiocentesis on ECH CG dilatation of the left atrium was marked, left ventricle was not enlarged, left ventricular contractile ability of the myocardium is satisfactory. The discrepancy between the sheets of pericardium behind the posterior wall was 4.1 cm; of the inferior wall was 2.5 cm., of the lateral was 4,5 cm., of the right ventricle - 2.3 cm., of the right atrium - 3.0 cm. Vienna cava inferior was expanded, collapsed on inspiration> 50%. The clinical manifestations of heart failure was at level II NYHA.
Thus, the presented clinical case proves once again that when searching for the causes of heart failure, the patient should be aware of the possible genesis of neoplastic lesions of the pericardium.

P2052
Clinical case of Takotsubo cardiomyopathy as an acute form of microvascular angina
I A Leonova[1]; S Boldueva[1]; M Ryzhikova[1]
[1]*North-Western Sate Medical University named I.I. Mechnikov, St-Petersburg, Russian Federation*

Features of the etiology, pathogenesis of stress-induced cardiomyopathy currently not well understood.
73 years women was hospitalized to the cardiology department due to the prolonged angina attack. Anamnesis: a long time arterial hypertension III degree. Patient had pressing pain in the chest, shortness of breath during physical exertion, psycho-emotional stress, in cold windy weather during few years. On ECG ST elevation in II, III, aVF, V3-6 was recorded. Troponin test was positive. The diagnosis was acute ST elevation inferior-lateral myocardial infarction. Urgency coronary angiography (CA) was performed: a balanced type of blood supply , the left descending artery without hemodynamically significant changes can be traced all over with a sharp drop in the diameter of the lumen in the distal - apical parts of the branches 3 of the order can not be traced (a symptom of "charred tree"), MPG = 0. Arteries without hemodynamically significant stenoses. Surgical treatment was not performed. Echocardiogram: EF = 49 %, the apex akinesia , hypokinesia of middle segments of all walls, dyskinesia of apex of the right ventricle, severe mitral regurgitation . According to the control echocardiogram on the 12th day the EF was 63 % , hypokinesia of apex of the left ventricle, mitral regurgitation I. Patient felt slight chest pain during exertion and emotional stress. After 1 month on echocardiogram EF was 65 %, there is no violation of contraction zone. Due to the rapid and significant positive trend of disease, the reversibility of the changes according to the echocardiogram, as well as data CA (coronary arteries without hemodynamically significant changes, the lack of branches of order 3 anterior descending artery), the diagnosis of myocardial infarction is excluded. Most likely, the patient had Takotsubo cardiomyopathy due to microvascular angina. To confirm the diagnosis perfusion positron emission tomography of the heart carried out. In a series of cardiac

tomograms performed alone, indicated moderate hypoperfusion of the myocardium in the apex of the heart, local contractility disturbances have been identified. By cold pressor test hypoperfusion in all segments of the anterior and lateral walls of the left ventricle, in the interventricular septum was revealed. Pharmacological test with adenosin: in the 5th minute of the sample registered oppressive chest pain, typical for the patient; revealed hypoperfusion of the myocardium in the apex; contractility zone violation have not been established. Thus, this is a case of acute form of microvascular angina as cardiomyopathy Takotsubo.

Atrial Fibrillation - Pathophysiology and Mechanisms

P2053

Apixaban successfully resolved left atrial appendage thrombus in patients with end stage renal disease with dialysis

YM Park[1]; MS Cha[1]; J Moon[1]; W-J Chung[1]; M-S Shin[1]; IS Choi[1]
[1]*Gil Hospital , Gachon University of Medicine & Science, Incheon, Korea Republic of*

Introduction: We report a patient requiring dialysis with left atrial appendage (LAA) thrombus which was successfully resolved with apixaban
Methods: N/A
Results: A 62-year-old female who had a history of end stage renal disease (ESRD) with dialysis was referred to our electrophysiology department due to paroxysmal atrial fibrillation (AF). Anticoagulation therapy with warfarin was started, because her CHADS2-VASc score was 4 (hypertension, diabetes, congestive heart failure, and female gender) as well as amiodarone for rhythm control. Trans-esophageal echocardiography was performed which revealed thrombus in left atrial appendage (LAA). Tachycardia-bradycardia syndrome was documented, therefore, catheter ablation was planned. Follow up TEE identified still remained thrombus despite approximately 1 year of anticoagulation therapy with warfarin. Therefore, warfarin was switched to the direct factor Xa inhibitor, apixaban 5mg bid. After four months of apixaban treatment, TEE revealed complete resolution of LAA thrombus. Finally, catheter ablation was performed without any complication and the patient has been in sinus rhythm thereafter under continued anticoagulant treatment with apixaban. Neither thromboembolic nor bleeding events did not occur during follow up for > 9 months.
Conclusion: Factor Xa inhibitor, apixaban, can successfully and safely resolve the LAA thrombus refractory to warfarin in patients with ESRD requiring dialysis.

Ventricular Arrhythmias and SCD - Treatment

P2054

Iatrogenic factors induce electrical storm in heart failure patients

SY Songyun Chu[1]; QH Sheng[1]; J Jiang[1]; J Zhou[1]; YS Ding[1]
[1]*Peking University First Hospital, Department of Cardiology, Beijing, China People's Republic of*

Purpose: Electrical storm is multiple episodes of ventricular tachycardia (VT) or ventricular fibrillation (VF) within 24 hours. Exacerbation of heart failure often becomes leading cause of the electrical instability. Iatrogenic factors, however, has not been paid enough attention.
Case: A 60-year-old man presented for palpitations and multiple shocks of ICD within one day. The patient had ischemic cardiomyopathy and ICD implanted after a syncope attack and VT demonstrated in our center 2 year ago. Standard medical therapy including ß-blocker, ACE-inhibitor, aspirin and statin were taken regularly thereafter. The patient had an attack of VT and received a shock at 16th, September, 2015. With heart failure symptoms, he was admitted into local hospital. Because of deterioration of heart function and hypotension, ß-blocker was stopped and dopamine and dobutamineintravenous infusion was started. At 12th, October, 2015, the patient had a VT attack and received 6 anti-tachycardia pacing (ATP) and 1 shock therapy. Bolus dose of amiodarone(300mg)was intravenous injected. Then continuous intravenous infusion of amiodarone(1000mg/h for initial 6 hours and 500mg/h thereafter) was given. Oral amiodarone (600mg/d) was also started to prevent recurrence of VT. Five days later (17th, October, 2015),the patient felt palpitation and lost his consciousness. Continuous ECG monitoring demonstrated VT reoccurred, but ATP therapy has no effect. Eight shocks were delivered from ICD, but also failed to convert the VT. Additional 3 shocks from external defibrillator (200J, biphasic wave) terminated the VT successfully. However,VT reoccurred the following day. ATP therapy was ineffective before a shock from ICD ended the VT. When the patient was transferred to our hospital with amiodarone continuous infusion, QTc was more than 600ms. Amiodarone was stopped. Multiple paroxysmal VTs were noticed when QTc longer than 500ms. QTc decreased gradually with cessation of amiodarone and supplementation of potassium and magnesium. Small dose of ß blocker was initiated and titrated. With the QTc decreased little by little, no more VT was observed.
Conclusion: Keep up with standardized secondary prevention medications are critical for heart failure patients. Withdrawal of ß-blockers was associated with elevated mortality while continuation of them even in patients hospitalized with decompensated heart failure improved treatment success. And intravenous inotropes should only be used as a bridge to further aggressive measures, or in selective patients with evident hypoperfusion or shock.
On the other hand, amiodarone has been demonstrated to significantly improve survival from cardiac arrest and reduce the frequency of ventricular tachyarrhythmia, and it has been recommended as treatment for electrical storm. However, one must be cautious when use amiodarone and keep close monitoring on QTc changes and early warning signs, especially for patients with decompensated heart failure.

Recordings - Episode list:

No.	Detection time	Type	Details	Predetection RR	Pretermination RR
29	Dec 9, 2016 6:26:56 PM	VF	Duration: 17s; Shocks delivered: 1	288	711
	Nov 29, 2016 12:44:02 PM	Follow-up			
28	Nov 10, 2016 12:40:42 AM	Periodic IEGM	Monitoring only	---	---
27	Aug 12, 2016 12:40:42 AM	Periodic IEGM	Monitoring only	---	---
	Jun 14, 2016 1:15:30 PM	Follow-up			
26	May 14, 2016 12:40:42 AM	Periodic IEGM	Monitoring only	---	---
25	Mar 25, 2016 8:13:47 AM	SVT	Monitoring only; Duration: 12s	379	401
	Mar 1, 2016 12:56:46 PM	Follow-up			
24	Feb 27, 2016 8:45:03 PM	VF	Duration: 20s; Shocks delivered: 1	327	856
23	Feb 14, 2016 12:40:42 AM	Periodic IEGM	Monitoring only	---	---
	Jan 12, 2016 12:51:22 PM	Follow-up			
22	Nov 16, 2015 12:40:42 AM	Periodic IEGM	Monitoring only	---	---
	Oct 21, 2015 1:19:55 PM	Follow-up			
21	Oct 18, 2015 5:05:18 PM	VT1	Duration: 1min 40s; ATP: 6; Shocks delivered: 1; Shocks aborted: 1	377	599
19	Oct 17, 2015 3:28:50 AM	SVT	Monitoring only; Duration: 41min 40s	396	563
17	Oct 17, 2015 1:35:25 AM	VT1	Duration: 1h 29min 18s; ATP: 6; Shocks delivered: 8	366	397
16	Oct 16, 2015 2:08:57 AM	SVT	Monitoring only; Duration: 35s	396	403
12	Oct 16, 2015 12:50:35 AM	SVT	Monitoring only; Duration: 38s	392	402
4	Oct 12, 2015 1:38:22 PM	VT1	Duration: 1min 10s; ATP: 6; Shocks delivered: 1	376	535
	Sep 22, 2015 2:06:17 PM	Follow-up			
3	Sep 16, 2015 5:35:27 PM	VT1	Duration: 1min 12s; ATP: 6; Shocks delivered: 1	365	599
1	Aug 18, 2015 12:40:42 AM	Periodic IEGM	Monitoring only	---	---

Ventricular Arrhythmias and SCD - Pathophysiology and Mechanisms

P2055

Sudden cardiac death due to reversible hypertrophic cardiomyopathy. Could it be possible?

P Paloma Jorda[1]; E Arbelo[1]; A Garcia-Alvarez[2]
[1]*Hospital Clinic de Barcelona, Electrophysiology & Genetic Cardiopathies, Barcelona, Spain*; [2]*Hospital Clinic de Barcelona, Heart failure and cardiac transplantation, Barcelona, Spain*

A case of a 36-year-old man who suffered out-of-hospital cardiac arrest in 2011 is presented. It occurred at rest and first rhythm identified was ventricular fibrillation (VF). He was competing in athletics at that time, with no previously clinical history.
Echocardiography and CMR showed concentric hypertrophy that was severe at inferolateral wall (18 mm at this level, total LV mass 93.6 g). LVEF was normal (53.5%). RV was no hypertrophic or dilated. Non gadolinium late enhancement was observed. Cardiac valves function was normal.
Channelopathies were excluded as flecainide test was negative, ergometry did not induce arrhythmias, QT interval was normal and electrophysiological study showed normal conduction system intervals and no arrhythmias during stimulation were induced.
Sudden cardiac death was attributed to an underlying hypertrophic cardiomyopathy (HCM) and an implantable cardiodefibrillator (ICD) was implanted. Cessation of competition exercise was recommended.
After discharge, the study of infiltrative diseases causing hypertrophy ruled out Fabry disease (normal a -galactosidase activity test) and familial amyloidosis (normal TTR genotype).
Five months after the first episode the patient suffered two ICD discharges while sleeping (at 6 AM) due to VF. Beta-blockers were started. No more discharges have been registered.
The genetic analysis showed a mutation of uncertain significance in the titin gene and a probably pathogenic mutation for Brugada syndrome (BS) in sodium channel a-subunit gene (SCN5A p.825 L>P). No sarcomeric mutations related to hypertrophic cardiomyopathy were found.

During the follow-up, six years after the first event, echocardiography demonstrated that the hypertrophy had reverted from 18 mm initially in the inferolateral wall to a maximum of 12 mm in the septum.

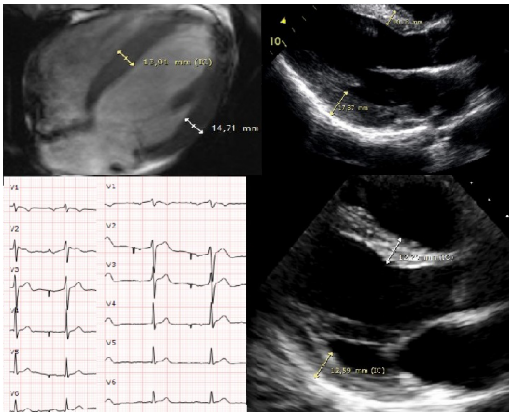
Given the practical resolution of ventricular hypertrophy we have assumed that ventricular hypertrophy observed initially was induced by exercise (HCM phenocopy).

The type of ventricular arrhythmias and the SCN5A mutation (probably pathogenic for BS) point a channelopathy as the underlying cause arrhythmias in this case.

Basal ECG with upper chest leads shows ECG type 2 for Brugada syndrome and atrial stimulation due to sinus dysfunction (typical in BS patients with SCN5A mutation). Negativity in flecainide test in 2011 is possibly a false negative (reported in 36% of cases). Ajmaline test to confirm the diagnosis of BS is pending at the moment of abstract submission.

This case shows the importance and the difficulty in the differential diagnosis of the aetiology of ventricular arrhythmias. In addition, it clearly shows how a hypertrophic myocardium can be observed in a wide spectrum of circumstances. Prognostic and therapeutic implications will be greatly different depending on the underlying condition.

Figure 1. Studies in 2011 on the top. Below, ECG and last control echo (2017).



Congestion: how to detect with new technologies

2076

Negative prognostic value of residual congestion by bioimpedance vector analysis at discharge in patients with decompensated heart failure

A Soloveva[1]; M Bayarsaikhan[1]; A Kuchaeva[1]; S Villevalde[1]; Z Kobalava[1]
[1]*Peoples' Friendship University of Russia (RUDN University), Department of Internal Diseases, Moscow, Russian Federation*

Objective: Congestion is the principal cause for admission with decompensated heart failure (DHF). The aim of the study was to evaluate hydration status during hospitalisation, rate and prognostic value of residual congestion in patients with DHF using bioimpedance vector analysis (BIVA).
Methods: 148 patients with DHF (99 male, 71 ± 11 years (M ± SD), arterial hypertension 95%, myocardial infarction 42.5%, atrial fibrillation 65%, diabetes mellitus 42.5%, chronic kidney disease 26%, ejection fraction (EF) 41 ± 14%, EF < 40% 44.6%, baseline NT-proBNP 4148 (1635;5567) pg/ml) were included in 6-month prospective study. Hydration status was assessed by BIVA on admission and discharge, using resistance (R) and reactance (Xc) standardized by height (h). Deviation from the 50th, 75th and 95th vector percentile of the healthy reference population was considered as mild, moderate and severe hyperhydration. Hyperhydration by BIVA at discharge was defined as residual congestion. Outcomes data were available for 138 patients. Mann-Whitney and Pearson chi-squire tests, multiple regression analysis were performed. P < 0.05 was considered significant.
Results: Baseline mild, moderate and severe hyperhydration was revealed in 19, 32.4 and 48.6% of patients. At discharge 1.4 and 34.4% of patients had dehydration and euvolemia, 64.2% - residual congestion by BIVA (mild, moderate and severe in 25.7, 31.1 and 7.4% of cases respectively).
Patients with vs without residual congestion did not differ by clinical and demographic characteristics (except for higher rate of oedema on admission and discharge), comorbidities, baseline NT-proBNP and EF, but had more pronounced baseline BIVA hyperhydration and lower R/h and Xc/h decrease despite more intensive diuretic therapy - longer and higher dose of iv furosemide therapy (7 (5;9) vs 6 (4;8) days, p = 0.037, total dose (640 (420;940) vs 360 (240;780) mg, p = 0.012) and maximum daily dose (100 (80;160) vs 80 (60;120) mg, p = 0.032)), lower rate of switching to per os furosemide therapy (80 vs 94%, p = 0.019) and thiazide therapy (9.5 vs 24.5%, p = 0.042).
Independent predictors for residual congestion were oedema at discharge (odds ratio (OR) 7.35 (95% confidential interval (CI) 2.85;18.98), p < 0.001) and baseline severe hyperhydration by BIVA (OR 4.37 (95% CI 2.08;9.18), p < 0.001).
Patients with vs without residual congestion had higher rate of 6-month all cause death (16.9 vs 4.1%, p = 0.029). Residual congestion was determined to be a predictor for 6-month all cause death (OR 4.76, 95% CI 1.03;22.08), p = 0.048).
Conclusions: Residual congestion was revealed in 64.2% of patients and was associated with more prominent baseline BIVA hyperhydration, lower hydration dynamics, more intensive loop diuretic therapy. Residual congestion had negative impact on 6 month outcomes and was independently associated with higher all-cause death.

2077

The real way to reduce Heart Failure hospitalizations and Heart Failure associated deaths: Lessons from the extended IMPEDANCE-HF trial

M Michael Kleiner Shochat[1]; A Shotan[1]; I Kleiner[2]; JM Weinstein[2]; I Dahan[1]; M Kazatsker[1]; A Asif[1]; S Meisel[1]
[1]*Hillel Yaffe Medical Center, Heart Institute, Hadera, Israel*; [2]*Saroka Medical Center, Cardiology, Beer Sheva, Israel*

Results of the IMPEDANCE-HF trial have shown that lung impedance (LI)-guided treatment reduces hospitalizations for heart failure (HF) and decreases HF-related mortality. The main trial was extended for an additional year to accrue more data on predictors of hospitalizations due to HF. The main aim of the study was to prove that HF patients with higher degree of long-standing pulmonary congestion are hospitalized more often.
Methods Study population included 266 patients, with HF and LVEF = 35% in New York Heart Association class II-IV. Patients were randomized (1:1) to a control group treated by clinical assessment and a LI-guided group whose therapy was also assisted by LI. Patients were examined and LI measured monthly in our outpatient clinics. Noninvasive LI measurements were performed with the high-sensitive device. Assessment of the degree of pulmonary congestion was by the new index ?LIR, measured at each visit and calculated as ?LIR = {1- [currently measured LI/normal baseline (calculated for each patient)] × 100} expressed as percentage. The annual average ?LIR for each patient was calculated as the mean of all ?LIR measurements at each consecutive year of follow-up.
Results The total follow-up period was 642 years in the LI-guided group and 510 years in the control group (p = 0.001). Groups were similar with respect to baseline characteristics. There were 249 and 475 HF hospitalizations (mean 0.39 and 0.93 per × year of follow up) in the LI-guided and control groups, respectively (p < 0.001). There were 56, 22 and 73, 51 all-cause and HF-associated death cases in the LI-guided and the control groups, respectively (p < 0.001). Hazard Ration (HR) for HF hospitalizations was higher in control in compare with LI-guided group [HR = 2.56, 95% CI: 1.8-3.7, P < 0.00001], (Anderson-Gil Model). Figure 1 shows the dynamics of pulmonary congestion in study groups during the follow-up period as represented by ?LIR, demonstrating a significantly lower level of pulmonary congestion in the LI-guided group compare with the control group during the study (p < 0.001). Conclusion The Extended IMPEDANCE-HF demonstrated that pre-emptive LI-guided therapy of HF patients reduced pulmonary congestion significantly more effectively than by treatment according to clinical assessment only. This effect appeared to be consistent during the whole study period. Since groups were similar with respect to baseline characteristics, we proposed that the main reason for reducing the number of HF hospitalizations and improving survival was better decongestion achieved in the monitored group.

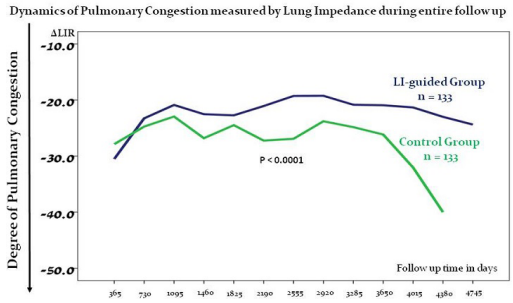


Figure 1

2078

Troponin and Lung Impedance based model for prediction Heart Failure readmission

M Michael Kleiner Shochat[1]; A Shotan[1]; M Kazatsker[1]; I Kleiner[2]; JM Weinstein[2]; I Dahan[1]; A Asif[1]; S Meisel[1]
[1]*Hillel Yaffe Medical Center, Heart Institute, Hadera, Israel*; [2]*Saroka Medical Center, Cardiology, Beer Sheva, Israel*

The IMPEDANCE-HF trial has shown that lung impedance (LI)-guided treatment reduces hospitalizations for heart failure (HF) and decreases HF-related mortality. The aim of the current sub-analysis was to evaluate whether troponin level elevation during admission and the degree of pulmonary congestion at discharge after HF hospitalization can predict time to the next readmission.
Methods: Study population included 266 patients with HF and LVEF = 35% in New York Heart Association class II-IV. Noninvasive LI measurements were performed with a high-sensitive device. Assessment of the degree of pulmonary congestion was assessed by the new index ?LIR= {[1-currently measured LI/normal baseline (calculated for each patient)] × 100} expressed as percentage. High sensitive troponin was evaluated 6-12 hours after admission for HF.
Results: There were 155 HF hospitalizations with available troponin level. LI was performed per protocol during every admission. Median troponin level was 44 ng/ml.

Troponin levels during HF hospitalization were divided into 3 categories: 0-13 ng/ml-normal range, 13.1-44.0 ng/ml (mildly elevated < median), and values> 44.0 ng/ml (elevated>median). Pulmonary congestion, assessed by ?LIR at discharge, was defined as mild pulmonary congestion: 0 to -20% (in comparison with normal individual basal LI), moderate pulmonary congestion: -20.1 to -35%, and severe pulmonary congestion: -35.1 to -60%. The respective times to readmission according to troponin groups were 304, 295, and 176 days ($p < 0.001$ only for elevated> median troponin subgroup). Median time to readmission according to the degree of pulmonary congestion at discharge was 496 days for mild pulmonary congestion, 370 days for moderate pulmonary congestion and 44 days for severe pulmonary congestion at discharge ($p < 0.01$). Time to HF death after discharge was not significantly dependent on troponin level but tended to correlate with it ($p = 0.06$). However, it was significantly dependent on the level of pulmonary congestion at discharge ($p < 0.001$). Conclusion Risk stratification of readmission and HF death after hospitalization for HF exacerbation is possible using troponin level during admission and the degree of pulmonary congestion at discharge. Mildly elevated troponin is not useful for risk stratification. The level of pulmonary congestion at discharge for HF hospitalization, as assessed by lung impedance, is a very strong predictor of the time for readmission and HF-associated death.

2079

Association between body mass index and b-lines by lung ultrasonography in patients with chronic and acute heart failure

P Brainin[1]; B Claggett[2]; K Dwyer[3]; A Merz[4]; M Silverman[1]; V Swarmy[1]; T Biering-Sorensen[5]; J Rivero[2]; E Lewis[2]; S Cheng[2]; J Mc Murray[6]; S Solomon[2]; E Platz[1]

[1]Brigham and Women's Hospital, Department of Emergency Medicine, Boston, United States of America; [2]Brigham and Women's Hospital, Division of Cardiovascular Medicine, Boston, United States of America; [3]Brown University, Department of Emergency Medicine, Rhode Island Hospital, Providence, United States of America; [4]Harvard Medical School, Boston, United States of America; [5]Gentofte University Hospital, Cardiology, Copenhagen, Denmark; [6]University of Glasgow, Institute of Cardiovascular and Medical Sciences, Glasgow, United Kingdom

Funding Acknowledgements: Gangsted Foundation, Internal Funds from Herlev and Gentofte University Hospital, Lundbeck Foundation, Julie von Müllens Foundation

Background: Identification of B-lines by lung ultrasonography (LUS) is useful for assessment of pulmonary congestion, however, the impact of body mass index (BMI) on B-line prevalence is not known.
Purpose: We sought to evaluate the relationship between BMI and B-line prevalence in patients with chronic heart failure (HF) and acute HF.
Methods: We analyzed ambulatory chronic HF (n = 118) and hospitalized acute HF (n = 177) patients (mean age, 70 years, 64% men, mean BMI 29 kg/m^2) undergoing echocardiography (mean ejection fraction, chronic HF: 45%; acute HF: 41%) and LUS examination in 8 chest zones. The sum of B-lines was quantified offline, blinded to clinical findings. Patients were divided into categories of BMI: lean (< 25 kg/m^2), overweight (25 to 29.9 kg/m^2), obese (30 to 34.9 kg/m^2), severely obese (= 35 kg/m^2) and B-line groups: 0-2, 3-6 and >6. Patients with BMI>50 kg/m^2 were excluded (n = 7).

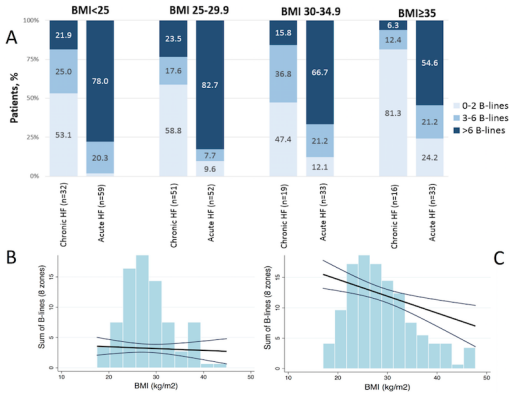


Fig1: (a) barchart (b-c) spline plots

Results: The number of B-lines was lower in patients with chronic HF (mean B-lines 3, range 0-17; P < 0.001) than those with acute HF (mean B-lines 12, range 0-36) (Figure 1a). In chronic HF there was no significant association between either continuous or categorical B-line number and continuous or categories of BMI (P trend = 0.17; rho=-0.16, P = 0.09). These findings remained consistent after adjustment for age and sex (P overall trend = 0.62; Figure 1b). By contrast, in acute HF patients the number of B-lines decreased significantly with increasing BMI both in continuous and categorical analyses (P trend = 0.003; rho =-0.21, P = 0.005) and after adjustment for age and sex (P overall trend = 0.002; Figure 1c). However, in more than half of severely obese patients with acute HF >6 B-lines could still be identified.
Conclusion: Patients with acute HF demonstrated a higher number of B-lines on LUS than those with chronic HF. The relationship between B-lines and BMI among patients with HF is less clear, and should be considered hypothesis generating and further examined in future, larger cohorts.

2080

Dynamic of pulmonary congestion assessed by clinical signs and lung ultrasound in patients with decompensated heart failure

F Cabello Montoya[1]; O Lukina[1]; A Soloveva[1]; A Safarova[1]; S Villevalde[1]; Z Kobalava[1]

[1]Peoples' Friendship University of Russia (RUDN University), Department of Internal Diseases, Moscow, Russian Federation

Introduction: In the past two decades, lung ultrasound (LUS) has emerged as an effective tool in the evaluation of pulmonary congestion. The aim of the study was to assess the incidence and severity of pulmonary congestion by evaluation of B-lines and their dynamic changes during hospitalization in decompensated heart failure (DHF).
Material and Methods: Routine clinical assessment, chest X-ray and lung ultrasound (LUS) were performed in 167 patients with DHF (men 62%, age 69 ± 12 years (M ± SD), arterial hypertension 94%, anamnesis of myocardial infarction 56%, atrial fibrillation 65%, ejection fraction (EF) 41 ± 14%, EF <40% 47%, baseline NT-proBNP 3674 (1466; 6413) pg/ml). Standart eight-zone LUS examination was performed. Sum of B-lines <5 was considered as normal, 6-15, 16-30 and >30 - as pulmonary congestion (mild, moderate and severe respectively). Presence of pulmonary congestion (PC) at discharge was considered as residual PC. Mann-Whitney, McNemar and Wilcoxon tests were performed. P <0.05 was considered statistically significant.
Results: During hospitalization incidence of clinical signs of PC decreased: orthopnoea from 80 to 16%, dyspnoea at rest from 34 to 0%, dyspnea at exertion from 97 to 42%, bilateral pulmonary rales from 82 to 9%, congestion on chest radiographs 65 to 16%, hydrothorax on chest radiographs 44 to 10%, p <0.05.
Presence of at least one of clinical (orthopnoea or rales) or radiological sing of PC was revealed in 34.1% cases.
On admission mild, moderate and severe PC occurred in 4.2, 30.5 and 65.3% of patients respectively. At discharge normal LUS profile was observed in 58.1% of patients. Mild, moderate and severe PC occurred in 31.7, 8.4 and 1.8% cases.
During hospitalization the median of B-lines sum decreased from 35 (27;55) to 5 (3;9) (relative ?-85.7 (-92;-75)%) p <0.001.
Patients with vs without residual PC had higher median of B-lines sum on admission (45 (29;60) vs 34 (25;49), p = 0,002) and at discharge (10 (8;15) vs 3 (3;4), p <0.001), lower relative ?B-lines (-67 (-82;-58) vs -91 (-94;-85)%, p <0.001).
Conclusion: Significant decrease of B-lines and incidence of clinical signs of pulmonary congestion during hospitalization was observed. Pulmonary congestion at discharge was observed in 34.1% by clinical data or chest radiographs and in 41.9% by LUS.

2081

Device measured rapid shallow breathing index reflects changing respiratory patterns but minute ventilation reflects changing activity during worsening heart failure in ambulatory patients

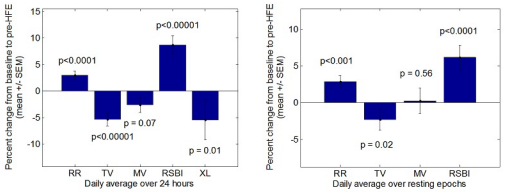
J Boehmer[1]; M Aktas[2]; A Capucci[3]; RS Gardner[4]; M Gold[5]; G Molon[6]; P Thakur[7]; R Sweeney[7]; Y Zhang[7]; Q An[7]; V Averina[7]; S Rials[8]

[1]Penn State Hershey Medical Center, Hershey, United States of America; [2]University of Rochester, Rochester, United States of America; [3]Marche Polytechnic University of Ancona, Ancona, Italy; [4]Golden Jubilee National Hospital, Clydebank, United Kingdom; [5]Medical University of South Carolina, Charleston, United States of America; [6]Sacro Cuore Hospital, Cardiology Department, Negrar, Italy; [7]Boston Scientific, St. Paul, United States of America; [8]Ohio Health Heart and Vascular, Columbus, United States of America

Funding Acknowledgements: Boston Scientific

Background: Respiratory distress is common in heart failure (HF) and a primary driver for HF hospitalizations. Minute Ventilation (MV), a product of respiratory rate and tidal volume, is known to be elevated in HF patients due to ventilation/perfusion (V/Q) mismatch. However, it is not known if changes in MV accurately reflect emergence of rapid shallow breathing patterns in ambulatory patients preceding a HF event.

Methods: The MultiSENSE trial enrolled 900 patients implanted with a COGNIS CRT-D and followed them up to 1 year. Device software was modified to permit collection of chronic diagnostic sensor data including impedance based respiration rate (RR) and tidal volume (TV), which was used to compute MV (= RR*TV) and Rapid Shallow Breathing Index (RSBI = RR/TV), and activity (XL). Daily averages were separately computed over entire 24 hours as well as during resting epochs. HF events (HFEs) were independently adjudicated and defined as HF admissions or unscheduled visits with intravenous HF treatment. Relative changes preceding HFEs were computed between a baseline 30-60 days prior to HFEs (BL) and 3-day pre-HFE (ST) as (ST-BL)/BLx100% and reported as mean ± SEM. Significance was tested using Wilcoxon signed-rank test.
Results: 900 patients followed for a year experienced 192 HFEs. Using 24-hour averages, significant changes were observed in RR, TV and RSBI indicating the emergence of rapid shallow breathing pattern leading up to HFE. MV average over 24 hours showed nonsignificant decrease coincident with decreased patient activity but showed no change when daily averaging was limited to resting epochs. In contrast, RR, TV and RSBI were significantly changed even at rest in directions consistent with the emergence of rapid shallow breathing pattern.
Conclusion: Device measured rapid shallow breathing is significantly elevated in the three day epoch preceding HFEs, whereas minute ventilation is not, in both 24-hour as well as resting period daily averages. Automatic ambulatory longitudinal monitoring of changes in rapid shallow breathing patterns may enable better monitoring for emerging respiratory distress in HF patients.



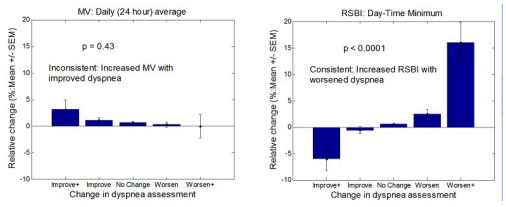
2082

Device measured rapid shallow breathing index and not minute ventilation reflects changes in dyspnea status in ambulatory heart failure patients

J Boehmer[1]; M Aktas[2]; A Capucci[3]; RS Gardner[4]; M Gold[5]; G Molon[6]; P Thakur[7]; R Sweeney[7]; YI Zhang[7]; Q An[7]; V Averina[7]; S Rials[8]
[1]Penn State Hershey Medical Center, Hershey, United States of America; *[2]University of Rochester, Rochester, United States of America*; *[3]Marche Polytechnic University of Ancona, Ancona, Italy*; *[4]Golden Jubilee National Hospital, Clydebank, United Kingdom*; *[5]Medical University of South Carolina, Charleston, United States of America*; *[6]Sacro Cuore Hospital, Cardiology Department, Negrar, Italy*; *[7]Boston Scientific, St. Paul, United States of America*; *[8]Ohio Health Heart and Vascular, Columbus, United States of America*

Funding Acknowledgements: Boston Scientific

Background: Dyspnea is common in heart failure (HF) patients and a primary driver for HF hospitalizations. Minute Ventilation (MV), a product of respiratory rate (RR) and tidal volume (TV), is known to be elevated in HF patients due to ventilation/perfusion (V/Q) mismatch. However, it is not known if changes in MV accurately reflect changes in dyspnea status in ambulatory HF patients over time.



Methods: The MultiSENSE trial enrolled 900 patients implanted with a COGNIS CRT-D and followed them for up to 1 year. Device software was modified to permit collection of chronic diagnostic sensor data including impedance based RR and TV, which was used to compute MV (RR*TV) and Rapid Shallow Breathing Index (RSBI = RR/TV). Dyspnea status was assessed on a 3-point scale (0 = No dyspnea, 1 = dyspnea on exertion, 2 = dyspnea at rest) at routine follow-up visits scheduled either every three months if the patients had remote monitoring, or every 6-8 weeks if not. Changes in dyspnea scores between follow-ups were calculated: Improve+ (2->0), Improve (2->1 or 1->0), No change, Worsen (0->1 or 1->2), and Worsen+ (0->2). Relative changes in the respiration parameters between the start (ST) and end (ED) of each epoch were calculated as (ED-ST)/STx100%, reported as mean ± SEM for each category and compared across categories using Kruskal-Wallis test.
Results: Of 4717 total follow-up intervals with dyspnea assessments, 3388 had no change, 561 had 1-point worsening, 41 had 2-point worsening, 689 had 1-point improvement, while 37 had 2-point improvement. 24-hour average MV was not significantly different between dyspnea change categories ($p = 0.42$) and changed inconsistent with expectation (i.e. increased MV with improved dyspnea assessment). In contrast changes in 24-hour average RSBI ($p = 0.03$) as well as day-time minimum RSBI ($p < 0.0001$) were significantly different between categories and consistent with expectation (i.e. increased RSBI with worsening dyspnea)
Conclusion: Changes in RSBI correlated with changes in patient's dyspneic status (i.e. increased rapid shallow breathing with worsening dyspnea status) whereas MV did not. Automatic longitudinal measurements of day-time minimum RSBI may better quantify the dyspneic status in ambulatory HF patients, enabling continuous monitoring of dyspnea in HF patients.

2083

Longitudinal function and right ventricular remodeling ratio in acute heart failure: a non invasive measurement of right dysfunction and outcome

A Alberto Palazzuoli[1]; G Ruocco[2]; M Beltrami[2]; O De Vivo[2]; R Nuti[2]
[1]Santa Maria Alle Scotte Polyclinic, Siena, Italy; *[2]University of Siena, Cardiovascular Diseases Unit, Department of Internal Medicine , Siena, Italy*

Background: In acute heart failure (AHF) the development of right ventricle (RV) dilation and failure is a signs of advanced disease and poor prognosis.
Purpose: In this study we sought to evaluate a new index including TAPSE and end diastolic diameter (EDD) of RV with respect to the well known TAPSE/PASP ratio; to compare these two formulas (TAPSE/PASP and TAPSE/EDDRV) in terms of outcome prediction in patients with preserved (pEF) or reduced ejection fraction (rEF).
Methods: Patients with AHF were included in this study. In each subject, the echocardiography was performed within 12 hours from admission, by two experienced cardiologists according to the instructions provided by the American Society of Echocardiography. We estimated the systolic PASP by continuous Doppler at tricuspid valve level. The TAPSE was obtained by placing the M-mode cursor lateral tricuspid annulus. EDD of RV was measured at the basal level by 4 chamber view. Patients were classified in pEF or rEF on the basis of EF cut-off 50%. We also assessed the diastolic function pattern by the analysis of transmitral and tissue Doppler waves.
Results: Of 157 patients enrolled, 90 had HFrEF and 67 had HFpEF, median age was 80 [77-85] years and 53% were women. Overall, the median BNP was 1,007 [768-1,540] ng/L, median TAPSE/PAPs 0.408 [0.305-0.533] and the median TAPSE/EDD RV was 0.454[0.356-0.591]. ROC curve analysis showed that the increase of PASP (AUC 0.60[0.51-0.69];$p = 0.03$), EDDRV (AUC 0.71[0.63-0.79];$p < 0.001$) and BNP (AUC 0.62[0.53-0.71];$p = 0.01$) were able to predict poor outcome; conversely, a reduction of TAPSE was related to poor prognosis (AUC 0.38[0.29-.46;$p = 0.01$). Univariate analysis showed that both a TAPSE/EDDRV < 0.454 (HR 3.36 [1.90-5.95]; $p < 0.001$) and a TAPSE/PASP < 0.408 (HR 2.16 [1.28-3.65]; $p = 0.004$) were related to poor outcome. After adjustment for potential confounders, multivariable analysis confirmed the prognostic role of TAPSE/EDDRV < 0.454 (HR 3.76 [1.60-8.84]; $p = 0.002$) and persistence of congestion at discharge (HR 4.23[2.04-8.77]; $p < 0.001$).
Conclusions: In AHF the poor RV longitudinal function/diameter ratio is an additional criteria for identification of RV dysfunction and elevated pulmonary pressure. This new formula appear to predict outcome in both pEF and rEF patients.

2084

Liver stiffness is associated of with hyperhydration and does not reflect liver fibrosis in decompensated heart failure

A Soloveva[1]; ? Bayarsaikhan[1]; M Naumenko[2]; A Abramov[1]; I Garmash[1]; S Villevalde[1]; Z Kobalava[1]
[1]Peoples' Friendship University of Russia (RUDN University), Department of Internal Diseases, Moscow, Russian Federation; *[2]Vinogradov City Clinical Hospital, Department of Pathology, Moscow, Russian Federation*

Objective: Over the last several years the relationship of liver stiffness (LS) with congestion in decompensated heart failure (DHF) have been discussed. The aim of the study was to assess LS by the transient elastography (TE) and its associations with hyperhydration by bioimpedance vector analysis (BIVA) in DHF.
Methods: LS by TE and hydration status by BIVA were measured in 123 patients with DHF on admission and discharge (81 male, 71 ± 11 years (M ± SD), arterial hypertension 94%, myocardial infarction 45%, atrial fibrillation 69%, diabetes mellitus 44%,

chronic kidney disease 25%, left ventricular ejection fraction (EF) 41 ± 14%, EF < 40% 46%, baseline NT-proBNP 3820 (1840;5486) pg/ml). In TE 10 valid measurements were required with success rate of >60%. LS = 5.8 was considered normal and LS = 5.9, 7.2, 9.5 and 12.5 kPa was considered as fibrosis (F1-F3 METAVIR score) and cirrhosis (F4) according to thresholds in studies with chronic liver disease. Hydration status was assessed by BIVA using resistance (R) and reactance (Xc) standardized by height (h). Wilcoxon adn Spearman tests were performed. P < 0.05 was considered significant.

In 6 patients died during hospitalisation liver biopsy was reviewed. Hematoxylin-eosin slides from liver autopsy specimens were examined in 6 persons died during hospitalisation. Pathologist didn't know of LS values. Histologic features of cardiac hepatopathy and congestive hepatic fibrosis score (CHFS) based on the pattern of fibrosis were assessed.

Results: On admission normal LS was observed in 21.1% of patients, abnormal LS = 5.9, 7.2, 9.5 and 12.5 kPa - in 8.1, 11.4, 11.4 and 48% of patients. At discharge normal LS was observed in 24.4% of patients, abnormal LS = 5.9, 7.2, 9.5 and 12.5 kPa - in 15.4, 11.4, 16.3 and 32.5% of patients.

During hospitalisation the median value of LS decreased from 12.3 (interquartile range 6.3;25.1) to 9.2 (5.9;14.4) kPa (?LS=-2.8 (-10.4;0.3) kPa), p < 0.001. R/h and Xc/h increased from 250 ± 64 to 287 ± 58 Om/m and from 21 ± 8 to 26 ± 7 Om/m (?R/h 37 (10;64) Om/m, ?Xc/h 4.7 (1.2;8.9) Om/m), meaning decongestion (p < 0.001 for both comparisons). Patients' weight decreased from 87 ± 20 to 82 ± 18 kg, p < 0.001 (?weight -4(-7;-2) kg).

?LS correlated with ?R/h (r=-0.42), ?Xc/h (r=-0.44) and ?weight (r = 0.46).

In 6 died patients LS was >12.5 kPa, in 1 case - 8 kPa. Liver fibrosis was observed in all slides but was not associated with LS. CHFS 2B (moderate portal fibrosis and central zone fibrosis, with accentuation of fibrosis in the portal zone) was revealed in 5 cases with corresponding LS 25.7, 22.3, 21.8, 16.9 and 8 kPa, CHFS 3 (bridging fibrosis) - in 1 case with LS 20.4 kPa and CHFS 4 (cirrhosis) - in 1 case with LS 17.3 kPa.

Conclusions: LS was associated with congestion by BIVA and didn't correlate with degree of histology liver fibrosis. During hospitalization decrease of LS correlated with decrease of weight and decongestion by BIVA parameters.

2085

Relationship of clinical congestion to biomarker activation and outcome in patients with heart failure: findings from BIOSTAT-CHF

P Pellicori[1]; G James-Rae[1]; A Voors[2]; C Lang[3]; M Metra[4]; G Filippatos[5]; P Ponikowski[6]; F Zannad[7]; J Khan[1]; A Mcconnachie[1]; JGF Cleland[1]

[1]University of Glasgow, Robertson Centre for Biostatistics, , Glasgow, United Kingdom; *[2]University Medical Center Groningen, Groningen, Netherlands*; *[3]University of Dundee, Dundee, United Kingdom*; *[4]University of Brescia, Brescia, Italy*; *[5]National & Kapodistrian University of Athens, Athens, Greece*; *[6]Wroclaw Medical University, Wroclaw, Poland*; *[7]University Hospital of Nancy , Nancy, France*

Aims: There is no universal method to assess and grade congestion. We used the clinical value of different clinical signs of congestion to construct a congestion score, and determined its relationship to novel biomarkers reflecting different disease pathways.

Methods and Results: Patients enrolled in The BIOlogy Study to TAilored Treatment in Chronic Heart Failure (BIOSTAT-CHF) were clinically assessed at baseline. Apart from the 3rd heart sound, each clinical sign of congestion was associated with an increase in all-cause mortality (ACM) or the composite of ACM and HF hospitalisation (HFH).

A congestion score was constructed for those with a complete set of relevant data (1589 patients (63%), based on lung auscultation (normal or presence of crepitations at a single or both lung bases), jugular venous pressure (not visible, uncertain, raised), peripheral oedema (none, ankles, below or above knees), hepatomegaly (absent or present) and orthopnoea (absent or present) with one point attributed for each degree of severity and a total possible score of nine.

124 in-patients (11%) and 202 out-patients (43%) were free of congestion and had the lowest risk of ACM (8% and 6% respectively) and of ACM/HFH (26% and 10% respectively) at 1 year. Risk increased progressively with increasing congestion score; overall, those who scored = 4 had roughly a 3-fold higher risk of ACM (HR: 3.33 (95%CI: 2.39-4.64, p < 0.001) or ACM/HFH (HR: 2.71 (95%CI: 2.12-3.47), p < 0.001) than those who scored 0.

Serum concentrations of all 31 measured biomarkers correlated significantly with clinical congestion score; natriuretic peptides, endothelin and some novel biomarkers of inflammation or fibrosis (Pentraxin-3 and WAP4C) had the strongest associations.

Conclusions: Clinical congestion score provides strong prognostic information but their evaluation may require considerable clinical skill. Serum concentrations of many biomarkers are associated with congestion, which might explain their association with prognosis. Whether other biomarkers add value to natriuretic peptides for tracking changes in the severity of congestion is uncertain

Moderated Posters - How to manage organ dysfunction in acute heart failure

2086

Blood glucose values spanning hypoglycemia and hyperglycemia during a heart failure hospitalization is associated with prolonged length of stay in patients with history of diabetes

S Sarkar[1]; J Koehler[1]
[1]*Medtronic Plc., Moundsview, United States of America*

Introduction: Patients with diabetes are at an increased risk for worsening heart failure (HF). We investigated whether changes in blood glucose during HF hospitalization influences length of stay (LOS).
Methods: HF hospitalizations (HFH) were retrospectively identified in patients with cardiovascular disease from the de-identified Optum EHR database during 01/2011-03/2017. HFHs were included for analysis if patient had history of diabetes prior to admission and if there was administration of intravenous acute HF therapy (diuretic or vasodilator or inotrope) during hospital stay. Valid fasting and random blood glucose measurements during hospital stay were included for analysis and postprandial measurements were excluded. The minimum and maximum glucose values during each hospital stay were categorized into 6 groups (table) using well established thresholds of 90 mg/dL and 140 mg/dL. The median LOS in the 6 groups were compared using Kruskal-Wallis Test and pairwise comparisons were performed using the Wilcoxon Rank Sum Test.
Results: A total of 164,178 HFH identified in 102,437 patients (72 ± 12 years, 51% male) met inclusion criteria and had a valid glucose measurement during HFH. The number and % of HFH in each blood glucose group and their associated length of stay statistics are shown in table. Over half of HFHs had blood glucose spanning both < 90 mg/dL and >140 mg/dL during the hospital stay. Median length of stay is different between different range of blood glucose values ($p < 0.001$) with patients with a large range of blood glucose values spanning from hypo to hyper glycemia having two-time longer LOS compared to patients with blood glucose in normal range during HFH ($p < 0.001$).
Conclusion: Large proportion of HFHs have a range of blood glucose that spans from hypo to hyper glycemia during hospital stay and these patients had a longer LOS in the hospital. Whether stricter management of blood glucose during HFH will lead to more effective acute HF therapy during admission needs further investigation.

		Length of stay (days)	
Blood glucose groups (thresholds in mg/dL)	Number of HFH (%)	Median (IQR)	Mean (SD)
maxGlucose < 90	297 (0.2)	3 (2-4)	3.4 (4.2)
minGlucose < 90 and maxGlucose ≥ 90 and maxGlucose ≤ 140	7925 (4.8)	4 (3-7)	5.8 (10.9)
minGlucose < 90 and maxGlucose > 140	82961 (50.5)	6 (4-11)	10.4 (22.7)
minGlucose ≥ 90 and maxGlucose ≤ 140	7592 (4.6)	3 (2-5)	3.9 (4.8)
minGlucose ≥ 90 and minGlucose ≤ 140 and maxGlucose > 140	56163 (34.2)	4 (3-7)	5.8 (9.1)
minGlucose > 140	9240 (5.6)	3 (2-4)	3.4 (3.0)

2087

Worsening renal function during decongestion among patients hospitalized for heart failure: findings from the escape trial.

M Marat Fudim[1]; SJ Doerfler[1]; A Coles[1]; SJ Greene[1]; LB Cooper[1]; M Fiuzat[1]; CM O'connor[1]; JG Rogers[1]; RJ Mentz[1]
[1]*Duke Clinical Research Institute, Cardiology, Durham, United States of America*

Funding Acknowledgements: American Heart Association and NIH T32

Background: Worsening renal function (WRF) is commonly encountered as patients are decongested during a hospitalization for acute heart failure (HF), but the incidence and prognostic implications of WRF in the setting of different measures of decongestion are unclear.
Purpose: Compare the agreement rate between various measures of decongestion and compare the prognostic implications of WRF in the setting of these measures of decongestion.
Methods: Patients (N = 433) from the Evaluation Study of Congestive Heart Failure and Pulmonary Artery Catheterization Effectiveness (ESCAPE) were included and classified into 4 groups by measures of decongestion during hospitalization: hemodynamic (right atrial pressure = 8 mmHg and/or wedge pressure = 15 mmHg at discharge), physical exam (= 1 sign of congestion at discharge), hemoconcentration (any increase in hemoglobin) and estimated plasma volume using the Hakim formula (5% reduction in plasma volume). WRF was defined as creatinine increase > 0.3 mg/dl during hospitalization. The association between WRF and 180-day all-cause death was assessed using Cox proportional hazards regression analysis adjusted for age, sex, and BMI stratified by decongestion status via this different measures.
Results: Successful decongestion was observed in N = 124 (60%) of patients by hemodynamics, N = 204 (49%) by clinical exam, N = 173 (47%) by hemoconcentration and N = 165 (45%) by plasma volume. There was no agreement between the hemodynamic assessment and other decongestion measures in up to 43% of cases. WRF was observed in 41% of patients, with a lower rate among patients with successful decongestion and higher rate (up to 60%) among patients with unsuccessful decongestion. Inadequate decongestion at discharge was associated with worse outcomes (Figure). Among patients decongested at discharge, in-hospital WRF was not significantly associated with the hazard of all-cause death at 180 days, irrespective of the measure of decongestion examined (Figure).
Discussion: In this clinical trial cohort of patients hospitalized for HF, although there was disagreement across common measures of decongestion, in-hospital WRF was not associated with increased hazard of all-cause mortality among patients successfully decongested at discharge.

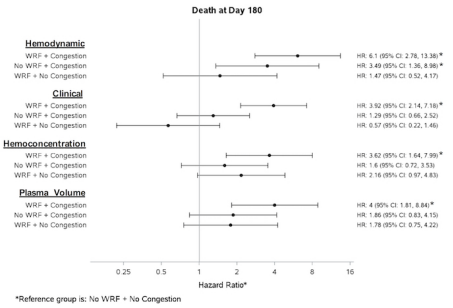


Figure: Adjusted 180 day all-cause death stratified different measures of congestion/decongestion. Proportional hazards regression analysis adjusting for age, body mass index and sex. * indicates a significant association with reference (No WRF and no Congestion) p<0.01, rest p>0.05. CI=confidence interval, HR=hazard ratio, WRF=worsening renal function.

Figure

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Neurocognitive deficits in cardiogenic shock are not acutely reversed with haemodynamic optimisation

M R Monique R Robinson[1]; H Khalid[1]; S Alkindi[1]; L Njoroge[1]; T Schwab[1]; M Khayata[1]; GH Oliveira[1]
[1]*University Hospitals Cleveland Medical Center, Cardiology, Division of Heart Failure and Transplantation, Cleveland, United States of America*

Background: Cardiogenic shock (CS) is characterized by altered mentation secondary to poor cardiac output and decreased cerebral perfusion. There is a paucity of data to demonstrate the relationship of haemodynamic (HD) parameters, including cardiac output and index and formal metrics of neurocognitive function (NCF) for patients with CS.

Purpose: Evaluate neurocognition in patients with CS and monitor NCF changes that occur with HD optimisation of CS.
Methods: The Montreal Cognitive Assessment (MoCA) is a validated tool for assessing global and subcategories of NCF (abstract thought, naming, data recall, and orientation). For patients with cardiogenic shock admitted to a specialised heart failure intensive care unit, with a cardiac index of = 2.2 L/min/m2), HD monitoring, and clinical optimisation was undertaken. MoCA assessment was done prior to the inception of standardised medical therapies and daily until HD monitoring was completed.
Results: A total of 21 patients were enrolled: 19% were female, 67% Caucasian, 72% with non- ischaemic cardiomyopathy. One patient had a history of cerebrovascular accident and 3 patients had a history of antecedent depression. Mean left ventricular ejection fraction (LVEF) was 23 ± 16 % , baseline HD assessment demonstrated central venous pressure (CVP) 13 ± 6 mmHg, pulmonary artery systolic pressure (PASP) 53 ± 15 mmHg, pulmonary artery diastolic pressure (PADP) 26 ± 8 mmHg, pulmonary capillary wedge pressure (PCWP) 22 ± 6 mmHg, cardiac output (CO) 3.6 ± 1 L/min, cardiac index (CI) 1.8 ± 0.1 L/min/m2, systemic vascular resistance 1748 ± 547 dynes-sec/cm5 , pulmonary arterial O2 saturation (SvO2): 54 ± 7 %. The average duration of HD monitoring was 2.7 ± 2.4 days. Baseline global MoCA score was 21 ± 4 and there was subnormal performance in each subcategory of NCF. Following medical management for CS, there was statistically significant HD improvement with CVP 13 ± 6 vs. 9 ± 6 mmHg p 0.008, PASP 53 ± 15 vs. 48 ± 15 mmHg p 0.06, PCWP 22 ± 7 vs. 15 ± 6 mmHg p 0.014, CO 3.6 ± 1 vs. 5.2 ± 1.2 L/min p < 0.001, CI 1.8 ± 0.1 vs. 2.6 ± 0.6 p < 0.001
Despite HD improvement, there was no significant difference in MoCA scores 21 ± 4 vs 23 ± 5, p 0.11.
Baseline MoCA scores correlated with baseline SVR (Spearman's rho = 0.6, P = 0.009), but there was no significant correlation between post-optimization hemodynamics and MoCA.
Conclusions: Patients with cardiogenic shock have demonstrable neurocognitive deficits that persist even following acute intensive care haemodynamic optimisation. Future work is required to explore the role that sustained HD stability plays in improving NCF.

2089

Worsening renal function prevalence and risk factors among brazilian patients with decompensated heart failure

P P M Spineti[1]; M E C Magalhaes[1]; F P Taniguchi[2]; S T Montenegro[3]; J D Souza Neto[4]; A A V De Paola[5]; L E P Rohde[6]; L G Passaglia[7]; K R P Pereira[8]; M M Vasconcellos[9]; M A M Da Silva[10]; J A Figueiredo Neto[11]; M A V Guedes[12]; V S Barzilai[13]; D C Albuquerque[1]
[1]State University of Rio de Janeiro, Pedro Ernesto University Hospital, Rio de Janeiro, Brazil; [2]HCor - Hospital do Coração, São Paulo, Brazil; [3]Pernambuco University, PROCAPE, Recife, Brazil; [4]Messejana Hospital, Fortaleza, Brazil; [5]Federal University of São Paulo, São Paulo Hospital, São Paulo, Brazil; [6]Federal University of Rio Grande do Sul, Hospital das Clínicas de Porto Alegre, Porto Alegre, Brazil; [7]Federal University of Minas Gerais, Hospital das Clínicas, Belo Horizonte, Brazil; [8]Hospital das Clínicas Gaspar Vianna, Belém, Brazil; [9]National Institute of Cardiology, Rio de Janeiro, Brazil; [10]Santa Casa de Misericórdia de Maceio, Maceio, Brazil; [11]Federal University of Maranhão, University Hospital , São Luís, Brazil; [12]Ana Nery Hospital, Salvador, Brazil; [13]Instituto de Cardiologia do Distrito Federal, Brasilia, Brazil

On behalf of: Best Clinical Practice in Cardiology (BPC) Program
Funding Acknowledgements: Brazilian Health Ministry (PROADI-SUS), American Heart Association (AHA), Brazilian Society of Cardiology (SBC)

Background: Worsening renal function (WRF) is associated with poorer prognosis in patients admitted with decompensated heart failure (DHF). Little is known about its incidence and risk factors in Brazil.
Purpose: To determine the incidence and risk factors to WRF at discharge among patients included in the Best Clinical Practice in Cardiology Program (BPC).
Methods: Longitudinal prospective study. Patients admitted for DHF between February 14, 2016 and December 24, 2017, in 15 centres throughout Brazil, were included in the study. WRF was defined as an absolute increase of = 0.3mg/dL in serum creatinine (SCr) between admission and discharge. Uni- and multivariate analyses were performed to identify WRF risk factors.
Results: 807 were included in the BPC Program, 11(5.3%) were under HD, 75(9.3%) died during the hospitalization and 64(7.9%) missed admission or discharge SCr measurements and were excluded from analysis. Data from the remaining 657 patients showed that 58.1% were male; with mean age of 59.7 +/- 14.5 years, 21.9% ischemic aetiology with a median ejection fraction of 33.0 %(25.0-48.0%). WRF incidence was 20.2%. It was associated with diabetes mellitus (46.3 x 35.9, p 0.034), previous use of hydralazine (15.0 x 9.2%, p 0.047), nitrates (23.3 x 13.7, p 0.007) or loop diuretics (78.2 x 68.5, p 0.033), haemoglobin (12.2 x 12.9mg/dL, p0,003), SCr (1.21 x 1.27, p < 0.0001), systolic (121 x 117mmHg, p0,009) and diastolic (80x70mmHg, p 0.033) blood pressure at admission, in univariate analysis. In multivariate analysis only previous use of loop diuretics remained associated with WRF (p 0.049). The WRF group had a longer length of stay 19 (9-32) x 15 (8-30) days (p 0,047). Conclusion: Previous use of loop diuretics was the only risk factor identified for WRF. Patients discharged with WRF had a longer hospital stay.

2090

Relationship between changes in brain natriuretic peptide and worsening renal functions in acute heart failure

Y Horiuchi[1]; N Wettersten[1]; P Murray[2]; A Maisel[1]
[1]University of California San Diego, Division of Cardiovascular Medicine, San Diego, United States of America; [2]University College Dublin, Department of Nephrology, Dublin, Ireland

Funding Acknowledgements: Abbott Laboratories and Alere, Inc.

Background: In acute heart failure (AHF), relationships between changes in brain natriuretic peptide (BNP) and worsening renal function (WRF) and its prognostic implications have yet to be fully determined.
Purpose: We aimed to investigate the prognostic value of WRF in relation to changes in BNP.
Methods: The Acute Kidney Injury NGAL Evaluation of Symptomatic heart failure Study (AKINESIS) was a prospective, international, multicenter study of AHF patients. We analyzed the relationship between a decrease in BNP and WRF in relation to in-hospital and 1-year mortality. Severe WRF was a sustained increase of = 0.5 mg/dl or = 50% in creatinine and non-severe WRF was a non-sustained increase of = 0.3 mg/dl or = 50%. WRF with clinical deterioration was non-severe WRF with renal replacement therapy, inotrope use or mechanical ventilation. Decreased BNP was defined as a = 30% reduction in the last measured BNP compared to admission BNP.
Results: Among 814 patients, the incidence of WRF was not different between patients with or without decreased BNP (non-severe WRF, 33% vs. 31%, p = 0.549; severe WRF, 11% vs. 9%, p = 0.551; WRF with clinical deterioration, 8% vs. 10%, p = 0.425). Decreased BNP was associated with better in-hospital and 1-year mortality regardless of WRF, while WRF was associated with worse outcomes only in patients without decreased BNP (Table 1 and Figure 1). In multivariate Cox regression analysis, decreased BNP, severe WRF, and WRF with clinical deterioration were significantly associated with 1-year mortality.
Conclusions: Decreased BNP was associated with better in-hospital and long-term outcomes. WRF was only associated with adverse outcomes in patients without decreased BNP.

Table 1. In-hospital mortality

	non-severe WRF (+)	non-severe WRF (-)
Decreased BNP	0%	1%
Non-decreased BNP	13%	3%
	severe WRF (+)	severe WRF (-)
Decreased BNP	0%	1%
Non-decreased BNP	22%	5%
	WRF with clinical deterioration (+)	WRF with clinical deterioration (-)
Decreased BNP	0%	1%
Non-decreased BNP	30%	4%

BNP, brain natriuretic peptide; WRF, worsening renal function

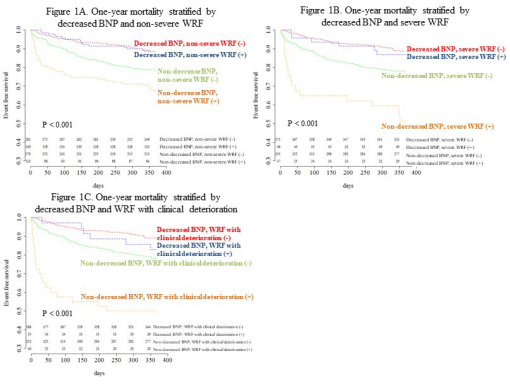

Figure 1

2091

Clinical characteristics and in-hospital outcomes of elderly patients with acute heart failure admitted to different settings of care: data from the ATHENA registry

A Herbst[1]; F Orso[1]; A Pratesi[1]; G Biagioni[1]; F Fedeli[1]; S Parlapiano[1]; C Ghiara[1]; A Lo Forte[1]; G Ciuti[2]; C Tozzetti[2]; F Bacci[2]; M Di Bari[1]; N Marchionni[3]; A Ungar[1]; S Baldasseroni[1]

[1]Careggi University Hospital (AOUC), Department of medicine and geriatrics, Florence, Italy; *[2]Careggi University Hospital (AOUC), Department of emergency and internal medicine, Florence, Italy*; *[3]Careggi University Hospital (AOUC), Cardiothoracovascular Department, Florence, Italy*

On behalf of: ATHENA Study group

Background: Acute heart failure (AHF) is a common disease that typically affects the elderly. Clinical registries should represent the so-called "real world", however, HF registries may maintain a certain level of selection bias by including only patients hospitalised in cardiology wards. Administrative data show that only a minority of these patients (about a quarter) is hospitalised in cardiology units, with the majority being admitted to internal medicine and geriatric settings of care.
Purpose: to compare the clinical characteristics and in-hospital prognosis of elderly patients hospitalised for AHF in the settings of care of usual management: cardiology, internal medicine and geriatrics.
Methods: data derived from the ATHENA retrospective observational study which included elderly patients (= 65 years) admitted with diagnosis of AHF (worsening or de novo) to the Emergency department (ED) of a tertiary University teaching-hospital and transferred to the above described settings of care in the period 01.12.2014-01.12.2015.
Results: 401 patients composed the study population; 15.2% were hospitalised in cardiology, 14.7% in geriatrics and 70.1% in internal medicine. Mean age was 83.5 years, resulting higher in geriatrics (86.9 years) versus internal medicine (83.4 years) and cardiology (81.0 years), P = 0.001. Females were 52.6%: 55.7% in cardiology, 52.7% in internal medicine and 49.2% in Geriatrics (P = 0.770). Patients with HFpEF were 47.4% and were hospitalised less frequently in Cardiology (36.8%) compared to geriatrics (55.1%) and internal medicine (48.6), P = 0.147. In-hospital mortality was 8.9% and it was higher in geriatrics (18.6%) compared to cardiology (14.8%) and internal medicine (5.7%), (P = 0.002). Independent predictors of in-hospital mortality were evaluated using multivariate analysis adjusting for age, gender and comorbitidies (Charlson comorbidity score). Barthel index (an index of functional status) (OR 0.98, 95%CI 0.97-1.00, p = 0.028), systolic blood pressure in the emergency department (OR 0.96, CI = 0.93-0.99, p = 0.014), cognitive impairment (OR 5.33, CI = 1.16-24.40, p = 0.031) and the setting of care were found to be correlated with in-hospital mortality. Particularly, a protective correlation could be observed with the admission to cardiological setting of care (geriatrics vs cardiology OR 13.23, 95%CI 1.80-97.07, p = 0.011; internal medicine vs cardiology OR 12.32; 95%CI 2.25-67.54).
Conclusions: elderly patients with AHF differ significantly in terms of clinical characteristics and in-hospital prognosis according to the different settings of care. In this population in-hospital mortality seems to be correlated with clinical variables already known to impact prognosis, but also with typical geriatric variables such as functional status and cognitive impairment and with setting of care of assignment after the emergency department, with a protective effect of management in cardiological settings.

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Relationship between sleep-disordered breathing or its treatment and post-discharge outcomes in patients hospitalized due to acute decompensated heart failure

H Matsumoto[1]; T Kasai[1]; S Suda[1]; A Murata[2]; S Yatsu[2]; M Shimizu[2]; J Shitara[2]; T Kato[2]; M Hiki[2]; H Daida[2]

[1]Juntendo University School of Medicine, Department of Cardiovascular Medicine, Cardiovascular Respiratory Sleep Medicine, Tokyo, Japan; *[2]Juntendo University School of Medicine, Department of Cardiovascular Medicine, Tokyo, Japan*

Funding Acknowledgements: Resmed, Philips-Respironics, Fukuda-Denshi

Introduction: In patients hospitalized due to acute decompensated heart failure (ADHF), Residual risk for worse post-discharge clinical outcomes remains to be clarified. However, limited data regarding influence of sleep-disordered breathing (SDB) and its treatment by positive airway pressure (PAP) on post-discharge clinical outcomes in patients hospitalized due to ADHF are available.
Hypothesis: In patients hospitalized due to ADHF, presence of SDB is associated with worse post-discharge clinical outcomes, which can be reversed by PAP therapy.
Methods: After the initial improvement of ADHF, overnight polysomnography was performed on consecutive hospitalized patients whose left ventricular ejection fraction (LVEF) = 45% between May 2012 and December 2014. SDB was defined as an apnea-hypopnea index = 15. Patients with SDB were subdivided into those with or without PAP treatment. The risk for composite of all-cause mortality and readmission were assessed by stepwise multivariable Cox proportional model.
Results: Overall, 114 patients including 76 with SDB (28 with PAP treatment) and 38 without SDB were enrolled. At a median follow-up of 6.8 months, 44 patients had clinical events (39%). In the stepwise multivariable analysis, SDB was associated with increased risk of clinical events (hazard ratio [HR], 3.41; P = 0.005). Among SDB patients, stepwise multivariable analysis showed that PAP treatment was associated with reduced risk of clinical events (HR 0.37; P = 0.027).
Conclusion: In patients with reduced LVEF hospitalized due to ADHF, presence of SDB affected post-discharge clinical outcomes adversely, which may be reversible by PAP therapy. Thus, following ADHF, hospitalized patients with reduced LVEF should be evaluated for SDB and considered for SDB treatment prior to discharge.

Clinical Case Corner 6 - Such a big, big heart: cases of (pseudo)hypertrophy

2093

Identification of a novel LAMP2 gene variant: key role of genetic testing in the diagnosis of Danon disease

V Novelli[1]; A Bisignani[2]; G Pelargonio[2]; G Primiano[3]; FD Tiziano[4]; P Zeppilli[5]; S Servidei[3]; F Crea[2]; MG Genuardi[4]
[1]Polyclinic Agostino Gemelli, Centro Benito Stirpe per la morte improvvisa del Giovane Atleta- Institute of Genomic Medicine, Rome, Italy; *[2]Polyclinic Agostino Gemelli, Polo di Scienze Cardiovascolari e Toraciche, Rome, Italy*; *[3]Polyclinic Agostino Gemelli, Department of Neurology, Rome, Italy*; *[4]Catholic University of the Sacred Heart, Institute of Genomic Medicine, Rome, Italy*; *[5]Catholic University of the Sacred Heart, Institute of Sport Medicine, Rome, Italy*

Danon disease (OMIM 300257) is an X-linked lysosomal storage disorder, characterized by hypertrophic cardiomyopathy (HCM), skeletal myopathy and variable intellectual disability. This condition accounts for ~ 4% of HCM patients, affecting both genders, with a severe and early onset phenotype in males. Genetic variants in LAMP2 gene are the main cause of this fatal condition. Here, we describe a novel LAMP2 pathogenic variant, demonstrating the utility of including this gene in the HCM genetic testing.
A 16-year-old male, with a family history of sudden cardiac death (SCD), was referred to our center with a diagnosis of HCM of one year ago when he was admitted for palpitations in a secondary hospital. His mother died for suspected post partum dilated cardiomyopathy (DCM) when she was 24 years old. Upon admission to our institution, the patient was symptomatic for palpitations, with evidence of biventricular hypertrophy on the echo and atrial tachycardia during ECG monitoring. Neurological examination revealed mild intellectual disability, mild weakness of distal upper and lower limb muscles and bilateral pes cavus. Because the phenotype was unclear, suggesting an early onset HCM, with a suspected family history of SCD, genetic testing was performed. A custom HCM sequencing panel including 12 genes associated with HCM and related phenotypes was adopted.
Results of the genetic testing showed a novel hemizygous 1 bp deletion, c.453delT, in LAMP2.
These results have rapidly driven the clinics through the diagnosis of Danon disease. Further analysis, including muscle biopsy (Figure 1), confirmed the diagnosis of this fatal condition, providing the indication for a heart transplant.
In conclusion, this case highlights the clinical utility of genetic testing in the differential diagnosis of conditions in the spectrum of HCM, suggesting the importance of including the LAMP2 gene in targeted NGS panels used for genetic diagnosis of HCM.

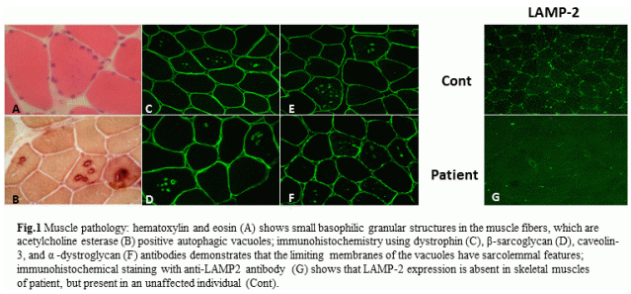


Fig.1 Muscle pathology: hematoxylin and eosin (A) shows small basophilic granular structures in the muscle fibers, which are acetylcholine esterase (B) positive autophagic vacuoles; immunohistochemistry using dystrophin (C), β-sarcoglycan (D), caveolin-3, and α -dystroglycan (F) antibodies demonstrates that the limiting membranes of the vacuoles have sarcolemmal features; immunohistochemical staining with anti-LAMP2 antibody (G) shows that LAMP-2 expression is absent in skeletal muscles of patient, but present in an unaffected individual (Cont).

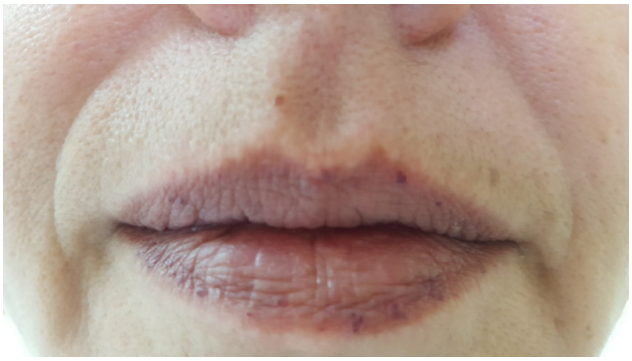
Fig. 1 Muscle Biopsy

2094

Hypertrophic obstructive cardiomyopathy: a disguise for fabry disease?

S Sebatian Militaru[1]; R Adam[1]; R Trambitasu[2]; A Munteanu[1]; A Dulamea[3]; E Rusu[3]; R Jurcut[1]
[1]Institute of Cardiovascular Diseases Prof. C.C. Iliescu, Cardiology, Bucharest, Romania; *[2]County Emergency Hospital of Brasov, Brasov, Romania*; *[3]Fundeni Clinical Institute, Bucharest, Romania*

Hypertrophic cardiomyopathy can be the expression of many etiologies, called phenocopies, and identifying and differentiating them can be a challenge.
We present the case of a 49 year-old patient, with perioral angiokeratoma, acroparesthesia, a history of cryptogenic stroke and obstructive HCM (diagnosed 6 years prior), who was referred to our center for cardiac evaluation. Family history included: a sister deceased at 54 while on dialysis, who's eldest son also died at age 27 while on dialysis.
Lab work-up showed slight renal dysfunction (small proteinuria, normal creatinine), and above normal levels of Troponin I (0.024 ng/ml) at resting state. The ECG showed sinus rhythm, LVH, short PR interval (~120 ms), without a delta wave. Echographic evaluation: concentric LVH, papillary muscle hypertrophy, normal systolic function, longitudinal dysfunction and a gradient of 48 mmHg in the LV ejection tract in Valsalva at rest. Ophthalmologic evaluation showed cornea verticillata, a FD specific sign. The patient was tested with genetic and enzymatic tests of Fabry disease, which confirmed the diagnosis: a heterozygote pathogenic mutation of the GLA gene was detected (c.[797A>C](p.[Asp266Ala]), aGal levels of 1,2 μmol/L/h (cut-off > 1,2 μmol/L/h) and Lyso-Gb3 level of 6,3 ng/mL (cut-off 0 - 3,5 ng/mL). During family screening, the patient's son was evaluated clinically, ECG and echocardiographicaly, and showed no cardiac involvement, but had angiokeratoma, acroparesthesia and anhydrosis, mild renal involvement and aGal level of 0. The second son of the patients sister was also found by family screening to have chronic kidney disease with creatinine levels of 2.3 mg/dl and proteinuria, and a confirmed diagnosis of FD. The patient, her son and her nephew all began enzyme replacement therapy, which can improve their life expectancy.
The main problem illustrated by this case is the importance of differential diagnosis in cardiomyopathies, as it has been proven that early enzyme treatment in Fabry disease can stop or slow disease pregression.
Fabry disease diagnosis can be suspected using clinical and paraclinical "red flags", in the present case these are: history of stroke at a young age, family history of renal failure, angiokeratoma, acroparesthesia, short PR, slightly high troponin level, proteinuria, concentric LVH with papillary muscle hypertrophy. Correct diagnosis of a phenocopy of HCM can save or prolong the life of FD pts by starting enzyme therapy, especially when accompanied by careful family screening.



Perioral angiokeratoma

2095

TTR familial amyloidosis - never forget phenocopies in hypertrophic cardiomyopathy

A Adriana Mursa[1]; M Serban[1]; A Jercan[2]; S Badelita[2]; C Stan[3]; BA Popescu[1]; C Ginghina[1]; D Coriu[2]; R Jurcut[1]
[1]Institute of Cardiovascular Diseases Prof. C.C. Iliescu, Bucharest, Romania; *[2]Fundeni Clinical Institute, Hematology, Bucharest, Romania*; *[3]Fundeni Clinical Institute, Nuclear Imaging, Bucharest, Romania*

Introduction: and case report: Left ventricular hypertrophy (LVH) unrelated to pressure overload leads to a first diagnosis of hypertrophic cardiomyopathy (HCM), but carefully putting together the puzzle of clinical picture, family history, electrocardiography and multimodality imaging can point further, revealing the path to the right diagnosis and therapeutic approach.
We present the case of a 49 years old female who presented to our clinic complaining of exertion dyspnea and palpitations in the last year. The patient has also been complaining of distal paresthesia for the last 5 years. From her family history we retain the mother who died at 49 years old after progressive severe loss of mobility and 4 maternal uncles with neuropathy.
The ECG showed sinus rhythm, low voltage in limb leads and trifascicular block (Ist degree AV block, LAFB, RBBB). Echocardiography revealed non obstructing HCM with maximal wall thickness of 16 mm, preserved left ventricular (LV) ejection fraction (50%), restrictive pattern of diastolic dysfunction, severely decreased wall motion velocities, LV global longitudinal strain -12.1%, with apical sparring. Biologically: BNP 141 pg/ml, normal creatinine and plasma protein electrophoresis and immunofixation. The 99Tc-HDP nuclear scan showed moderate late cardiac enhancement suggesting TTR amyloidosis. The PCR genetic test was positive for the mutation Glu54Gln (GAG-CAG) on the Third exon of TTR gene, a mutation known as specific to the Romanian population.
Discussion: Behind the diagnosis of HCM can sit either sarcomeric forms, or a large variety of metabolic or other genetic or non-genetic disorders. Sometimes, finding the right diagnosis leads to specific therapeutic possibilities. Genetic TTR amyloidosis is a differential diagnosis to AL amyloidosis and wild-type, senile amyloidosis. Red flags which led to diagnosing this phenocopy of HCM were LVH combined with low voltage and conduction disturbances on ECG, apical sparing on LV longitudinal strain map and finally cardiac enhancement at 99Tc-HDP nuclear scan, all in association with neurological symptoms in the patient and the family. Comparing to AL amyloidosis without treatment, TTR amyloidosis carries out a better outcome, but often progresses to intractable heart failure and death due to systolic heart failure or dysrhythmia. Not all cases present cardiac involvement, most patients having only neurological symptoms (also depending on the exact mutation - interestingly, our patient has a region-specific genetic variant). Several therapeutic options exist for TTR amyloidosis, some are still under development.
Conclusion: The present case illustrates how a red flag approach including multimodality imaging, combined with inter-specialist collaboration can lead to the right diagnosis.

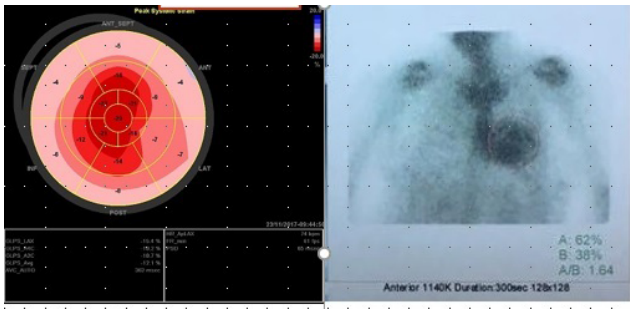


Figure 1

2096
FABRY DISEASE OR SARCOMERIC HYPERTROPHIC CARDIOMYOPATHY?

H Hedvig Takacs[1]; V Nagy[1]; J Borbas[1]; A Tringer[1]; B Csanyi[1]; L Hategan[1]; I Nagy[2]; Z Hegedus[3]; T Forster[1]; R Sepp[1]
[1]University of Szeged, Second Department of Internal Medicine and Cardiological Center, Szeged, Hungary; *[2]Biological Research Centre of Szeged, Institute of Biochemistry, Szeged, Hungary*; *[3]Biological Research Centre of Szeged, Institute of Biophysics, Szeged, Hungary*

Funding Acknowledgements: GINOP-2.3.2-15-2016-00039

Hypertrophic cardiomyopathy (HCM) is a primary myocardial disease typically caused by gene mutations encoding proteins of the cardiac sarcomere. HCM-like phenocopies, e.g. the cardiac manifestation of Fabry disease, make differential diagnosis of HCM cases particularly challenging.
In this case report we describe the detailed genetic analysis of a female patient with a HCM phenotype. At first presentation, the 49 years old female patient complained permanent chest pain, shortness of breath and very low exercise capacity. Cardiac evaluation proved hypertrophic cardiomyopathy with severe asymmetric left ventricular hypertrophy (LV max at the anterior septum: LVmax: 27 mm), without left ventricular outflow tract obstruction. During regular follow up, the patient had no episodes of cardiac decompensation, however echocardiography revealed grade II. diastolic dysfunction with a maximum NTpBNP level of 244 pg/ml. Cardiac MRI confirmed increased left ventricular mass (LVM: 169 g) and the significant hypertrophy of the anterior septum in the basal and mid segment. Though the patient had no dermatological, ophthalmological, audiological and renal symptoms; electroneurography indicated low-grade polyneuropathy. Based on this, genetic screening was performed for Fabry disease, which revealed a c.376A>G (p.Ser126Gly) pathogenic mutation in the GLA gene. Levels of lysoGb3 (= 1,8 ng/ml) was repeatedly in the normal range. In order to prove the cardiac involvement of Fabry disease unequivocally, myocardial biopsy was performed, which did not show histological evidence of Fabry disease. Subsequently, extended screening of 103 cardiomyopathy genes with next generation sequencing proved a most likely pathogenic frameshift mutation, p.Ala1056fs, of the MYBPC3 gene.
Based on the above findings, it is probable that hypertrophic cardiomyopathy was due to the MYBPC3 sarcomere gene mutation and not the cardiac manifestation of Fabry disease in this case.

2097
Double silent threat- case report of asymptomatic patient with cardiac transthyretin amyloidosis and multivessel coronary artery disease

M Monika Gawor[1]; M Franaszczyk[2]; M Spiewak[3]; B Milosz-Wieczorek[3]; M Marczak[3]; M Opolski[4]; Z Bilinska[5]; J Grzybowski[1]
[1]Institute of Cardiology, Department of Cardiomyopathies, Warsaw, Poland; *[2]Institute of Cardiology, Department of Medical Biology, Warsaw, Poland*; *[3]Institute of Cardiology, CMR Unit, Warsaw, Poland*; *[4]Institute of Cardiology, Department of Interventional Cardiology and Angiology, Warsaw, Poland*; *[5]Institute of Cardiology, Unit for Screening Studies in Inherited Cardiovascular Diseases, Warsaw, Poland*

A 49-year-old male was referred to our institution for further evaluation because of abnormalities in the standard 12-lead electrocardiogram (ECG). The patient suffered from recurrent rhinitis due to deviated nasal septum- ECG was performed in preparation for septoplasty. Otherwise, he was completely asymptomatic, without fatigue, exertional dyspnoea, chest pain or syncope.
On physical examination the patient was normotensive, lungs were clear on auscultation, the liver was not enlarged, jugular veins were normal, there was no oedema of lower extremities. The baseline level of NT-proBNP was 925,8 (range 0-125) pg/mL, and hs-cTnT was 38.2 (range 0-14) ng/L. No significant pathology was present on chest X-ray. ECG demonstrated sinus rhythm with low QRS voltage in the limb leads and nonspecific ST-T wave changes (Fig. 1A). Echocardiography revealed concentric hypertrophy of left ventricle (LV) with a maximal wall thickness of 16 mm at interventricular septum. Posterior wall diameter was 14 mm. Left atrial anterior-posterior diameter was 42 mm. Cardiac magnetic resonance (CMR) scan confirmed the presence of concentric LV hypertrophy with a maximal wall thickness of 16 mm and increased myocardial mass indexed for the body surface area (LV mass index [LVMI] 101 g/m2, range 58-91). Systolic function of the LV was decreased with EF 40%. The right ventricular function was in normal range. Moreover, diffuse subendocardial areas of late gadolinium enhancement (LGE) was found. Results of CMR suggested cardiac amyloidosis (Fig. 1B).
Coronary computed tomography angiography showed chronic total occlusion in the middle segments of the right coronary artery (RCA). Moreover stenosis in the left main coronary artery, in the middle segments of the left anterior descending artery (LAD), in the proximal segments of the first diagonal branch and in the proximal segments of the left marginal artery were detected. Patient underwent invasive coronary angiography with fractional flow reserve (FFR) evaluation. Only stenosis in the LAD was identify hemodynamically relevant (FFR = 0.77). Percutaneous coronary intervention using drug eluting stents was performed for occlusion in RCA and for stenosis in LAD (Fig. 1C, 1D). Endomyocardial biopsy was also performed. Transthyretin (TTR)-related amyloid deposits was detected. Genetic analysis revealed Phe33Leu mutation in the TTR gene. Neurological and haematological examination revealed no abnormalities. Patient was referred to the liver transplantation.
The case we describe underscores the importance of ECG as a screening tool in cardiology. Our patient would not have underwent the whole diagnostic process that led to such fatal discovery, unless ECG had been performed in the first place. Although several months after diagnosis patient was still completely asymptomatic, with good exercise tolerance during ECG exercise testing, follow-up showed further deterioration of LV function and increase in NT-proBNP and hs-cTnT levels.

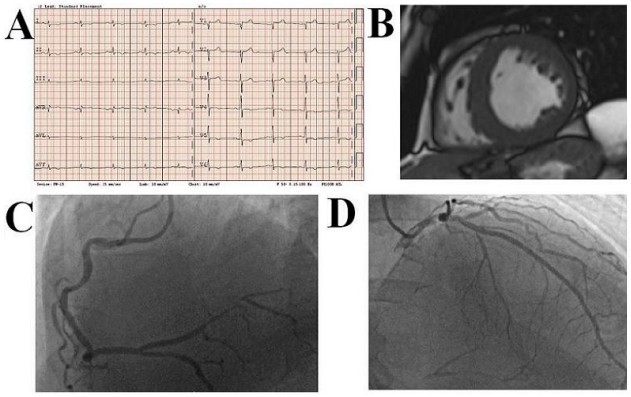


Figure 1

2098

Surgical treatment of hypertrophic obstructive cardiomyopathy in a patient with prior alcohol septal ablation and artificial cardiac pacemaker

K Rudenko[1]; V Lazoryshynets[1]; L Nevmerzhytska[1]; P Danchenko[2]
[1]*Amosov Institute of Cardiovascular Surgery AMS of Ukraine, Kiev, Ukraine*;
[2]*National O.O. Bohomolets Medical University, Kiev, Ukraine*

Introduction: 18-year-old female patient, hospitalized on 07.08.2017, and presented with complaints on chest pain at rest, exertional dyspnea, periodic attacks of palpitations, limited physical activity, and dizziness.
Instrumental examination data were the following:
- TTE: Hypertrophic obstructive cardiomyopathy (HOCM), systolic pressure gradient (SPG) = 80 mm Hg. Systolic anterior motion of the anterior leaflet of the mitral valve. EDV = 59 ml; ESV = 22 ml; SO = 37 ml; EF = 62%. IVS: basal part = 2 cm; medial part = 1,0 cm.
- Coronaroventriculography: Intramural passage of the mid-third of LAD LCA with 50-70% systolic compression.
- Heart CT: Asymmetric hypertrophy of LV myocardium (width = 20 mm, length = 125 mm). Significant trabecularity of the anterior wall of the LV myocardium (non-compacted myocardium).
- ECG: Sinus rhythm, HR = 67/min, singular ventricular extrasystoles. Complete right His bundle branch block.
The following diagnosis was established: hypertrophic cardiomyopathy, obstructive form, mild mitral valve regurgitation, initial stage of pulmonary hypertension, state after implantation of artificial cardiac pacemaker, state after alcohol septal ablation, heart failure, functional capacity III, objective assessment B (NYHA). On 16.08.2017 there was conducted a surgical treatment. The extent of surgical intervention included: extended superficial myectomy of interventricular septum (0,5 cm ? 1,0 cm ? 1,0 cm), resection of 5 secondary chordae of the anterior leaflet of the mitral valve, mobilization of the anterior and posterior groups of papillary muscles of the mitral valve (applying approach of professor P. Ferrazzi, Monza, Italy), LAD LCA debridging, plastic of P2 segment of the posterior leaflet of the mitral valve with transseptal approach. Intraoperative TEE showed no clinically significant SPG on LVOT and mitral valve (SPG = 20 mm Hg, mild mitral valve regurgitation).
In post-operative period patient received antibacterial, antiarrhythmic, antianginal, antihypertensive, and anticoagulation therapy. Follow-up examination in 10 days showed decrease of the degree of mitral regurgitation (SPG = 28 mm Hg) and absense of systolic compression of LAD LCA. On 26.12.2017 there was performed an extraction of the artificial cardiac pacemaker and implanted a dual chamber ICD for the purpose of prophylaxis of sudden cardiac death.
Summary. Surgical intervention is a "gold standard" of treatment of HOCM. Performance of extended superficial myectomy of the IVS with resection of secondary chordae of the anterior leaflet of the mitral valve followed by mobilization of the anterior and posterior groups of papillary muscles of the mitral valve (applying approach of professor P. Ferrazzi, Monza, Italy) is the most optimal choice for definitive repair of this pathology. Debridging can be successfully performed in patients with obstructive form of hypertrophic cardiomyopathy in case of LAD LCA systolic compression.

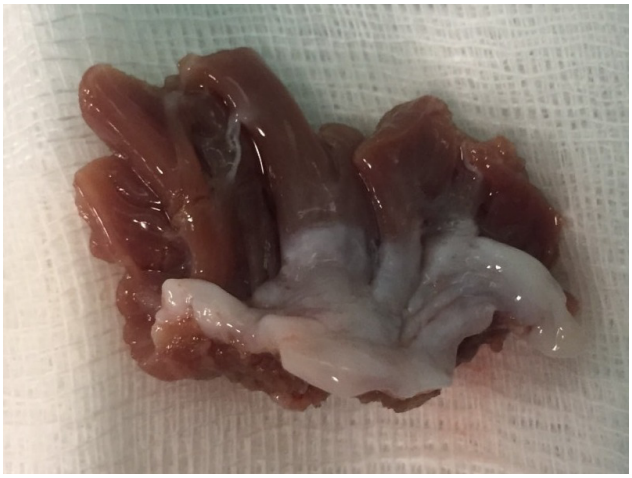


Fig. 1. A part of resected myocardium

Shortness of breath: a common presentation of an uncommon form of cardiac amyloidosis

X Xin Zhang[1]; A Jaffe[1]
[1]*Mayo Clinic, Rochester, United States of America*

Introduction: Dyspnea is a common initial complaint in the cardiologist's office. We present a case of cardiac amyloidosis presenting as isolated dyspnea in an elderly man.
Case Presentation: An 84-year-old man presented to cardiology clinic for one year of progressive dyspnea on exertion without other associated symptoms. His past medical history was notable for coronary artery bypass grafting (CABG) in 2007. Physical exam revealed a blood pressure of 161/78, heart rate 75 bpm at rest, and an oxygen saturation of 96% on room air. After walking 10 feet on flat ground, he became tachycardia to 102 bpm and his oxygen saturation fell modestly to 93%. The remainder of his exam was unremarkable. He demonstrated no signs of valvular heart disease or congestive heart failure by physical examination.
A chest x-ray demonstrated an AV pacemaker and mild cardiomegaly. ECG was consistent with dual chamber pacemaker. Transthoracic echocardiogram (TTE) showed left ventricular ejection fraction of 60 % and thickened left ventricular walls. Left and right coronary angiogram revealed patent bypass grafts.
A technetium Pyrophosphate (PYP) scan was obtained to evaluate for possible transthyretin (TTR) amyloidosis given the patient's advanced age and thickened left ventricular myocardium. PYP scan showed increased uptake in the left ventricular myocardium consistent with TTR cardiac amyloidosis. Furosemide was started for management of volume status. He is currently exploring long term treatment options, including doxycycline /tauroursodeoxycholic acid (TUDCA).
Discussion: Wild type transthyretin cardiac amyloidosis is responsible for sporadic cardiac amyloidosis in the elderly. Also termed "senile amyloidosis," it affects 25-36% of patients older than 80 years although severe symptoms are less common [1]. Consequently, it is less frequently considered as a cause of dyspnea. Presenting symptoms include heart failure, angina, and arrhythmias [1]. While amyloid deposition on histopathology is the gold standard, PYP scan has been shown to have 97% sensitivity and 100% specificity for TTR amyloidosis in some studies [1]. Treatment is currently focused on management of heart failure symptoms, but there are investigational drugs that target TTR production and degradation under study [1] [2].
Conclusion: It is important to consider TTR cardiac amyloidosis in elderly patients who present with unexplained heart failure symptoms. PYP scan is a non-invasive tool for diagnosis and may mitigate the need for a tissue biopsy.

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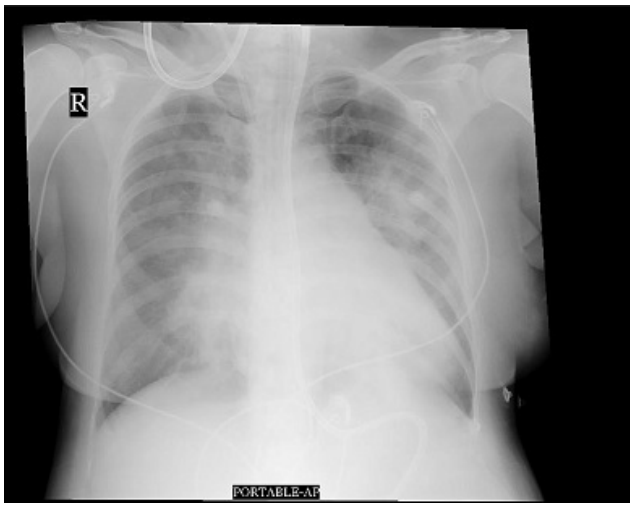
Acute massive pulmonary edema and cardiogenic shock: an unusual presentation of hypertrophic obstructive cardiomyopathy

VIPIN Mughilassery Thomas[1]; IJAZ Majeed[1]; FAHD El Sayed[1]; DOAA Elkholy[1]
[1]*Al Ain Hospital, Cardiology, Al Ain, United Arab Emirates*

Case Summary: This 58- year-old female known to have some cardiac disease was transferred from a peripheral hospital in acute pulmonary edema and cardiogenic shock. She was intubated and mechanically ventilated following respiratory failure. She presented there with history suggestive of respiratory infection of one week followed by progressive shortness of breath of two days duration. She received

intravenous Furosemide and was on Dopamine infusion from the referring hospital. But her condition deteriorated and hence shifted to our Center. On arrival in the ER, her Blood Pressure was 77/48 mm Hg and Chest x-ray showed massive pulmonary edema. ECG showed left ventricular hypertrophy(LVH) with strain pattern. Her WBC count and CRP were elevated.Trans Thoracic Echo demonstrated severe concentric LVH with asymmetrical septal hypertrophy (ASH), severe left ventricular outflow tract (LVOT) obstruction with peak gradient of 100 mmHg, small LV cavity and systolic anterior motion (SAM) of mitral valve with severe MR. LV systolic function was normal with impaired LV relaxation. Patient was admitted to ICU. She was on Dopamine and Nor-epinephrine Infusion but remained resistant to treatment. Both medications were discontinued and started her on Phenylephrine Infusion. Intravenous Furosemide and fluids were administered judiciously. In order to relieve the dynamic LVOT obstruction, Esmolol bolus and infusion were started and overlapped with oral beta blocker therapy. Subsequently her condition improved and repeat Echocardiography showed marked reduction in LVOT gradient and MR. Her coronary angiography was normal. Patient had a protracted course of illness due to cardiogenic shock leading to multi-organ involvement but she recovered over a period of time and underwent Trans-Mitral Surgical Myectomy and Mitral Valve repair following cardiac MRI.



Conclusion: This unusual case illustrates the complex hemodynamics and challenging management of HOCM presenting with acute pulmonary edema and cardiogenic shock. LVOT obstruction in HOCM is dynamic and the degree of obstruction depends more on cardiac contractility and loading conditions.Decrease in LV preload and augmentation of myocardial contractility increase the LVOT obstruction. Usual inotropes and vasopressors are contraindicated in such situation with the exception of Phenylephrine. Betablocker and Phenylephrine increase the ventricular volume and decrease the LVOT obstruction. Patient was resistant to treatment with standard medical therapy and the use of beta blocker and Phenylephrine helped to reduce the LVOT gradient and improve the condition of the patient.

2100

Hypertrophic cardiomyopathy or light chain cardiac amyloidosis?

A Ntalianis[1]; E Repasos[1]; E Tseliou[1]; E Kastritis[1]; D Ziogas[1]; E Papadopoulou[1]; M Tselegkidi[1]; Z Tsoumani[1]; A Koutsoukis[1]; N Makris[1]; I Stamoulopoulos[1]; A Cohen[1]; MA Dimopoulos[1]; S Toumanidiss[1]; I Paraskevaidis[1]
[1]*University of Athens Medical School, Dept of Clinical Therapeutics, Alexandra Hospital, Athens, Greece*

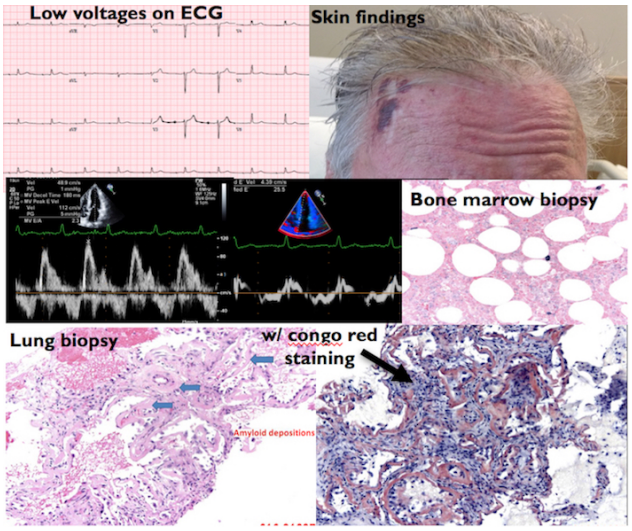
A 54 year old female with a history of hypertrophic cardiomyopathy, thrombopenia and transient ischemic attack presents in the outpatient heart failure clinic because of deteriorating shortness of breath the last 6 months. Her ECG showed LV hypertrophy, her chest X-ray right pleural effusion, NT-proBNP was measured at 5852 pg/mL, hemoglobin at 12.3 mg/dL and heart echo showed a sparkling hypertrophic interventricular septum (22 mm) with left ventricular outflow tract obstruction (with a peak gradient of 101 mmHg) and right ventricular hypertrophy. Protein immunoelectrophoresis showed an increase of IgM ?. Fat and bone marrow biopsy revealed amyloid deposits. The suspicion for cardiac amyloidosis with pre-existing hypertrophic cardiomyopathy was raised but cardiac MRI was non-diagnostic. Heart biopsy was finally decided which showed hypertrophic cardiomyopathy and the patient was finally and successfully submitted to surgical myectomy.

2101

Piecing out the puzzle of AL amyloidosis

PP Poorna Pushkala Natarajan[1]; MT Slawsky[1]; J Hernandez-Montfort[1]
[1]*Baystate Medical Center, Cardiology - Advanced heart disease, Springfield, United States of America*

A 66 year old male with type 1 diabetes, coronary artery disease status (CAD) post stenting of left anterior descending artery in 2010 and B/L carpal tunnel surgery presented with chills, drenching sweats and shortness of breath (SOB) at rest. On further history, his SOB had progressed gradually over 2 years from class I then to class IV with associated fatigue and lower extremity weakness. Workup over 1.5 years including stress echo, lower extremity doppler and lumbar spine MRI were normal. In the interim 2 years between initial onset of SOB and current presentation, he developed orthostasis and hypotension leading to discontinuation of anti hypertensives. Hypoglycemic episodes became frequent and was attributed to long standing autonomic neuropathy from diabetes. Atrial fibrillation was diagnosed and symptomatic junctional bradycardia led to pacemaker placement. He endorsed easy bruising and spontaneous cutaneous bleeding thought to be from sun exposure. During his current admission, he was treated for pneumonia without improvement.



Amyloid Echo and Histology

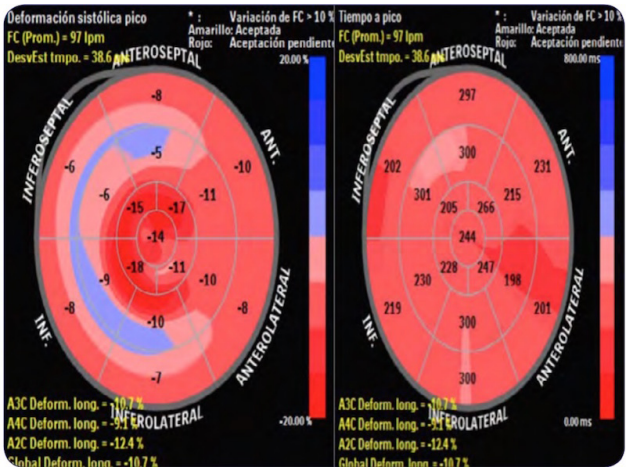
On exam, he appeared ill with Kussmauls sign, bibasilar crackles and lower extremity edema. Labs revealed CKD, and disproportionately elevated NT Pro BNP at 25184 pg/ml. Electrocardiogram (ECG) had low voltage complexes. Echo showed mild concentric left ventricular hypertrophy, preserved ejection fraction, Grade III diastolic dysfunction and low e' velocity (4 m/s). Chest CT showed ground glass opacities that were biopsied, which revealed amyloid deposition in alveolar septa. Kappa fraction of free light chain was elevated with kappa/lambda ratio of 52.95. 99mTc PYP scanning was negative. Bone marrow biopsy showed 15% plasma cells and 14 : 16 translocation. A diagnosis of AL amyloidosis was made. Diuresis and chemotherapy with bortezomib was initiated. Renal function worsened with proteinuria, and kidney biopsy showed amyloid casts. He underwent plasmapheresis. Patient deteriorated quickly and ultimately succumbed to this disease.
Amyloidosis results from extracellular deposition of amyloid fibrils which are misfolded precursor proteins with proteolytic resistant beta pleated sheet configuration. The prognosis is determined by the organ involved and type of amyloid. It is increasingly recognized that up to 13 % of heart failure with preserved ejection fraction cases are misdiagnosed cardiac amyloidosis. AL amyloidosis most commonly affects the kidneys, but 60 % of cases can involve the heart. In our patient, despite classical features such as carpal tunnel syndrome, orthostasis, low voltage on ECG, heart block, autonomic neuropathy and progressive dyspnea, diagnosis was delayed due to the symptoms of amyloid being shared by type I diabetes and preexisting CAD. This emphasizes the importance of unbiased evaluation of clinical presentation, attention to subtle clinical and non cardiac clues, education among cardiologists since early referrals and diagnosis can improve the prognosis of the disease.

2102

Cardiac amyloidosis

D David Gonzalez Calle[1]; P Luengo Mondejar[1]; E Villacorta Arguelles[1]; M Sanchez Ledesma[1]; A Elvira Laffond[1]; M Lopez Serna[1]; A Barrio Rodriguez[1]; I Cruz Gonzalez[1]; PLM Sanchez Fernandez[1]
[1]*University of Salamanca, Salamanca, Spain*

A previously healthy 43-year-old patient presented to the emergency department he refers progressive dyspnea.
Physical examination suggested systemic congestion. On the electrocardiogram, low voltages were observed, while chest X-ray findings were signs of pulmonary congestion and enlargement of the cardiac silhouette.
With the diagnosis of first episode of congestive heart failure, and a deposit disease being suspected, the patient is admitted to the cardiology department in order to complete the study. Imaging diagnostic tests performed were highly suggestive of deposit disease: on echocardiogram, moderate ventricular hypertrophy, together with a strain pattern and restrictive dysfunction were observed (picture 1), while on cardiac magnetic resonance imaging (cMRI) a late enhancement ring pattern affecting the free wall of the right ventricle was present. Given these results, amyloidosis was the main suspected diagnosis. Therefore, a proteinogram was performed, in which a monoclonal l light chain peak was observed. Bone marrow aspiration confirmed the presence of Multiple Myeloma (15% plasma cells, 94% malignant). A myocardial biopsy was performed, and histologic analysis revealed the presence of extracellular material positive for Congo red stain and apple-green birefringence.



Picture 1

At the moment, with the diagnosis of Multiple Myeloma and AL Amyloidosis, chemotherapy with bortezomib, cyclofosfamide and dexametasone is initiated, considering the possibility of a sequential transplantation (heart and hematopoietic). After beginning chemotherapy, the patient's clinical condition deteriorates, with progressive worsening of his hemodinamic status despite of increasing-dose inotropic support. A intraaortic balloon pump (IABP) is placed, persisting heart failure (INTERMACS 1). It is decided to refer the patient to the reference centre for transplantation. Upon arrival to the transplantation centre, given the patient's clinical situation and progression in spite of inotropic treatment and IABP, bridge therapy with central ventricular assistence (centrimag) is placed. The patient remains hemodinamically stable for two weeks, when cardiac transplantation is performed. After 30 days of hospital admission, the patient is discharged with good medical state. New cycles of chemotherapy were administered, and after six months of treatment, autologous stem cell transplantation was performed, without further complications. Ten months after stem cell transplantation, the patient remains stable and asymptomatic, and is currently being followed in outpatient consultation.
As cardiac amyloidosis is a low-incidence disease, studies performed are series of cases with a small number of patients. However, from our experience -albeit limited-, we deem it necessary to initiate agressive treatment from the beginning, given the poor prognosis of the disease, being cooperation between different professionals essential for the adequate management of the patient.

2103

Cardiac sarcoidosis: don't lose sight of the forest for the trees

S Ng[1]; J Pan[1]
[1]*St Thomas' Hospital, London, United Kingdom*

Sarcoidosis is a systemic non-caseating granulomatous disease of unknown aetiology with an estimated prevalence of 10 - 20 per 100,000 population. Cardiac involvement (cardiac sarcoidosis (CS)) is observed clinically in 5% of patients with systemic sarcoidosis but autopsy studies have reported that subclinical CS is observed in up to 70% of cases. As CS has diverse clinical presentations, its diagnosis can be a major challenge to clinicians.
We describe an anxious but otherwise fit and well 43 year-old African lady who presented with worsening dyspnoea, intermittent palpitations and dizziness. Her admission 12-lead electrocardiogram (ECG) showed fixed T-wave inversions in precordial leads V4-V6 and ST depression in the inferior leads II, III and AVF with non-dynamic serum troponins. Her chest X-ray revealed bilateral hilar lymphadenopathy with reticular shadowing in the right lower zone. She had asymmetric left ventricular hypertrophy of the posterolateral walls with normal ejection fraction and no evidence of LVOT obstruction on an echocardiogram. On the coronary care unit, the patient developed recurrent symptomatic monomorphic ventricular tachycardia (VT) despite commencing intravenous amiodarone. An endomyocardial biopsy revealed non-caseating granuloma confirming cardiac sarcoidosis. The patient had an implantable cardioverter-defibrillator due to poor response to trials of steroids.
This case highlights the dilemma in diagnosing a concurrent presentation of cardiac and pulmonary sarcoidosis. Non-specific symptoms of dyspnoea and palpitations with a suggestive chest X-ray focuses clinicians' on the diagnosis of isolated pulmonary sarcoidosis. This delays initiation of corticosteroids or immunosuppression as spontaneous remission of pulmonary sarcoidosis occurs in 90% of patients. This is further complicated by the rarity of systemic sarcoidosis, especially CS, with more common diagnoses such as pulmonary embolism, myocardial infarction and lower respiratory tract infections considered before cardiac sarcoidosis.
Whilst myocardial involvement with sarcoidosis is more frequent in patients with cardiac symptoms, asymptomatic cardiac involvement is not uncommon. Hence, early and accurate diagnosis of cardiac involvement in sarcoidosis is crucial to prevent associated morbidity and mortality. The diagnosis of CS is often difficult with non-specific ECG and echocardiographic findings. As such, there should be a low index of suspicion for cardiac involvement in all patients with systemic sarcoidosis. Advanced cardiac imaging modalities have an increasingly important role in evaluating for cardiac sarcoidosis. However, the role of advanced imaging in diagnosing and guiding treatment remains unclear. A risk-stratification method is needed to guide therapy and aid decision-making to prevent sudden cardiac death, such as in the case highlighted above, with an ICD implantation.

2104

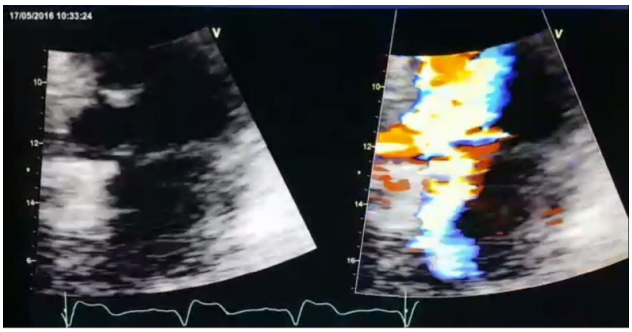
An unusual clinical presentation of hypertrophic cardiomyopathy

A E Vijiiac[1]; C Iorgulescu[1]; DA Radu[1]; M Guran[1]; M Dorobantu[1]
[1]*Emergency Clinical Hospital Floreasca, Cardiology Department, Bucharest, Romania*

The most frequent, well-studied and fearsome complications of hypertrophic cardiomyopathy (HCM) are complex ventricular arrhythmias, while little data exist on the prevalence of severe cardiac conduction disturbances in patients with HCM. We report the case of a patient whose presentation with symptomatic high grade atrioventricular (AV) block led to the diagnosis of obstructive HCM.
A 51 year-old previously healthy male was admitted for a 48-hour history of near syncope, intense fatigue and dyspnea on minimal exertion. His family history was unremarkable. On physical examination, he had a heart rate of 40 beats/min, a blood pressure of 140/70 mm Hg, a respiratory rate of 25 breaths/min and a soft systolic murmur at the left lower sternal border. His ECG revealed a Mobitz II second degree AV block, with electrical criteria of left ventricular hypertrophy. His echocardiography showed a septal thickness of 18 mm, with a dynamic left ventricular outflow tract (LVOT) gradient (25 mm Hg at rest, 82 mm Hg at the Valsalva maneuver) and systolic anterior motion of both mitral leaflets with severe eccentric mitral regurgitation. Coronary angiogram was normal. A permanent DDD pacemaker was implanted with apical placement of the ventricular lead, with prompt resolution of the patient's symptoms. The follow-up echocardiography showed a decrease of the LVOT gradient to 50 mm Hg.
Proposed mechanisms for AV block in HCM are: fibrosis, necrosis or cystic abnormalities of the conduction system, luminal narrowing of the intramural coronary arteries or iatrogenic complication of septal reduction therapies. Consequently, (pre)syncope in HCM can be explained not only by LVOT obstruction and tachyarrhythmias, but also by bradyarrhythmias. There seems to be a connection between the occurrence of conduction disturbances and certain mutations in HCM, such as PRKAG2 mutation or those leading to neuromuscular disorders or Fabry disease. In our patient, genetic study was not performed because he refused testing. However, he did not have any extracardiac manifestation suggestive of a phenotype consistent with the above-mentioned mutations.

DDD pacing can treat both the outflow obstruction and the AV block. In our patient there was a moderate decrease in LVOT gradient, but as he remained asymptomatic, we decided to optimize the beta-blocker therapy, without referring him for a septal reduction strategy. His clinical course was proof that the mechanism of his symptoms was the conduction disturbance.

While the incidence of malignant arrhythmias in HCM is well established, conduction disturbances may also occur, although far less frequently. Furthermore, this association might prompt to certain mutations, especially when corroborated with specific clinical features. One must keep in mind AV block as a possible cause of sudden death or syncope in patients with HCM. It might be prudent to monitor for the development of abnormal AV conduction in these patients.



Zoom on the mitral valve (A4C) showing systolic anterior movement and severe mitral regugitation

SAM with severe mitral regurgitation

Poster Session 4

Atrial Fibrillation - Epidemiology, Prognosis, Outcome

P2111

Antithrombotic therapy improves long-term prognosis in patients with atrial fibrillation and heart failure -A report from the CHART-2 Study-

T Takashi Shiroto[1]; Y Sakata[1]; K Nochioka[1]; R Abe[1]; T Oikawa[1]; S Kasahara[1]; M Sato[1]; H Aoyanagi[1]; M Miura[1]; J Takahashi[1]; S Miyata[2]; H Shimokawa[1]
[1]Tohoku University Graduate School of Medicine, Department of Cardiovascular Medicine, Sendai, Japan; *[2]Tohoku University Graduate School of Medicine, Department of Evidence-based Cardiovascular Medicine, Sendai, Japan*

On behalf of: The CHART-2 Investigators
Funding Acknowledgements: Japan Agency for Medical Research and Development

Background: Atrial fibrillation (AF) is one of the major comorbidities in patients with heart failure (HF). Antithrombotic agents, especially anticoagulants (ACs), are widely used for AF patients to prevent thromboembolic events including stroke. However, it remains to be fully elucidated whether ACs, anti-platelets (APs), and their combination improve long-term prognosis in AF patients, especially in those with HF.
Purpose: To elucidate whether antithrombotic therapy (ATT) improves long-term prognosis of AF patients.
Methods: Our Chronic Heart Failure Analysis and Registry in the Tohoku District (CHART) -2 Study is a multicenter observational study, enrolling cardiovascular patients with and without HF in Japan (N = 10,219). In the CHART-2 Study, we examined the merits and demerits of the contemporary ATT in 3,221 consecutive AF patients with and without HF.
Results: We divided AF patients into 4 groups based on ATT at enrollment; without ATT (w/o ATT, N = 368), ACs alone (N = 1,073), APs alone (N= 838), and both of them (ACs & APs, N = 942). As compared with w/o ATT group, all other 3 groups had significantly improved all-cause mortality (adjusted hazard ratio (aHR) 0.66, 0.75, and 0.67 for ACs, APs, and ACs & APs, respectively, all $P < 0.05$) and cardiovascular mortality (aHR 0.64, 0.62, and 0.57, respectively, all $P < 0.05$), and the beneficial effects of ATT were noted only in AF patients with HF but not in those without HF (Table).
Conclusions: These results indicate that ATT improves long-term prognosis in AF patients with HF but not in those without HF.

P2112

Heart failure in patients with non-valvular atrial fibrillation. Insight from the national observational cross-sectional registry.

L Lubos Urban[1]; Z Slegrova[2]; K Chroust[2]; G Kaliska[3]
[1]National Institute of Cardiovasc Diseases - NUSCH, Bratislava, Slovak Republic; *[2]DSC Services, Brno, Czech Republic*; *[3]Central Slovakia Institute of Cardiovascular Diseases, Banska Bystrica, Slovak Republic*

On behalf of: SLOV-FIB investigators
Funding Acknowledgements: Slovak Heart Rhythm Assosciation, Boehringer-Ingelheim

Background: Atrial fibrillation (AF) is the most common arrhythmia in heart failure (HF). AF increases risk of stroke, impairs cardiac function and worsen the outcome of HF pts.
Purpose: of our analysis was to evaluate clinical profile and real-life management strategies in the subgroup of pts with non-valvular (NV) AF w/ or w/o concomitant HF.

	NVAF w/ HF (N = 587)	NVAF w/o HF(N = 1388)	p value
Age (years ± SD)	74.9 ± 9.6	70.8± 10.0	p <0.001
CHA2DS2Vasc score (excl.HF) ± SD	4.2 ± 1.6	3.4 ± 1.7	p <0.001
HAS-BLED score ± SD	2.3 ± 1.2	1.8 ± 1.1	p <0.001
Rhythm control (N; %)	203; 34.6%	722; 52%	p <0.001
Renal insufficiency (N; %)	195; 33.2%	222; 16%	p <0.001
Creatinine (umol/l ± SD)	102.1 ± 63.5	91.1 ± 36.9	p <0.001
Pts w/ thromboembolic event (N; %)	114; 19.4%	219; 15.8%	p <0.01
Pts w/ bleeding event (N; %)	68; 11.6%	126; 9%	p = 0.02

P2111 Table

	All (N = 3,221)	AF patients with HF (N = 1,983)	AF patients without HF (N = 1,238)									
	Events/ Number	Adjusted HR*	95% CI	P value	Events/ Number	Adjusted HR**	95% CI	P value	Events/ Number	Adjusted HR***	95% CI	P value
w/o ATT	61/368	Reference	45/189	Reference	16/179	Reference						
ACs alone	166/1,073	0.64	0.46-0.89	0.009	133/706	0.58	0.40-0.84	0.004	33/367	0.85	0.41-1.77	0.661
APs alone	120/838	0.62	0.44-0.88	0.008	88/466	0.58	0.39-0.86	0.007	32/372	0.65	0.31-1.35	0.245
ACs & APs	150/942	0.57	0.40-0.80	0.001	113/622	0.53	0.36-0.77	0.001	37/320	0.64	0.30-1.36	0.248

Comparison of cardiovascular mortality between AF patients with and without HF
*adjusted with age, BMI, BNP, diabetes mellitus, diastolic BP, diuretics, eGFR, Hb, history of brain disorder and HF, LA dimension, LV dimension, LVEF and NYHA functional class. **adjusted with age, BMI, BNP, diastolic BP, LA dimension, LV dimension, LVEF, eGFR, Hb, history of brain disorder and HF and NYHA functional class. ***adjusted with age, BNP, diabetes mellitus, diuretics, Hb, history of brain disorder, ischemic HF, LV dimension and paroxysmal AF. Abbreviations: ACs, anticoagulants; AF, atrial fibrillation; APs, antiplatelets: ATT, antithrombotic therapy; BMI, body mass index; BNP, brain natriuretic peptide; BP, blood pressure; CI, confidence interval; eGFR, estimated glomerular filtration ratio; Hb, hemoglobin; HF, heart failure; HR, hazard ratio; LA, left atrium; LV, left ventricle; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association.

Methods: All 1975 consecutive pts with NVAF that visited 150 out-patient cardiology clinics during 10 days period were included into national cross-sectional registry.
Results: Subgroup of 587 pts (29.79%) suffered from HF; 146 pts (24.9%) classified as non-ischemic cardiomyopathy (non-iCMP), 411 pts (70%) as ischemic cardiomyopathy (iCMP) and 30 pts (5.1%) w/ other cause. Most NVAF/HF pts had preserved left ventricular ejection fraction (LVEF) = 50% (252 pts; 42.9%), HF group of mid range LVEF 40-49% comprises of 189 pts (32.2%) followed by 114 pts (19.4%) with systolic HF (LVEF <40%; HFrEF). HFrEF was more frequent among pts with non-iCMP compared to iCMP (28.8% vs. 19.5%, p <0.001). DC cardioversion in HF pts was not associated with more TE events when compared to pts w/o HF (12.5% vs. 12.6%), but NYHA = III pts had much more TE events than those with less severe HF (58.3% vs. 22.6%, p = 0.017) irrespective of LVEF. Among NVAF/HF pts, only 4(0.7%) underwent AF ablation and only 15(2.6%) were implanted with ICD/CRTD. All 587 NVAF/HF pts fulfilled ESC 2016 criteria for anticoagulation, but anticoagulants were used in 512 pts (87.2%); Warfarin 216 (36.8%), Dabigatran 116 (19.8%), Rivaroxaban 90 (15.3%), Apixaban 90 (15.3%). Clinical characteristics and outcomes are summarized in table.
Conclusion: HF is important concomitant condition in almost 1/3 of pts with NVAF. Such pts have higher risk of TE as well as bleeding events. Thanks to our real-life analysis it was possible to identify pts at highest risk of adverse outcome and underuse gaps of current AF/HF therapies that have an impact on morbidity and mortality.

P2113
Relevance of device detected atrial arrhythmias in patients with cardiac implantable electronic devices (CIEDs) in a real world scenario.

SHYAM Sasidharan[1]; V V Radhakrishnan[1]; K Sunitha Viswanathan[1]; P N Gupta[1]; A George Koshy[1]
[1]Government Medical College, Thiruvananthapuram, Cardiology, Thiruvananthapuram, India

Introduction: : CIEDs with an atrial monitoring lead offers the advantage of continous monitoring of atrial rhythm.However the clinical and therapeutic implications of High Rate Atrial Events (HRAE) or Device Detected Atrial Fibrillation (DDAF) is unclear.
Purpose: To study the frequency,pattern and treatment of device detected atrial arrhythmias and its association with clinical outcomes.
Methods: 155 patients with CIEDs with an atrial lead were recruited.Those with a minimum duration of 3 months of interrogated data were included and those with clinically detected atrial arrhythmias were excluded from the study.Relevant information were obtained by direct interview of the patient,with a prespecified proforma during their routine follow up visits.All patients underwent device interrogation and the electrograms(EGM) of all reported HRAEs were meticulously examined.
Results: 155 patients were enrolled in the study.The mean age of the study population was 58 years.Majority (97.4%) had a dual chamber pacemaker implanted and the most common indication for device implantation was SA nodal disease(77.4%).The mean duration of interrogated data was 6.7 months.HRAEs were reported in 69(44.5%) of which 28(18.1%) were atrial fibrillation(DDAF),16(10.3%) were artifacts and 25(16.1%) were other supraventricular tachyarrhythmias. In the present study stroke/Transient Ischemic Attacks/peripheral embolism/heart failure/Acute coronary syndromes were the clinical events which were studied.Among those with Device Detected Atrial Fibrillation(DDAF) 9 patients (32.14%) had 10 events and in the group without DDAF ,17 patients (13.4%) had 17 clinical events.This association of Device Detected Atrial Fibrillation(DDAF) with a composite of all clinical events were found to be significant (?2 = 7.2471,df = 1,p = 0.007102).However no significant association between DDAF and incidence of stroke or heart failure independently, could be demonstrated (p = 0.093).The mean CHA2 DS2 VaSc score in patients with DDAF was 2.11 ± 1.8 . Most (71.2%) of the patients with DDAF were never evaluated further for Atrial Fibrillation and they were not on any treatment for AF.
Conclusion: The study reveals that DDAF is frequently found in patients with CIEDs.A composite of all clinical outcomes studied was found to be significantly associated with DDAF.The study also reveals that the current clinical practice often overlooks the presence of DDAF ,as evidenced by the large number of untreated patients with device detected atrial fibrillation,despite having a high risk of stroke.

Implantable Cardioverter / Defibrillator

P2114
Predictors of implantable cardioverter defibrillator intervention for life-threatening ventricular arrhythmias in systolic heart failure: role of reverse remodelling.

G Gianluca Mirizzi[1]; A Aimo[1]; V Castiglione[1]; A Giannoni[2]; G Vergaro[2]; M Piacenti[2]; L Panchetti[2]; U Startari[2]; A Rossi[2]; C Passino[1]; M Emdin[1]
[1]Sant'Anna School of Advanced Studies, Pisa, Italy; [2]Gabriele Monasterio Foundation, Department of Cardiovascular Medicine, Pisa, Italy

Background: Implantable cardioverter defibrillators (ICD) recognize and treat life-threatening arrhythmias in systolic HF. In primary prevention, however, the rate of appropriate ICD intervention is low, with complications potentially offsetting their benefit; more accurate prediction of arrhythmic events is thus highly anticipated. The impact of reverse remodelling (RR) well above the guidelines-recommended threshold of three months in predicting ICD intervention has not been properly assessed.
Purpose: to evaluate the impact of RR on ICD- treated life-threatening ventricular arrhythmia occurrence in systolic HF patients above three months.
Methods: patients with systolic HF (left ventricular ejection fraction - LVEF - < 40%) who underwent ICD implantation for primary prevention were evaluated regularly (6-months or yearly basis) via in-site device interrogation. ICD intervention for life-threatening ventricular arrhythmia (shocks for ventricular tachycardia - VT - or fibrillation -VF) were collected. Basal and 1-year echocardiograms were performed; RR was defined as an improvement of left ventricular end-systolic volume index (LVESVi) of at least 15%. Primary outcome was defined as appropriate ICD intervention for VT/VF (whatever came first).
Results: among 812 patients (83% males, 57% ischemic etiology, age 68 ± 10 years, LVEF 28 ± 6%, median NT-proBNP 1383 ng/L, interquartile range -IR- 733-3170, 87% betablockers, 82% ACE-inhibitors/angiotensin receptor blockers, 72% mineralcorticoid receptor antagonists), single chamber ICD were implanted in 14% of patients, dual chamber in 25%, subcutaneous in 1%, cardiac resynchronization therapy (CRT) devices in 60%. Shocks for VT were recorded in 7.3%, for VF in 7.1%, for aggregate VT/VF in 11.4%. RR occurred in 12.3% of patients; it occurred in 7.8% of patients with ischemic HF and in 18.2% of non-ischemic HF (p < 0.001). No treatment differences were found; CRT was however more common in non-ischemic group (71.9% vs. 51.1, p < 0.001). At follow-up (27 months, IR 11-55), systolic pulmonary arterial pressure (PAPs) and RR, but not LVEF, were independent predictors primary outcome occurrence (respectively, odds ratio - OR - 1.03, 5-95th confidence interval 1.01-1.06, p = 0.02 and OR 0.24, CI 0.06-0.99, p = 0.05) independently from CRT status. Primary outcome occurred in 8.3% of patients with RR and ischemic HF (3 out of 36 patients), while no events occurred in patients with RR and non-ischemic HF (0 out of 63 patients).
Conclusion: ICD intervention rate for VT/VF is low among patients with systolic HF and contemporary treatment; RR is associated with a reduced risk of ICD intervention, especially among patients with non-ischemic HF. Evaluation of left ventricular RR above 3 months could help identify a subgroup of patients with reduced risk of future life-threatening arrhythmias.

P2115
Haemodynamic Effects of Xenon versus Desflurane >Anaestehsia during ICD Implantation

J Jan Poelaert[1]; J Czapla[1]; I Remory Isabel[1]; V Umbrain[1]; S Beckers[1]; C Verborgh[1]
[1]Free University of Brussels (VUB), Brussels, Belgium

Funding Acknowledgements: Only Departmental Funding

Background: Patients scheduled for ICD implantation often suffer from a low ejection fraction with a critical preload/afterload balance. Intraoperatively, low left ventricular (LV) reserve and intravascular fluid shifts and negative inotropic effects make these interventions hazardous. Desflurane is an inhalational anaesthetic with favourable effects to ventricular contractility. In comparison with other inhalational anaesthetics, xenon results in a better cardiovascular stability.
Purpose: The aim of this study was to test the hypothesis patients with severely impaired LV systolic function show a better cardiovascular status with xenon versus desflurane anaesthesia. To the best of our knowledge, this is the first study comparing those two anaesthetics.
Methods: In this study, patients, scheduled for ICD implantation for malignant ventricular arrhythmias, were included. All showed a LV ejection fraction of < 0.35. Before induction of anaesthesia, an arterial line was inserted. Patients were assigned randomly to either xenon or desflurane anaesthesia, in conjunction with sufentanil. After induction of anaesthesia, a multiplane TOE probe was inserted, connected to an echocardiograph (Vivid Q, GE). Following variables were assessed before surgery after induction and haemodynamic stabilization, and after obtaining 1 MAC xenon or desflurane: aortic valve flow velocity (AVmax), time velocity integral (TVI),

Comparison between Xenon and Desflurane

N = 49	pre-xenon (n = 17)	xenon (n = 17)	pre-desflurane (n = 17)	desflurane (n = 17)
SV (ml)	59±24	57±69	73±34	51±78 *
CI (l/min.m^2)	2152±742	1699±1773 *	2598±977	1872±3317 **
AV max (m/s)	1.0±.3	.9±.6	1.2±.3	.9±1.5 **
TVI (cm)	16.5±6.3	15.4±6.2	22.2±8.5	17.5±4.3 *
Ea (mmHg/ml)	2.2±1.1	1.9±1.5	1.8±.8	1.8±2.0
LVESWS (g/cm^2)	64±68	62±74	72±157	77±182
Strain (%)	14.8±5.6	13.4±7.0	12.5±5.2	16.6±12.9 *#

* p < .05 pre versus inhalation anaesthetic; ** p < .01; # p < .05 between xenon and desflurane anaesthesia.

stroke volume (SV) and cardiac index (CI) calculation, arterial elastance (Ea) and LV end-systolic wall stress (LVESWS).

Results: Due to incomplete data sets or impossibility to analyze data, 17 patients remained in each subset to be analyzed.

Conclusions: Whereas SV decreased significantly after induction of anaesthesia, strain increased considerably only with desflurane. Xenon anaesthesia appears not to induce strain alterations.

Cardiac Resynchronization Therapy

P2116

Active fixation lead can improve clinical response to cardiac resynchronization therapy

M Mezzetti[1]; M Morelli[1]; L Caccamo[1]; M Casale[2]; P Busacca[1]
[1]*Santa Maria della Misericordia, Cardiology Division, Urbino, Italy*; [2]*Universitá di Messina, Dipartimento di medicina clinica e sperimentale, Messina, Italy*

In cardiac resynchronization therapy (CRT) the final location of a traditional passive fixation left ventricular lead (PFix) usually selected according to stability criteria, favourable pacing threshold and absence of phrenic nerve stimulation can be suboptimal because pacing is delivered far from the latest electrical activated site.

The most delayed sites, usually located in lateral (L) or posterolateral (PL) basal segments of the left ventricle (LV), can pose problem in terms of both stability and pacing threshold. The recently introduced active fixation lead (AFix) could overcome these issues, leading to a better electrical resynchronization (EResync) and ultimately improved response to CRT.

Objective: Electrical and clinical performances of 91 consecutive PFixs were compared with 42 consecutive AFixs in 133 heart failure (HF) patients with systolic dysfunction and prolonged QRS duration candidates to CRT.

Methods: The parameters assessing EResync were: (1) local LV activation time (LAT) calculated from QRS onset (QRSo) to the electrogram registered from the distal bipole of LV lead positioned in the final site, (2) LAT to QRS duration ratio (LAT/QRS), (3) duration of QRS obtained with biventricular pacing (QRSbiv) and (4) QRSbiv to QRS ratio (QRSbiv/QRS). The clinical endpoint was all cause mortality and/or unplanned HF hospitalizations.

Results: Clinical, echocardiographic and ECG parameters, number of coronary sinus veins (CSVs) and types of implanted devices (87 defibrillators, 65,5%) were similar in the two groups.

AFix achieved significantly better EResync parameters compared to PFix. In particular LAT was 119,8 ± 27 vs 99,3 ± 37msec (p = 0,002) respectively for AFix and PFix; LAT/QRS was 0,71 ± 0,13 vs 0,60 ± 0,19 (p = 0,002); QRSbiv was 135,3 ± 20 vs 143,34 ± 15msec (p = 0,04) and QRSbiv/QRS was 79,5 ± 11% vs 92 ± 15% (p < 0,001). L or PL vein was targeted in 97,2% with AFix vs 74,4% with PFix (p = 0,003) and basal segment was the target site in 30,6% and 5,2% with AFix and PFix respectively (p = 0,001). There was one dislodgment in PFix group vs no dislodgment in AFix group. AFix reduced significantly HF hospitalizations plus all-cause mortality compared to PFix (3,7% vs 40%, p = 0.038).

Conclusion: AFix was able to deliver LV pacing from significantly later activated sites located in L and PL basal LV segments compared to PFix, leading to a better electrical resynchronization and therefore to an improved clinical response to CRT.

P2117

Early prediction of cardiac resynchronization therapy response by non-invasive electrocardiogram markers

V Victor Perez Rosello[1]; NOA Nuria Ortigosa Araque[2]; VDT Victor Donoso Trenado[1]; JO Joaquin Osca[1]; OCP Oscar Cano Perez[2]; CF Carmen Fernandez[2]; AG Antonio Galbis[2]; LMD Luis Martinez-Dolz[1]
[1]*Hospital Universitario y Politécnico La Fe, Valencia, Spain*; [2]*Polytechnic University of Valencia, Valencia, Spain*

Cardiac resynchronization therapy (CRT) is an effective treatment for those patients with severe heart failure. Regrettably, there are about one third of CRT do not respond to it, which adversely affects the utility and cost-effectiveness of CRT.

In this project we assess the ability of a novel surface ECG marker, called energy of QRST, to predict

CRT response. This marker is obtained by mathematical analysis of the QRS, ST segment and T wave using the Stockwell transform.

We performed a retrospective exploratory study of the ECG previous to CRT implantation in 43 consecutive patients with ischemic (17) or non-ischemic (26) cardiomyopathy.

We defined response to CRT as an increase in LVEF= 5% or one who presented an improvement in NYHA functional class = 1 in absence of death by any cardiovascular cause, heart transplantation, or hospital admissionfor heart failure during a follow-up period of one year. We consider as super responders those patients with an increase in LVEF = 15% without cardiovascular death, heart transplantation, or hospital admission for heart failure.

This ECG marker showed statistically significant lower values for non-responder patients and, joint with the duration of QRS complexes (the current gold-standard to predict CRT response).

In this manner, the proposed ECG marker may be useful to predict positive response to CRT in a non-invasive way, in order to minimize unsuccessful procedures.

Median measure of energy of QRST

	Responders energy of QRST	Not responders enegy of QRST	p value
All	747.32	174.69	0.0134
Ischemic	1397.30	142.73	0.0068
Non ischemic	464.71	249.25	0.5408
With left Bundle branch block	576.16	178.05	0.0500
Without left bundle branch block	1203.80	169.65	0.1986

p values are obtained for Wilcoxon statistical test

Chronic Heart Failure - Pathophysiology and Mechanisms

P2118

Safety and tolerability of a first in class chymase inhibitor in clinically stable patients with left-ventricular dysfunction after myocardial infarction

M Senni[1]; L Kober[2]; S Nodari[3]; M Schou[4]; C Otto[5]; M Becka[6]; F Kanefendt[7]; BR Winkelmann[8]; G Gislason[9]; F Richard[10]; OW Nielsen[11]; M Gheorghiade[12]; HD Duengen[13]
[1]*Ospedale Papa Giovanni XXIII, Bergamo, Italy*; [2]*Rigshospitalet - Copenhagen University Hospital, Copenhagen, Denmark*; [3]*Civil Hospital of Brescia, Brescia, Italy*; [4]*Herlev Hospital, Herlev, Denmark*; [5]*BAYER AG, Experimental Medicine Cardiovascular and Hematology, Wuppertal, Germany*; [6]*BAYER AG, Research and Clinical Sciences Statistics, Wuppertal, Germany*; [7]*BAYER AG, Clinical Pharmacokinetics, Wuppertal, Germany*; [8]*Clinphenomics, Frankfurt am Main, Germany*; [9]*Gentofte University Hospital, Copenhagen, Denmark*; [10]*Praxis Dr. Richard, Erfurt, Germany*; [11]*Bispebjerg og Frederiksberg Hospital, Copenhagen, Denmark*; [12]*Northwestern University Feinberg School of Medicine, Chicago, United States of America*; [13]*Charite - Campus Virchow-Klinikum (CVK), Berlin, Germany*

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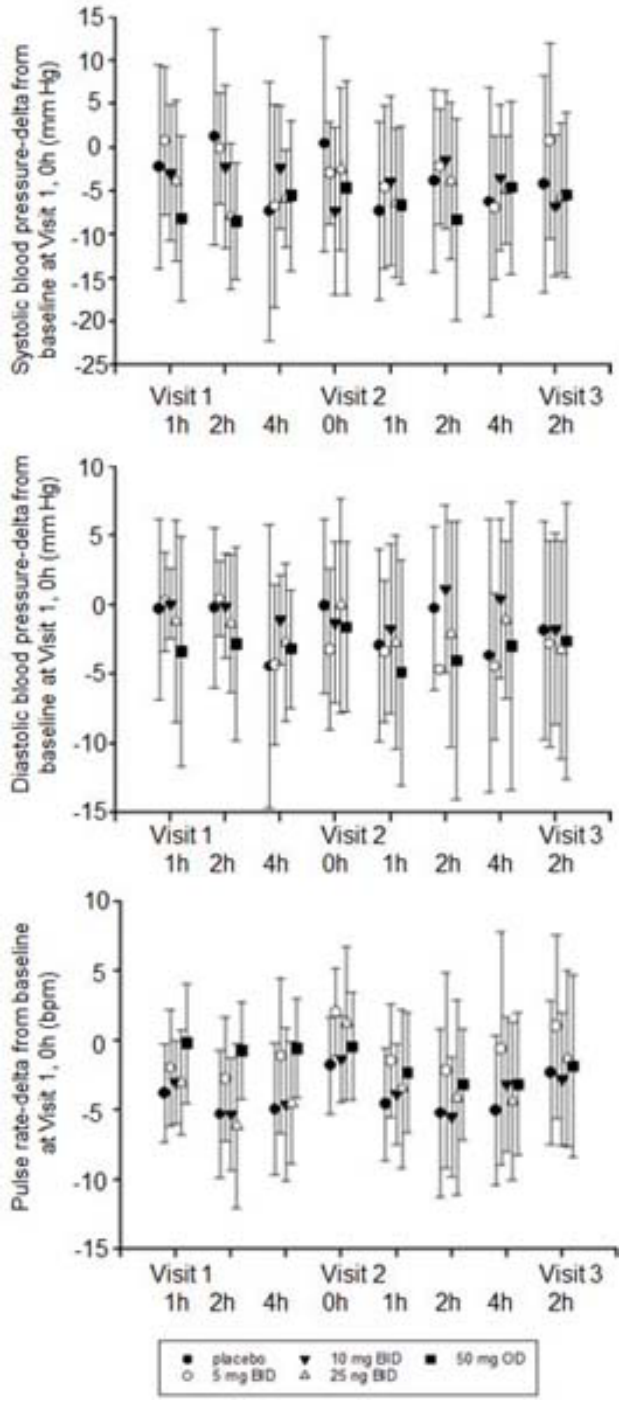
Introduction: Adverse cardiac remodelling represents the most important risk factor for the development of heart failure after myocardial infarction (MI). Chymase, a chymotrypsin-like serine protease, is secreted after tissue injury and generates



locally pro-fibrotic factors (such as angiotensin II (Ang II), TGF beta, and matrix metalloproteases) that contribute to adverse cardiac remodelling. An orally available chymase inhibitor is currently in clinical development as a first in class treatment for left-ventricular dysfunction (LVD) after acute MI. In healthy volunteers, it did not interfere with systemic Ang II levels or blood pressure. As chymase activity is increased in arteriosclerotic plaques and thus may contribute to systemic ANG II generation, it is currently unknown whether chymase inhibition would interfere with vital signs (blood pressure, pulse rate) in patients.

Purpose: This phase IIa study examined safety and tolerability of a novel chymase inhibitor in a chronic patient population suffering from LVD after MI.

Methods: A multicentre, multinational, randomized, placebo-controlled study was performed in clinically stable patients (40-79 years of age, LVEF = 45% due to MI in medical history at least 6 or more months before randomization) who were on stable evidence-based standard of care therapies for LVD post MI. These included an angiotensin converting enzyme inhibitor or angiotensin receptor blocker at doses of at least half the recommended target dose. Patients were treated for 2 weeks with either placebo (n = 12) or 4 different doses of the chymase inhibitor (5 mg twice daily (BID), n = 9; 10 mg BID, n = 9; 25 mg BID, n = 10; 50 mg once daily, n = 9). Four ambulatory visits (incl. one follow up visit) were performed. Safety and tolerability were monitored by ECG, safety lab, urinalysis, and adverse event questioning. Vital signs were measured in triplicates at selected time points before and after study drug administration on the ambulatory visits and at patients' home. Blood samples for pharmacokinetic and exploratory biomarker analyses were collected at the ambulatory visits.

Results: The chymase inhibitor was safe and well tolerated at all examined doses. 58.3% of patients treated with placebo and 27.0% of patients treated with active compound reported treatment emergent adverse events of mild to moderate intensity. There were no significant effects on potassium levels, biomarkers or vital signs (see attached Figure depicting deltas from baseline values as mean ± SD) compared to placebo treatment. Mean plasma concentrations of the chymase inhibitor increased with the administered dose.

Conclusion: The safety and tolerability profile as well as the absence of hemodynamic effects in a chronic patient population suffering from similar comorbidities and receiving similar co-medication as the envisaged later target population support future clinical trials with this chymase inhibitor in patients suffering from LVD after acute MI.

P2119

The relations between pro- and anti-inflammatory cytokines contractile ability of the myocardium in patients with coronary artery disease

VI Ruzov[1]; LG Komarova[1]; A Andrey Vorobev[1]; MV Krestyaninov[1]; H Khalaf[1]; M Mulenga[1]

[1]*Ulyanovsk State University, Ulyanovsk, Russian Federation*

Introduction: Studies have shown sufficient details describing cardio-depressive effects of TNF-alpha and there are conflicting reports on the relationship of pro-inflammatory cytokines IL-1b, IL-6 and anti-inflammatory cytokine IL-10 with myocardial dysfunction as the leading pathogenetic link of heart failure.

The aim of this study was to investigate the relation pro-inflammatory cytokines IL-1b, IL-6 and anti-inflammatory cytokine IL-10 with left ventricular ejection fraction which is an integral indicator of myocardial contractility.

Materials and Methods. The study involved 45 patients with coronary artery disease who underwent coronary revascularization in the form of bypass and stenting. The mean age of patients was 57 ± 8 years. According to their ejection fraction (EF), the patients were divided two groups: < 50% (10 patients) and 60% or more (35 patients).

The study of cytokines IL-1ß, IL-6, IL-10 was carried out using solid phase ELISA using the corresponding reagent kits. Ejection fraction was evaluated using Simpson's method.

The patients were on standard treatment regimens of the underlying disease - ACE inhibitors or Sartana, selective ß-blockers, statins, and antiplatelet agents.

Results: There was an inverse relationship between the concentrations of pro-inflammatory cytokines and EF. The most significant changes were observed with respect to the concentration of IL-6.

Thus, in patients with EF up to 50% the average value of the concentration of IL-1ß was 0.87 ± 0.69 pg / ml and 0.90 ± 1.62 pg / ml - in patients with EF above 60%

The mean value of IL-6 concentration in patients with EF up to 50% was 3.34 ± 2.50 pg / ml and 3.08 ± 1.93 pg / ml - in patients with EF above 60%.

Thus, variations in average values of IL-1ß in the patient groups with different ejection was 5%, and IL-6 was 10%. With regard to IL-10, we found a direct correlation between its concentration and EF. In the group of patients with an ejection fraction up to 50% the average value of IL-10 concentration was 3,91 ± 4,34 pg / ml, and 5,31 ± 4,57 pg / ml in patients with EF above 60%.

Fluctuations in the average value of IL-10 between the groups of patients with different ejection fraction was 25%.

Conclusions: We found a direct correlation between the contractile ability of the myocardium and the level of anti-inflammatory cytokine.

There is a feedback between the anti-inflammatory cytokines and the contractile ability of the myocardium.

Preservation of contractile ability of the myocardium is associated with high anti-inflammatory cytokine (IL-10) and low values of pro-inflammatory cytokines (IL-1ß and IL-6), which are comparable with the values of EF.

P2120

Predictors of galectin-3 in patients with heart failure and reduced ejection fraction

I Alexanian[1]; I Parisis[2]; V Bistola[2]; G Bakosis[2]; N Cholevas[2]; F Tzifi[1]; N Karamichalakis[1]; P Niarchou[1]; S Xydonas[1]; L Pappas[1]; K Letsas[1]; M Efremidis[1]; A Sideris[1]; G Filippatos[2]

[1]Evangelismos General Hospital of Athens, 2nd Department of Cardiology, Athens, Greece; *[2]Attikon University Hospital, Department of Cardiology, Athens, Greece*

Background: Immunoinflammatory activation has been recognized as an integral feature of heart failure (HF) pathophysiology. Galectin-3, a ß-galactoside-binding lectin, has been implicated in myocardial inflammation and fibrosis.
Purpose: We sought to determine the association between galectine-3 and clinical, echocardiographic and laboratory parameters in HF patients with reduced ejection fraction (Left Ventricular Ejection Fraction < 40%) (HFREF).
Methods: Clinical, echocardiographic and laboratory parameters were assessed in 87 consecutive patients with HFREF (age: 65.01 ± 9.58years, 56% ischemic HF) visiting our outpatient clinic. Galectin-3 concentrations in serum were determined by an automated quantitative test (VIDAS® Galectin-3, bioMerieux SA, France) using the ELFA technique. Statistical analysis was performed using SPSS 19.
Results: Serum galectin-3 levels were 21.77 ± 13.12ng/ml. Patients with NYHA III-IV had significantly higher serum galectin-3 than NYHA I-II (23.95 ± 14.63 vs. 16.20 ± 6.13, p = 0.001). HFREF patients of ischemic etiology had significantly increased serum galectin-3 compared to those with dilated cardiomyopathy (25.39 ± 15.30 vs. 17.11 ± 7.52, p = 0.001). In univariate analysis, right ventricular diameter (RVD) (r = 0.291, p = 0.036), pulmonary artery systolic pressure (PASP) (r = 0.396, p = 0.004), logNT-proBNP (r = 0.416, p = 0.001), serum urea (r = 0.730, p < 0.001) and creatinine (r = 0.723, p < 0.001) were positively correlated with serum galectin-3 concentrations, whereas Hgb (r= -0.249, p = 0.032) and serum Na (r= -0.330, p = 0.004) were negatively correlated with serum galectin-3. In multiple linear regression analysis, serum urea (B:0.302, 95%CI for B: 0.200 - 0.404, P < 0.001) was the only independent predictor of serum galectin-3 levels.
Conclusion: Serum urea independently predicted galectin-3 in HFREF patients after adjusting for NYHA, etiology of HF, RVD, PASP, logNT-proBNP, creatinine, Hgb and Na. This underscores that galectin-3 is a pleotropic molecule mediating immune response, inflammation, and fibrogenesis rather than specific to cardiac performance alone.

P2121

The role of Response-to-Diuretic in predicting prognosis in discharged heart failure patients after an acute decompensation.

M Feola[1]; M Testa[1]; S Ariotti[2]; C Ferreri[3]; GL Rosso[4]

[1]Cardiovascular Rehabilitation-Heart Failure Unit, Fossano, Italy; *[2]Cardiology Division, Mondoví, Italy*; *[3]School of Geriatry University of Turin, Turin, Italy*; *[4]Emergency 118 ASLCN1, cuneo, Italy*

The diuretic response demonstrated to be a robust independent marker of cardiovascular outcomes in acute heart failure (ADHF) patients. The objectives of this clinical research, will aim to: a) include diuresis into the formula for diuretic response (R-to-D) ; b) add to R-to-D the value of a pre-discharged determination of galectin-3 and BNP in predicting mid-term clinical outcome.
Methods: consecutive patients discharged alive after an ADHF were enrolled. All patients underwent BNP and galectin-3, a 6-minute walk test and an echocardiogram together with diuresis and body weight during diuretic administration. Death by any cause, cardiac transplantation and worsening HF requiring readmission to the hospital were considered cardiovascular events.
Results: 141 patients (95 males, age 73.8) were analysed (follow-up 17 months). During the follow-up 45 (31.9%) events were scheduled (19 cardiac deaths, 26 re-hospitalisation for HF). Patients who experienced CV-event had a worst renal function (p = 0.003), an higher BNP (p = 0.006) and galectin-3 (p = 0.008). At multivariate analysis, only R-to-D, galectin-3 and BNP showed a significant correlation with worst clinical prognosis (respectively p = 0.043; OR 6.01; p = 0.01; OR 8.9; P = 0.02 OR 10.38), independently to age and renal function. Kaplan-Meier curves depicted the powerful stratification using a R-to-D >1.2 kg/40mg furosemide (log rank 10.96 ; p = 0.0009). Adding R-to-D>1.2 mg/40 mg furosemide to galectin-3>17.6 pg/ml and BNP>500 pg/ml the predictive value improved (log rank 23.59; p = 0.0001).
Conclusion: adding R-to-D to Gal-3 and BNP, a single pre-discharge strategy testing seemed to obtain a satisfactorily predictive value in alive HF patients discharged after an ADHF episode.

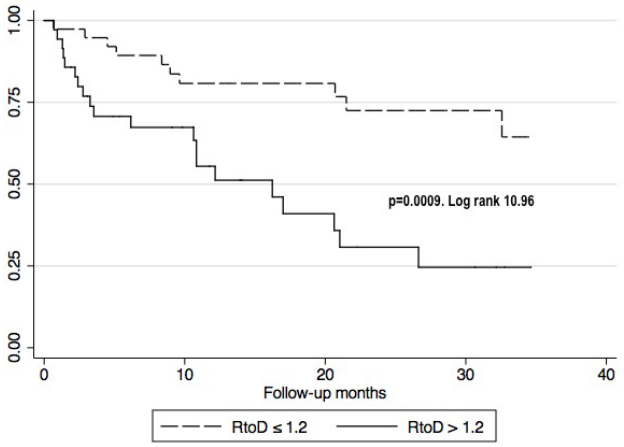


Figure 1

P2122

Mobile cardiopaging in toxic cardiomyopathy diagnostics in cancer patients

N Lyamina[1]; S Lyamina[2]; E Kotelnikova[1]; V Senchikhin[1]; T Lipchanskaya[1]

[1]Research Institute of Cardiology Saratov State Medical University named after V.I. Razumovskiy, Saratov, Russian Federation; *[2]Moscow State University of Medicine and Dentistry named after A.I. Evdokimov, Moscow, Russian Federation*

Background: The use of modern high-efficient cancer chemotherapy treatment in 5-35% of cases is accompanied by cardiotoxic effect varying from asymptomatic electrocardiography (ECG) changes to the development of acute coronary syndrome (ACS) and heart failure (CHF) that significantly impair the patients' life expectancy.
Purpose: Assessment of the feasibility of cardiopaging using due to improve the effectiveness of cardiotoxic effect diagnostics in cancer patients.
Methods: Remote management effectiveness was assessed in cardio-oncological patients with heart failure (CHF) (22 patients: 12 men, 10 women, 52.6 ± 5.5 y.o., NYHA 2.04 ± 0.25, ejection fraction 48.6 ± 6.5%). Patients were included in the study from 2 to 12 months after the chemotherapy start with 6 months follow-up period. Cardiopaging was performed on the principle of autotransmitting mobile devices and Internet application ECG Dongle. Asynchronous telecardiologic platform "CardioCloud" was used for information storage and analysis, telemedicine counseling. In CHF/chemotherapy group standard therapy was administered considering the patients' clinical status. ECG was registered 5 times a week. ECG was registered in addition in the case of any clinical symptoms present or according to the patients' desire. ECG registration duration was 10-20 minutes. ECG data were analyzed by an external doctor (an employee of the Cardiology Research Institute). Analysed data included mean heart rate, any rhythm or conduction disorders, dynamics of ST changes, QT duration. If necessary, medication was prescribed.
Results: Within 6 months not previously documented ECG changes were remotely registered in all CHF/chemotherapy patients. Among them sinus tachycardia was predominant (88%). Against the background of sinus tachycardia ventricular extrasystole of various gradations (38%), supraventricular extrasystole (24%), transient tachy-dependent bundle-branch blockages (9%) were registered. Atrial fibrillation paroxysms were observed in 2 patients. In 55% of patients complicated ECG disorders were registered in the form of sinus tachycardia and supraventricular rhythm disorders (extrasystole, episodes of atrial fibrillation) combination, and sinus tachycardia, ventricular extrasystole and ST depression. The majority pf detected violations were symptomatic (65%), in other cases patients did not complain. Within the framework of office counseling 7 (70%) patients had arterial hypertension (AH) of I-III degree. ß-blockers and ACE inhibitors were prescribed to correct the identified violations and AH.
Conclusions: Remote dynamic management of cancer patients with chemotherapy including ECG registration (= 5 times/week, 10-20 min) on the base of mobile cardiopaging combined with doctors' counseling is a sufficiently effective and accessible method of cardiotoxicity phenomenon diagnostics. The main advantage of the method is the possibility of early pharmacological correction in asymptomatic cardiovascular disorders.

P2123

Use of sacubitril valsartan in heart failure due to post-chemotherapy symptomatic ventricular dysfunction

V Gregorietti[1]; A Rojo[2]; R Coronel[2]; L Saglieti[2]; M Gregorietti[1]; M Muzzio[2]; A D Ortencio[3]; P Roura[1]; S Perrone[4]; AJ Daniele[3]
[1]Instituto Argentino de Diagnostico y Tratamiento, Cardiologia, Buenos Aires, Argentina; *[2]Sanatorio Sagrado Corazon, Cardiologia, Buenos Aires, Argentina*; *[3]Instituto de Oncologia Angel Roffo, cardiologia, Buenoa Aires, Argentina*; *[4]Hospital El Cruce, Trasplante Cardiaco, Hipertension Pulmonar, Florencio Varela, Buenos Aires, Argentina*

Background and objetives: Heart failure is a term used to define a constellation of symptoms and signs that are commonly attributed to the inability of the heart to produce a cardiac output that meets the demands of the body. It remains a deadly disease, affecting between 1-2% of the population, and is more common in the elderly, with around 6-10% of patients over 65 suffering from the condition. Sacubitril / valsartan (LCZ-696) is a combined neprilysin inhibitor and angiotensin AT1 receptor blocker approved in recent years for the treatment of chronic heart failure with reduced ejection fraction. In an area where there have been limited pharmacological advances in the last 10 years, this drug was a game changer and a great one. The optimal use of sacubitril / valsartan in clinical practice needs further investigation, in particular for patients with Cardiomyopathy induced by chemotherapeutic toxicity, as such patients are usually poorly represented in clinical trials.
Methods: 490 consecutive patients(p) with a history of breast cancer, who received treatment with chemotherapy, were enrolled prospectively from June 2016 to June 2017.
Ventricular dysfunction was detected through clinical, echocardiographic and laboratory tests.
For the statistical analysis the SPSS was used.
Results: 490 p, aged 69 ± 7.2 years, female 482(98.3%). 14 p presented ventricular dysfunction refractory to conventional treatment, all were optimally treated with beta-blockers, being with an average heart rate of 61 ± 9 bpm, so in this group it was decided to rotate the angiotensin II receptor blocker treatment to the sacubitril-valsartan combination, whose titration was adjusted to the clinical response and the hemodynamic parameters.
He was followed up at 14, 28 days and at 3 and 6 months.
It was observed that at 3 months the patients improved the ejection fraction of the left ventricle (average 23% to 36%). Improvement of ProBNP 934 pg / ml (basal), with an average reduction of 30% at follow-up, normalizing in 100% of patients followed up at 3 months. Improvement of CF III-IV to CF I-II is observed in 100% of patients. The dose of loop diuretics was reduced in all patients.
Conclusions: In patients with ventricular dysfunction secondary to chemotherapy and refractory to the tried-and-tested therapy, sacubitril valsartan has shown a good safety profile with excellent results in follow-up; and it would be a promising alternative in this cohort of patients.

P2124

Effect of severe functional mitral Regurgitation on novel hemodynamic findings in heart transplant candidates

Z Zubeyde Bayram[1]; C Dogan[1]; RD Acar[1]; B Guvendi[1]; T Unkun[1]; A Karaduman[1]; C Onal[1]; OY Akbal[1]; A Hakgor[1]; C Kaymaz[1]; N Ozdemir[1]
[1]Kartal Kosuyolu Heart Education and Research Hospital, Department of Cardiology, Istanbul, Turkey

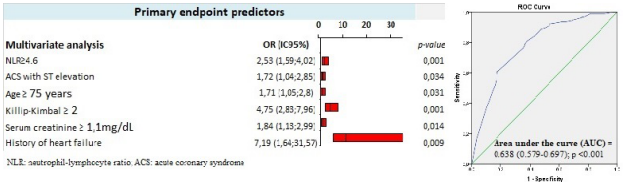
Background: A severe functional mitral regurgitation had additive factor for left ventricular filling pressure and pulmonary arterial pressures. We aimed to investigate the relationship between severe functional mitral regurgitation (FMR) and left ventricle stroke work index (LVSWI), left ventricular cardiac power index (LVCPI),right ventricle stroke work index (RVSWI), pulmonary artery pulsality index (PAPi), pulmonary arterial capacitance (PAC) and pulmonary arterial elastance (PAE) in patients who were heart transplant candidates. Methods and results. A total of 238 patients with left ventricle ejection fraction (LVEF) = 25%, NYHA class III-V and INTERMACS IV -VII were included to study and they were divided into two groups; namely; those with severe and non-severe FMR.The severe FMR was defined as effective regurgitation area = 20 mm2 and regurgitation volume = 30 ml. Seventy six patients had sever and 162 patients had non-severe FMR. There was no difference in terms of LVEF, NYHA and INTERMACS grades and heart failure duration among to groups (p>0.05). The CO, CI, SV, SVI, LVSWI and LVCPI were lower in severe FMR compared to non-severe FMR [3.1 ± 0.7 vs. 3.5 ± 0.89, p = 0.005; 1.6 ± 0.3 vs. 1.8 ± 0.5, p = 0.021; 35.0 ± 9.1 vs. 44.7 ± 15.8, p = 0.001; 19.0 ± 4.5 vs.23.4 ± 8.9, p = 0.003; 13.1 (10.8-18.5) vs. 17.1 (12.4-24.9), p < 0.001 and 0.32 (0.27-0.44) vs.0.38 (0.31-0.48), p = 0.004]. The systemic vascular resistance (SVR) was similar among to groups (22.0 ± 8.2 vs. 21.5 ± 7.9, p = 0.656).The pulmonary arterial systolic pressure, pulmonary wedge pressure were higher in patients with severe FMR than those with non-severe FMR (58.3 ± 16.0 vs. 49.3 ± 18.6, p = 0.001; 38.4 ± 11.5 vs. 30.7 ± 11.0, p < 0.001 and 25.9 ± 7.0 vs. 21.5 ± 7.4, p < 0.001). The RVSWI and PAPi were similar among to groups (6.5 ± 2.9 vs. 6.2 vs. 3.1, p = 0.416; 3.2 ± 2.0 vs. 3.7 ± 2.5, p = 0.232). The patients with severe FMR had higher PVR and PAE value and lower PAC than patients with non-severe FMR [4.0 (2.3-6.8) vs. 2.6 (1.2-4.3), p = 0.001; 1.5 (1.1-2.3) vs. 1.1 (0.79-1.68), p < 0.001 and 1.1 (0.78-1.74) vs. 1.5 (1.0-2.3), p = 0.001].
Conclusions: The patients with severe FMR had lower left ventricular cardiac performance assessed by CI, LVSWI, and LVCPI without increase in afterload (SVR), while they had higher pulmonary afterload assessed by PVR, PAC, and PAE without increase in right ventricular work defined by RVSWI and PAPi.

P2125

Neutrophil-lymphocyte ratio as a predictor of left ventricular systolic dysfunction and mortality after acute coronary syndrome

L Luis Graca Santos[1]; C Ruivo[1]; F Montenegro Sa[1]; R Ribeiro Carvalho[1]; J Correia[1]; F Saraiva[1]; A Antunes[1]; J Guardado[1]; F Soares[1]; S Pernencar[1]; J Morais[1]
[1]Hospital Santo Andre, Cardiology, Leiria, Portugal

Introduction: Inflammation plays a key role in the atherosclerotic process. Evidence supports the relationship between elevated inflammatory parameters and mortality in the context of acute coronary syndrome (ACS), which can be partially explained by higher levels of left ventricular systolic dysfunction (LVSD).
Purpose: To evaluate the association between the neutrophil-lymphocyte ratio (NLR), LVSD, and mortality in patients (pts) with ACS.
Methods: Unicentric and longitudinal retrospective study of 514 consecutively admitted pts with ACS and submitted to coronary angiography between January 2014 and December 2016. Clinical, demographic and laboratory data were obtained. NLRis defined as the ratio between absolute neutrophil count and lymphocyte count in peripheral blood at admission. The primary endpoint (PE) was a composite of LVSD (ejection fraction < 40%), in-hospital death from any cause or 1-year death from any cause. Two groups were defined according to the occurrence (or not) of the PE, and their characteristics compared. Statistically significant variables (p = 0.05, bilateral) were included in a binary logistic regression model in order to obtain predictors of mortality and LVSD. The estimated probabilities of model response were then analyzed using the Receiver Operator Characteristics (ROC) curve.
Results: The mean age was 65 ± 13 years, of which 373 were male (72.60%). The type of ACS was with ST elevation (STE) in 306 cases (59.50%). At the end of the follow-up, 122 (23,7%) pts reached PE. Mean RNL was higher in the cohort that reached PE (7.71 ± 6.59 vs. 5.11 ± 4.61, p = 0.001). The NLR cut-off that best predicted the PE was estimated at = 4.60 through ROC curve analysis, with a sensitivity of 65.6% and specificity 60.1% [area under the curve (AUC) = 0.638 (0.579-0.697); p < 0.001]. After multivariate analysis, NLR = 4.6 remained an independent predictor of mortality, as well as age = 75 years, ACS with STE, signs of heart failure (HF) at admission (Killip = 2), HF history, and creatinine = 1,1 mg/dL [picture]. A risk model encompassing all variables showed good discrimination (AUC 0.783 (0.735-0.832, p = 0.001) [picture]).
Conclusion: According to the present unicentric series of patients with ACS, NLR was an independent predictor of both LVSD and/or death from all causes in the short or medium term. It may be speculated that a greater neutrophilic inflammatory response leads to a worse prognosis in the ACS scenario, conjecturing it as a potential therapeutic target.



Primary endpoint predictors and ROCcurve

P2126

The effectiveness of coronary arteries revascularization in patients with chronic heart failure depending on a left ventricle ejection fraction

G Igimbayeva[1]; N Makhadiyeva[1]; A Zhashkeyev[2]; A Magzumov[2]; A Muhamediya[1]; A Akmaral Zhumabayeva[1]
[1]Karaganda State Medical University, Department of Therapeutic Disciplines, Karaganda, Kazakhstan; *[2]Karaganda Regional Cardiosurgery Centre, Karaganda, Kazakhstan*

Background: Coronary heart disease (CHD) is one of the main causes of mortality and morbidity all over the world, (Wolff G., Dimitroulis D., Andreotti F. and others;

Circulation: Heart Failure, January 2017). The great bulk of patients with CHD have a certain degree of chronic heart failure (CHF), and therefore CHF is a problem of public health. (Mosterd A., Hoes A.W. Clinical epidemiology of heart failure. Heart. 2007). Echocardiography is most often used diagnostic method of CHF, which able to assess left ventricle (LV) systolic function. It is advisable to study this problem, due to insufficiency of literature data about the effect of myocardial revascularization at various degrees of CHF in patients with CHD.

Purpose: To assess the effectiveness of coronary arteries revascularization in patients with CHF depending on left ventricle ejection fraction (LVEF).

Methods: We conducted retrospective study of 300 patients' medical histories with hemodynamically significant coronary artery stenosis requiring revascularization with balloon angioplasty and stenting, and with various functional classes of CHF. Stenting of one or more coronary arteries was undergone in all patients in Karaganda Regional Cardiosurgery Centre in 2015-2016. Every patients underwent echocardiography before stenting and 6 month after stenting. All patients were divided into 3 groups, accordingly to LVEF degree. The first group consisted of patients with a preserved LVEF (<50%), the second group consisted of patients with intermediate LVEF (49-40%), the third group patients were with reduced LVEF (< 40%). Pharmacological (dobutamine) stress echo was conducted in the third group patients to determining myocardial viability. Withdrawal criteria: patients with decompensated diabetes mellitus, reduced glomerular filtration rate (< 60 ml/min/1,73m^2 CKD EPI) and with severe disorders of liver function.

Results: According to the research data it was revealed that among 300 patients 56.3% were men and 43.1% were women. In each group the amount of patients were equal to 100 (33.3% in each group). Increasing of LVEF registered in patients of the first and the second groups (consequently from 53.78% to 59.31% and from 44.87% to 48.12%) 6 months after stenting. According to stress echocardiography in 78% of the third group patients there was identified no survival of the myocardial viability function in the zone of the blood supply affected artery. Accordingly, in the third group, there was no increase of LVEF after revascularization. It was registered the increasing of the LVEF from 25.36% to 41.12% in patients with preserved viability of the myocardium, after the stenting of the coronary arteries.

Conclusions: Therefore, the determination of myocardial viability function by echocardiographic data is important in determining the decisive tactics of managing patients with CHF. Revascularization is more effective in patients with preserved LVEF, which leading to LV systolic function increasing.

P2127

Relationship between diastolic dysfunction and electrophysiological remodeling of heart in patients with rheumatoid arthritis

L Liutsiia Feiskhanova[1]

[1]*Kazan State Medical University, department of hospital therapy, Kazan, Russian Federation*

Rheumatoid arthritis is autoimmune rheumatic disease characterized by injury not only the joints but also other organs, including the heart. It is known that the presence of rheumatoid arthritis increases the risk of fatal cardiovascular complications by 1.5 times compared to the general population.

Objective: to identify features of development of diastolic dysfunction in patients with rheumatoid arthritis.

Material and Methods: we examined 180 patients with rheumatoid arthritis. The activity of disease was defined according to the scale of the DAS-28. By echocardiography in 101 patients (group 1) were identified diastolic dysfunction of the left or both ventricles and in 79 patients (group 2) it was absent. Both groups were matched for age and sex. We determined the following echocardiographic parameters: mitral E/A, tricuspid E/A, end-diastolic dimension of left ventricle. In addition to echocardiography, patients underwent the vectorcardiography with the assessment of electrophysiological parameters: the squares of loops P, QRS, T, maximum vector (MV), MV-azimuth and MV- ascent. To compare two independent groups on quantitative grounds used nonparametric methods, the rank correlation and Mann-Whitney test. Differences were considered to be valid when p <0.05.

Results: when comparing the groups revealed that in the 1st group, DAS-28 was higher than in the 2nd (p <0,05): 5,575 [5,17; 6,15] and 5.32 [4,8; 5,8] respectively. In the 1st group, the square of loop QRS and the MV- ascent directly correlated with E/A of mitral valve (p <0.05), whereas in the 2nd group, we have established a direct relationship with end-diastolic dimension (p <0.05).

Conclusion: the results indicate that increased activity of rheumatoid arthritis contributes to the development of diastolic dysfunction of the myocardium. In addition, the decrease in E/A observed in diastolic dysfunction, accompanied by electrophysiological remodeling and reduction in electrical activity of the myocardium of the left ventricle, diagnosed during registration of vectorcardiogram. Moreover, even in the absence of diastolic dysfunction, a tendency to its development in the presence of electrophysiological remodeling. This demonstrates the relationship between early electrophysiological, structural-geometric changes in patients with rheumatoid arthritis. Early diagnosis allows for timely start prevention of remodeling in patients with rheumatologic diseases.

P2128

Heterogeneity of cardiac macrophages during wound healing following myocardial infarction: clinical data

A Aleksandra Gombozhapova[1]; Y Rogovskaya[1]; M Rebenkova[2]; J Kzhyshkowska[3]; V Ryabov[1]

[1]*Cardiology Research Institute, Tomsk National Research Medical Centre, Russian Academy of Sciences, Tomsk, Russian Federation*; [2]*National Research Tomsk State University , Tomsk, Russian Federation*; [3]*University of Heidelberg, Heidelberg, Germany*

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Introduction: Modern efficient acute care leads to reduction of acute infarct mortality but has contributed to an increase in the prevalence of heart failure. The necessity of better prevention and treatment of heart failure resulted in exploration of new therapeutic strategies to repair the infarct heart. Myocardial regeneration has become one of the most ambitious goals in prevention of adverse cardiac remodeling and consequent heart failure. Macrophages play a key role in transition from inflammatory to regenerative phase during wound healing following myocardial infarction (MI).

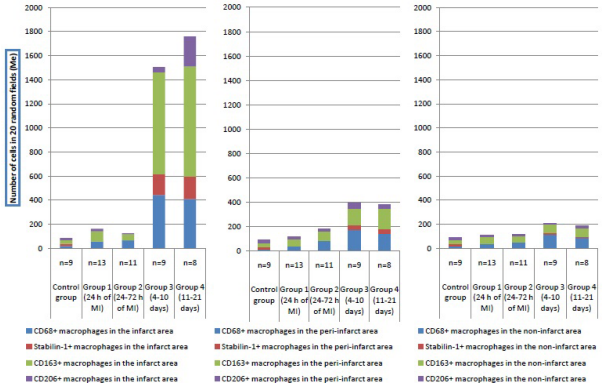


Figure 1

We have accumulated data on macrophage properties ex vivo and in cell culture. However, there is no clear information about phenotypic heterogeneity of cardiac macrophages in patients with MI.

Purpose: The purpose of the project was to assess cardiac macrophage infiltration during wound healing following myocardial infarction in clinical settings taking into consideration experimental knowledge.

Methods: The study included 41 patients with fatal MI type 1. All patients were divided into 4 groups depending on the timeline of MI histopathology. In addition to routine histopathological analysis, macrophages infiltration was assessed by immunohistochemistry. We used CD68 as a marker for the cells of the macrophage lineage, while CD163, CD206, and stabilin-1 were considered as M2-like macrophage biomarkers. Nine patients who died from non-cardiovascular causes comprised the control group.

Results: The figure (Figure 1) demonstrates results of immunohistochemical analysis. The intensity of cardiac macrophage infiltration was higher during the regenerative phase than during the inflammatory phase. In the control group the number of CD68+ and CD163+ macrophages was lower than in the infarct (IA), peri-infarct (PIA), and non-infarct areas during all phases of MI (p < 0.001). Simultaneously, the quantity of stabilin-1+ cells in the control group was higher in all the areas during inflammatory phase of MI (p = 0.01). In the control group the number of CD206+ macrophages was lower in all the areas during the reparative phase of MI (p = 0.003). We noticed that numbers of CD68+, CD163+, CD206+, and stabilin-1+ macrophages depended on MI phase. The number of CD68+ cells correlated with the day of MI in the IA (R = 0.67, p = 0.001) and in the PIA (R = 0.55, p < 0.001). There was similar relationship for CD163+ (IA: R = 0.61, p = 0.001; PIA: R = 0.66, p < 0.001), CD206+ (IA: R = 0.4, p = 0.02), and stabilin-1+ cells (IA: R = 0.6, p < 0.001; PIA: R = 0.42, p = 0.007).

Conclusions: Cardiac macrophage response following MI reminded a murine model. We observed heterogeneity of M2-like cardiac macrophages in patients with MI. Our study supported prospects for implementation of macrophage phenotyping in clinic. Improved understanding of phenotypic heterogeneity might become the

basis of a method to predict adverse cardiac remodeling and the first step in developing myocardial regeneration target therapy.

P2129

Relationships of angiotensin-(1-7) with left ventricular remodeling and diastolic disfunction in patients with arterial hypertension and type 2 diabetes

K Iushko[1]; S Koval[1]; I Snihurska[1]; T Starchenko[1]; D Miloslavskiy[1]
[1]L.T.Malaya Therapy National Institute of the NAMS of Ukraine, Department of Arterial Hypertension, Kharkiv, Ukraine

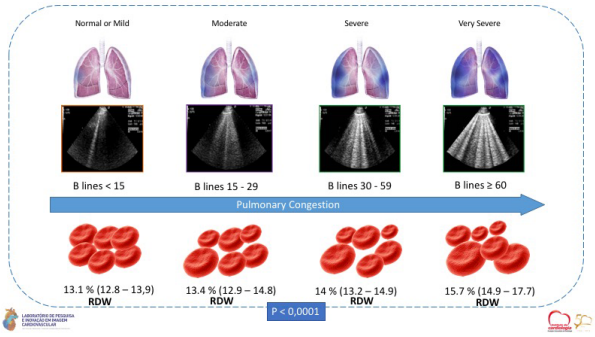
Introduction: Left ventricular (LV) remodeling and LV diastolic disfunction are the initial stages of the development of the heart failure in patients with hypertension. The angiotensin-(1-7) is the novel part of renin-angiotensin system, the metabolic product of angiotensin-II and the important protective cardiovascular factor, but its role in the development of both LV remodeling and LV diastolic disfunction in such combined pathology as arterial hypertension (AH) with type 2 diabetes (T2D) is not clear.
Purpose: The aim of the study was to determine the levels of angiotensin-(1-7) in patients with AH with concomitant T2D and to investigate its relationships with parameters of LV remodeling and LV diastolic disfunction.
Methods: The study involved 70 patients with AH of 2-3 degrees with concomitant T2D (34 men and 36 women) aged 40 to 70 years. The investigation complex included general clinical examination methods, the echocardiography with determination of the LV internal dimension at end diastole (LVIDed), septal wall thickness at end diastole, posterior wall thickness at end-diastole and calculation of the relative wall thickness, the LV mass (LVM) and LVM index. The types of cardiac remodeling we determined according 2013 ESH/ESC Guidelines. The LV diastolic function assessed using Doppler transmitral inflow pattern. Control group consisted of 16 healthy volunteers. The levels of angiotensin-(1-7) determined using ELISA.
Results: The levels of angiotensin-(1-7) in patients with AH and T2D were significantly lower than in the control group - 105,51(89,13;121,17) ng/l versus 128,77(120,02;276,49) ng/l, p <0,05. The correlation analysis revealed significant negative relationships of angiotensin-(1-7) levels with LVIDed (r=-0,37, p <0,01), LVM (r=-0,40, p <0,001) and LVM index (r=-0,41, p <0,001). Among the examined patients concentric remodeling of LV observed in 10 patients (14,3%), concentric LV hypertrophy - in 35 patients (50%), eccentric LV hypertrophy - in 25 patients (35,7%). The patients with concentric LV hypertrophy and eccentric LV hypertrophy had significant lower levels of angiotensin-(1-7) than in patients with concentric remodeling of LV - 107,5(88,2;119,6) ng/l and 101,4(84,2;111,8) ng/l versus 129,3(117,5;136,8) ng/l (? <0,01 and ? <0,01 respectively) but did not differ between themselves (p?0,05). Among examined patients the LV diastolic disfunction defined in 49 persons (70%). The levels of angiotensin-(1-7) in patients with LV diastolic disfunction were significantly lower than in patients with normal diastolic function - 101,1(87,9;116,6) ng/l versus 121,1(105,5;128,9) ng/l, ? <0,01.
Conclusion: The decreasing levels of angiotensin-(1-7) and negative relationships with LV parameters in patients with AH and T2D have been observed. The study showed, that angiotensin-(1-7) can plays an important pathogenetic role in the development of both LV remodeling and LV diastolic disfunction in hypertension patients with T2D.

P2130

The degree of pulmonary congestion assessed by lung ultrasound is directly correlated with the red cell distribution width

MH Marcelo Miglioranza[1]; RMM Vilela[1]; DL Shuha[1]; LH Saito[1]; RS Monteiro[1]; GMC Rovieri[1]; SG Alves[1]; VM Martins[1]; TJN Gomes[1]; TLL Leiria[1]; MM Rover[1]; CG Pereira[1]; RT Sant'anna[1]; RAK Kalil[1]
[1]Institute of Cardiology of Rio Grande do Sul - University Foundation of Cardiology, Porto Alegre, Brazil

Background: Measurement of red cell distribution width (RDW) has emerged as a promising prognostic marker in patients with cardiovascular disease and heart failure. However, the mediating mechanism of this interaction remains controversial. We aimed to determine if the degree of pulmonary congestion is directly correlated with higher RDW in heart failure outpatients with reduced ejection fraction (HFREF).
Methods: Cross-sectional study of HFREF outpatients. The outpatient evaluation included a complete clinical examination, NT-proBNP, echocardiogram and lung ultrasound (LUS) assessment. The degree of pulmonary congestion was obtained by LUS considering the sum of the number of B lines identified in 28 thoracic windows on the anterior and lateral sides of the right and left hemithorax.
Results: 97 patients (61% men, mean age 53 ± 13 years, 29% NYHA III-IV, average left ventricular ejection fraction 28 ± 4%, and 54% with dilated cardiomyopathy) were evaluated. The RDW indices were significantly correlated ($p < 0.001$) with NT-proBNP ($r = 0.56$), LUS ($r = 0.6$); E/e' ($r = 0.4$); right atrial pressure ($r = 0.47$). Clinically significant pulmonary congestion by LUS (B lines = 15) was present in 68% of the patients, which presented a higher RDW values than non-congestive patients: 14% (13-16) vs 13.1% (12-14) $p < 0.0001$. Severely congested patients (B lines = 30) had an even higher RDW values: 15% (13-16) $p < 0.0001$. Was also observed that patients with RDW = 14.05% had significantly more extravascular lung water than patients with RDW < 14%: 51 (30-96) vs 16 (7-31) B lines by LUS respectively ($p < 0.0001$). Conclusion: In an HFREF outpatient sample, RDW indices were proportionally higher as the number of B lines by LUS increased, suggesting that the degree of pulmonary congestion may contribute to the interaction mechanism of RDW as a prognostic marker.



Pulmonary Congestion Degree and RDW

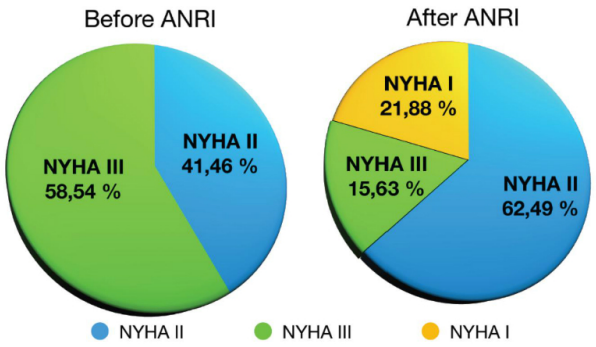
P2131

Early experience with sacubitril/valsartan in real life: impact in emergency room and hospital admissions among frequent flyers patients

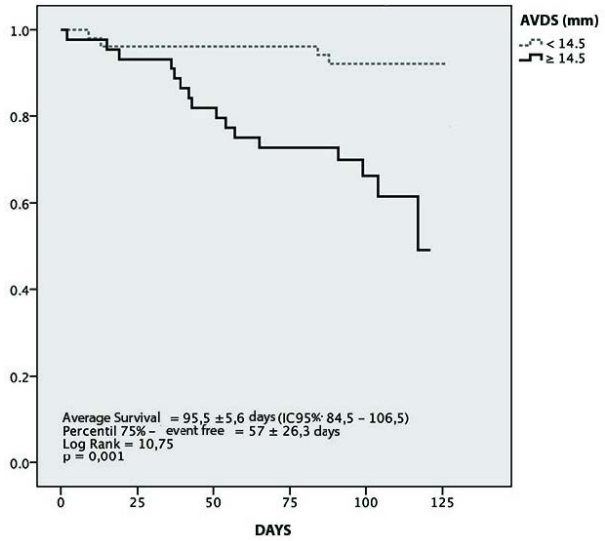
M Galvan Ruiz[1]; M Singh[1]; M Blanco-Nuez[1]; M Fernandez-De-Sanmamed-Giron[1]; M Groba-Marco[1]; R Montiel Quintero[1]; E Perez-Nogales[2]; JM Medina Gil[2]; E Caballero Dorta[1]; P Martin Lorenzo[1]; A Antonio Garcia Quintana[1]
[1]University Hospital De Gran Canaria "Dr. Negrin", Las Palmas de Gran Canaria, Spain; [2]University Hospital Insular of Gran Canaria, Las Palmas De Gran Canaria, Spain

Background: The treatment of heart failure (HF) with reduced ejection fraction (HFrEF) has recently changed with the introduction of sacubitril/valsartan (SV), an inhibitor of neprilysin and the angiotensin receptor (ANRI) enhancing the cardioprotective effect of natriuretic peptides as well as inhibiting the renin angiotensin system. This drug is recommended as a replacement for an ACEi or ARBs in ambulatory patients with symptomatic HFrEF despite optimal treatment. Patients with a recent hospital admission due to HF have an increased risk of new HF admissions, major adverse events and worse short-term prognosis.
Purpose: To analyse a subgroup of patients with HFrEF started on ANRI, with one or more hospital admissions or visit to the emergency department (ED) due a decompensation of HF, within one year prior to the initiation of ANRI.
Methods: A multicentre, ambispective study of 106 patients with HFrEF was carried out. After an initial analysis, 44 patients had at least one or more admissions or visits to the ED in the previous year of using the drug due to worsening HF. Patients were recruited between September 2016 and December 2017.
Results: In this cohort 77.3% were males with mean age 64.5 ± 11 years, and a mean follow-up time of 196 ± 132 days. 79.5% had hypertension, 53.2% diabetics, 59.1% dyslipidaemia, 36.4% AF, 25% ICD and 22.7% CRT. The most frequent etiology was ischemic heart disease (56.8%), idiopathic dilated cardiomyopathy 36.4%, 4.5% valvular etiology and 2.3% chemotherapy induced cardiotoxicity. The average baseline LVEF was 30%, the left ventricular end-diastolic diameter was 64.38 mm.
Regarding the side effects, we observed 13.6% symptomatic hypotension, 6.8% acute renal failure, 4.5% hyperkalemia, 4.5% nausea and vomiting and one patient asymptomatic hypotension. Likewise, we observed that 4 patients died during the follow-up period, and one of them due to HF.
Conclusions: Patients with recent admissions showed significant improvement of the functional class, less hospital admissions or visits to the ED related to HF, and lower NT-proBNP levels. It is important to identify these patients with worse prognosis, which could benefit at most of the treatment.

Hospital admissions and biochemistry	BeforeSV	AfterSV	P value
Admissionor visits to the ED (mean)	2.0	0.52	< 0.001
NT- proBNP (mean) pg/mL	4932	2317	0.004
Glomerularfiltration (mean)mL/min	66.22	63.14	0.088
Creatinine(mean) mg/dL	1.11	1.19	0.014
SerumPotassium (mean) mEq/L	4.35	4.55	0.034



Functional class before and after ANRI



Dyspnea Severity and Survival

P2132

Dyspnea severity in chronic heart failure outpatients is mainly related to prognosis than to pulmonary congestion degree

MH Marcelo Miglioranza[1]; MM Rover[1]; TJN Gomes[1]; GMC Rovieri[1]; LH Saito[1]; RMM Vilela[1]; RS Monteiro[1]; DL Shuha[1]; SG Alves[1]; VM Martins[1]; TLL Leiria[1]; RT Sant'anna[1]; RAK Kalil[1]

[1]Institute of Cardiology of Rio Grande do Sul - University Foundation of Cardiology, Porto Alegre, Brazil

Purpose: Dyspnea is one of the main symptoms assessed during a heart failure outpatient visit. However, data are scarce on literature demonstrating the association between dyspnea severity with pulmonary congestion or prognosis. Our aim was to determine the dyspnea scale accuracy in determining extravascular lung water and prognosis in heart failure outpatient clinic.
Methods: Ninety-seven patients admitted to a heart failure clinic due to advanced systolic HF (61% men, mean age 53 ± 13years, 27% postischaemic and 54% idiopathic cardiomyopathy) were enrolled. Dyspnea analog visual scale (100mm) evaluation was independently performed during the outpatient regular visit and correlated to lung ultrasound B lines (LUS), NTproBNP, E/e' ratio, NYHA class and Minnesota scale. Patients were followed up for a median period of 106 ± 12days (interquartile range: 89115days).
Results: Overall AVDS severity was 21mm ± 22, being higher in patients with significant pulmonary congestion at LUS (total Blines number>15) 24mm ± 24 vs 13mm ± 16 (p = 0.005). AVDS C statistic to determine pulmonary congestion at LUS was 0.63 (0.50.75) with 14mm cutoff (57% sensitivity and 61% specificity). AVDS was correlated with Minnesota (r = 0.42), NYHA class (r = 0.34), LUS (r = 0.36), E/e'ratio (r = 0.22) and NTproBNP (r = 0.24). During the follow-up period, 21 heart failure admissions occurred. The severity of dyspnea at AVDS was related to events with HR = 5.2 (1.8 15; p = 0.003) (see figure). AVDS C statistic to determine adverse events was 0.69 (0.56 0.83) with 14mm cutoff (76% sensitivity; 63% specificity; 90% negative predictive value; positive likelihood ratio = 2).
Conclusion: In an HF outpatient setting, dyspnea assessment by AVDS may help mainly to identify patients most likely to be admitted than to identify patients with pulmonary congestion. Due to the multifactorial dyspnea physiopathology, this simple evaluation could help to recognize patients at risk, whose treatment should be intensified.

P2133

The effect of resveratrol on non-invasive cardiologic and laboratory parameters in systolic heart failure

R Halmosi[1]; R Gal[1]; L Deres[1]; O Horvath[1]; D Praksch[1]; ZS Marton[1]; B Sumegi[2]; K Toth[1]; T Habon[1]

[1]University of Pecs, Medical School, 1st Department of Medicine, Division of Cardiology, Pecs, Hungary, Hungary; [2]University of Pecs, Medical School, Department of Biochemistry and Medical Chemistry, Pecs, Hungary

Funding Acknowledgements: GINOP-2.3.2-15-2016-00048, UNKP-17-4-I-PTE-209

Introduction: The positive effects of resveratrol on heart failure have already been evaluated in several experimental animal models, however, in human clinical trial they have not been confirmed.
Aim: The primary aim of our study was to assess the effect of resveratrol supplementation on left ventricular function in patients with heart failure with reduced ejection fraction (HFrEF).
Methods and materials: We enrolled 60 patients (age: 66.7 ± 11.04 years, 17 women and 43 men), who had heart failure with left ventricular systolic dysfunction (ejection fraction <40%). They were randomized into two groups. Daily 2x50 mg resveratrol was administered orally in the first group (n = 30) and placebo in the other group (n = 30). 56% of the enrolled patients had ischemic HFrEF. During the whole study period patients received optimal medical therapy for heart failure (ACEI/ARB, BB, MRA) in the same dose as before the randomization. On the day of randomization and 3 months later we performed echocardiography, lab test, impedance cardiography (ICG), six-minute walk test (6MWT) and quality of life questionnaire (QoL test).
Results: After the 3-month follow-up period the left ventricular ejection fraction improved significantly in the resveratrol group versus the placebo group (p <0.001). Lab test analysis showed that resveratrol supplementation significantly reduced the total cholesterol level (p <0.05), the LDL-C level (p <0.05) and the HDL-C level also (p <0.05) and had no overt effect on other metabolic parameters. 6MWT (p <0.05) and QoL test (p <0.05) significantly improved in the resveratrol group compared to the placebo group (p <0.05). ICG parameters did not show significant changes in either of the groups.
Conclusion Our results revealed that resveratrol supplementation added to standard medical therapy resulted in the improvement of left ventricular systolic function, exercise capacity and quality of life.

P2134

The rates of use of drugs that reduce mortality in patients with reduced ejection fraction in turkish population

T Kivrak[1]; MA Kobat[1]; O Karaca[1]; I Karaca[1]

[1]Firat University, Department of Cardiology, Elazig, Turkey

Background: Heart failure(HF) is associated with significant morbidity and mortality despite the use of medical therapies such as angiotensin-converting enzyme inhibitors, beta-adrenergic blockers, angiotensin receptor blockers, and mineralocorticoid receptor antagonists.
Purpose: Our purpose is to determine the number of patients receiving optimal medical treatment at first admission to heart failure policlinic to our hospital.
Methods: We collected demographic, laboratory, drug history, physical examination and echocardiographic parameters data at first admission to our heart failure policlinic(Table 1 and 2).We assessed 187 patients with reduced ejection fraction.
Results: In our trial, 51% of the patients were using ACE or ARB, 70% of the patients were using Beta-blocker, and 40% of the patients were using mineralocorticoid receptor antagonists(Table 3).The average ejection fraction was 29% in our trial.92% of the patients were NYHA class II and above(Table 4).
Conclusions: In our country, heart failure patients with reduced ejection fraction don't receive enough treatment.There are many reasons for this situation.In Turkey, general cardiologists treat about 80-100 patients in a day.However, many centers have not heart failure policlinic.For this reason, cardiologists can not leave enough time for chronic illness like heart failure.Heart failure policlinics in our country should become widespread, and these patients should be directed to heart failure policlinics.

TABLE

Drugs	Frequency(N:187)	Percent	Cumulative Percent
ACE/ARB	97	51	51
Spironolactone	75	40,1	40,1
Furosemide/Tiazide	97	51	51
BetaBloker	134	71,4	71,4
Ivabradine	13	7	7
Acetylsalicylic Acid	108	57,8	57,8
Digoxin	32	17,1	17,1
Statin	29	15,5	15,5
ARNI	2	1,1	1,1

Usage Rate of Drugs in Our Trial

P2135

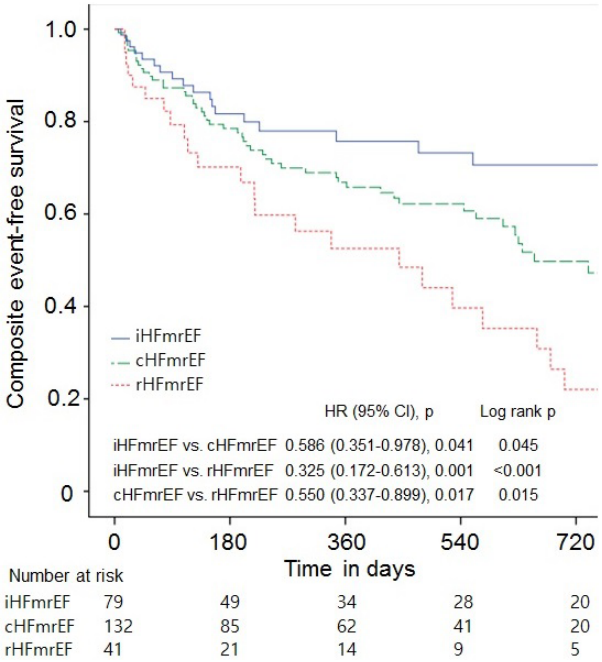
The association of ejection fraction change with clinical outcomes in heart failure with mid-range ejection fraction patients

JC Jeong Cheon Choe[1]; JH Choi[1]; SH Lee[1]; J Ahn[1]; JS Park[1]; HW Lee[1]; JH Oh[1]; HC Lee[1]; KS Cha[1]; TJ Hong[1]
[1]*Pusan National University Hospital, Department of Cardiology, Pusan, Korea Republic of*

Background: Heart failure with mid-range ejection fraction (EF) (HFmrEF) has been proposed as new category in recent guideline.
Purpose: We investigated the association of EF change with clinical outcomes in HFmrEF patients.
Methods: Of 252 consecutive patients with primary diagnosis of HFmrEF (EF 40-49%) and baseline and follow-up echocardiogram in an urban tertiary referral center from October 2013 to March 2017, 79 (31.3%) were in HFmrEF with improved EF (EF = 50% at follow-up echocardiogram) (iHFmrEF), 132 (52.4%) were in HFmrEF with consistent EF (EF 40-49% at follow-up echocardiogram) (cHFmrEF), and 41 (16.3%) were in HFmrEF with reduced EF (EF <40% at follow-up echocardiogram) (rHFmrEF) groups. We compared the characteristics and composite event (cardiovascular death and cardiovascular readmission).
Results: Compared with rHFmrEF or cHFmrEF groups, iHFmrEF group had significantly higher rates of female and coronary artery disease (CAD) with revascularization. There were similar in other characteristics among 3 groups. Composite event occurred in 100 patients (39.7%). After risk adjustment, iHFmrEF was associated with decreased risk of composite event compared with cHFmrEF (hazard ratio [HR] 0.586, 95% confidence interval [CI] 0.351-0.978, p = 0.041) and rHFmrEF (HR 0.325, 95% CI 0.172-0.613, p = 0.001). Significant contributors for improved EF included female (odds ratio [OR] 0.404, 95% CI 0.233-0.699, p = 0.001), CAD with revascularization (OR 0.361, 95% CI 0.208-0.630, p <0.001), and spironolactone use (OR 0.434, 95% CI 0.234-0.805, p = 0.008).
Conclusions: In HFmrEF patients, improved EF at follow-up echocardiogram was observed in approximately one-third of patients. Moreover, it was predictive for better clinical outcomes and affected by gender, CAD with revascularization, and spironolactone use.

The impact of EF change on outcomes

	iHFmrEF vs. cHFmrEF	iHFmrEF vs. rHFmrEF	cHFmrEF vs. rHFmrEF
Adjusted HR (95% CI), p	Adjusted HR (95% CI), p	Adjusted HR (95% CI), p	
All-cause death	0.721 (0.216-2.406), 0.595	0.189 (0.050-0.715), 0.014	0.322 (0.118-0.879), 0.027
CV death	0.802 (0.083-7.760), 0.849	0.378 (0.034-4.246), 0.430	0.466 (0.078-2.798), 0.404
Non-CV death	0.805 (0.184-3.526), 0.774	0.363 (0.067-1.954), 0.238	0.447 (0.106-1.891), 0.274
All readmission	0.863 (0.601-1.240), 0.426	0.681 (0.418-1.109), 0.123	0.719 (0.471-1.096), 0.125
CV readmission	0.575 (0.340-0.972), 0.039	0.323 (0.167-0.623), 0.001	0.559 (0.335-0.931), 0.025
Non-CV readmission	1.322 (0.792-2.206), 0.285	0.555 (0.245-1.256), 0.158	1.154 (0.532-2.504), 0.717
CV death and CV readmission	0.586 (0.351-0.978), 0.041	0.325 (0.172-0.613), 0.001	0.550 (0.337-0.899), 0.017
All-cause death and CV readmission	0.606 (0.374-0.982), 0.042	0.327 (0.180-0.592), <0.001	0.734 (0.582-0.927), 0.009



composite event free survival

P2136

Echocardiographic profile of heart failure patients with mid-range ejection fraction

VV Venzheha[1]; NT Vatutin[1]; AN Shevelok[1]; AN Zagoruiko[2]
[1]*Donetsk National Medical University, Hospital Therapy, Donetsk, Ukraine*;
[2]*Institute of Urgent and Recovery Surgery na V.K. Gusak , Donetsk, Ukraine*

Background: The 2016 European Society of Cardiology heart failure guidelines introduced the term "heart failure with mid-range ejection fraction" (HFmrEF) to refer to patients with heart failure and mildly reduced ejection fraction (EF). While structural and functional characteristics of heart failure with preserved and reduced EF are well described, echocardiographic pattern of HFmrEF remain unclear.
Purpose: The purpose of our trial was to study the echocardiographic profile in patients with HFmrEF.

Methods: The study included 110 patients (90 men and 20 women, mean age 60.4 ± 13.5 yaers) with stable coronary arterial disease and HFmrEF (40-49 %). All patients were screened by transthoracic echocardiography using the M-mode, bidimensional echocardiography and Tissue Doppler Imaging measurements with assessment of the main echocardiographic parameters: end-diastolic (EDV) and end-systolic volumes (ESV) and left ventricular (LV) dimensions indexed by body surface area (BSA), left ventricular myocardium mass index (LVMMI), left atrium (LA) anterior-posterior size, degree of mitral regurgitation (MR), pulmonary artery (PA) pressure, the presence and type of LV diastolic dysfunction (DD).
Results: According to echocardiographic results 27 % (95 % confidence interval (CI) 19.3 ± 36.0 %) patients with HFmrEF had severe LV dilatation (LV EDV index = 97 ml/m2). More than half (55 %, 95 % CI 45.1-63.8 %) of all patients had LV hypertrophy, the mean LVMMI was 144.3 ± 35.51 g/m2. Clinically significant (= 2 degree) mitral regurgitation and LA enlargement were revealed in 73 % (95 % CI 64.0-80.7 %) of cases, the mean value of LA size was 46.5 ± 8.15 mm. The first and second degree of pulmonary arterial hypertension (PAH) was registered in 45 % (95 % CI 36.2-54.9 %) and 18 % (95 % CI 11.5-26.0 %) of patients respectively, the mean PA pressure was 36.66 ± 12.58 mm Hg. LV DD was observed in 91 % (95 % CI 84.8-95.6 % patients, mild and moderate type were found with equal frequency (36 %, 95 % CI 27.6-45.6 %), while the prevalence of severe LV DD was 18 % (95 % CI 11.5-26.0 %).
Conclusion: About a quarter of patients with HFmrEF have severe LV dilatation. The prevalence of clinically significant mitral regurgitation and LA dilatation achieves 73 %, while the prevalence of PAH is about 63 %. Every second patient with HFmrEF has the LV hypertrophy. In most of cases (91 %) mildly reduced of LV EF combined with the LV DD.

P2137

Soluble ST2 in patients with heart failure with preserved ejection fraction and its prognostic value: results from the Aldo-DHF trial

F Baehr[1]; L Schleussner[1]; A Bobenko[1]; J Petutschnigg[1]; V Holzendorf[2]; R Wachter[2]; K Nolte[2]; A Duvinage[3]; HD Duengen[1]; C Hermann-Lingen[4]; M Halle[3]; G Hasenfuss[4]; B Pieske[1]; F Edelmann[1]
[1]Charite - Campus Virchow-Klinikum (CVK), Department of Cardiology, Berlin, Germany; *[2]University of Leipzig, Leipzig, Germany*; *[3]Technical University of Munich, Munich, Germany*; *[4]Georg-August University, Gottingen, Germany*

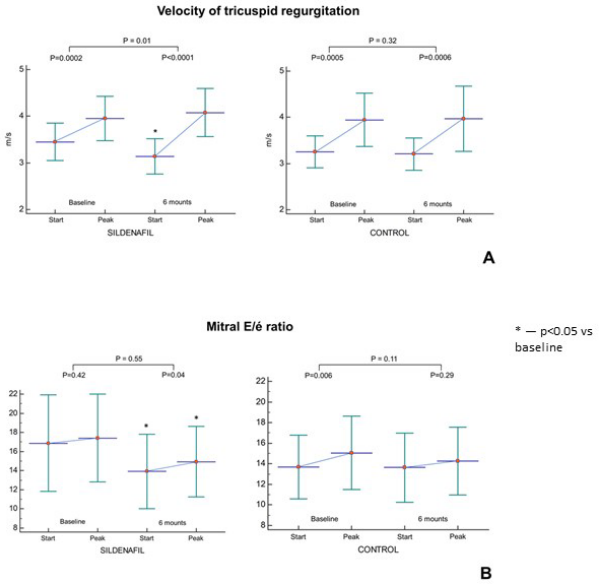
Background: sST2 is a novel serum biomarker that has been shown to be linked to myocardial dysfunction and fibrosis. Elevated sST2 levels are associated with an increased risk of mortality in heart failure with reduced ejection fraction. Myocardial fibrosis is a key contributor in the genesis of Heart failure with preserved ejection fraction (HFpEF) but data on ST2 in chronic HFpEF is scarce. The aim of this analysis was to define sST2 plasma levels in patients with stable HFpEF and its association with patient characteristics and outcome. Furthermore we investigated the interaction between spironolactone treatment and sST2 levels over time.
Methods and Results: sST2 levels were measured at baseline, at 6 and at 12 months in 415 patients of the Aldosterone in Diastolic Heart Failure trial (Aldo-DHF, n = 422). The association between different baseline sST2 levels (low (< 29.5ng/ml) middle (29.5-38.5ng/ml) and high (<38.5ng/ml) he change in sST2 and all-cause death or hospitalization, as well as the effect of treatment with spironolactone on sST2 levels were evaluated. Baseline sST2 was significantly higher in male patients. Furthermore,sST2 levels correlated positively with uric acid concentration (7,88ng/ml per 10mg/dl uric acid, p = 0,008), left ventricular ejection fraction (2,03ng/ml per 10% LVEF, p = 0,001) and left atrial volume index (LAVI)(0,12ng/ml per 1ml/m2, p = 0,031). After multivariable adjustment, sST2 showed no significant correlation to clinical parameters such as NYHA class, 6 min walk distance or Short Form 36 Health Survey- physical functioning. Difference in baseline sST2 level had no impact on all-cause death or hospitalization during 12 months follow up. Further analysis showed no significant effect of long term spironolactone treatment to sST2 levels.
Conclusion: In stable HFpEF patients sST2 levels are significantly higher in males than in females and are associated with uric acid, LVEF and LAVI. However, during 12month follow up sST2 did not show prognostic value for the combined endpoint all-cause death or hospitalization. Surprinsigly, long term treatment with spironolactone did not effect sST2 levels.

P2138

Sildenafil improves functional capacity and exercise hemodynamics in patients with HFpEF and predominantly combined pre- and post-capillary pulmonary hypertension

AG Artem Ovchinnikov[1]; AV Potekhina[1]; SV Gavryushina[1]; FT Ageev[1]
[1]Russian Cardiology Research and Production Complex, Moscow, Russian Federation

Aims: Data on clinical effectiveness of phosphodiesterase 5 (PDE5) inhibitors in heart failure with preserved left ventricular ejection fraction (HFpEF) show controversial.
Results: PDE5 inhibition targets pulmonary vessels and improves right ventricle function in pulmonary hypertension (PH). We aimed to investigate whether therapy with PDE5 inhibitor sildenafil improves exercise tolerability and exercise hemodynamics in patients with HFpEF and PH (presumably combined pre- and post-capillary [Cpc] as assessed via echocardiography).
Methods: In present randomized, controlled open single-center 6-month study we enrolled 28 patients with stable HF in NYHA functional class II?III; preserved EF



Changes in PASP (A) and PCWP (B).

(<50%); and PH due to left heart disease determined via echocardiography as high filling pressure (LV diastolic dysfunction grade II/III) and pulmonary artery systolic pressure (PASP) >40 mm Hg. According to pulmonary vascular resistance (PVR) >3 Wood units and/or transpulmonary gradient (TPG) >15 mm Hg, the presumable Cpc phenotype of PH was suggested. Patients were assigned to sildenafil group (25 mg TID for 3 months followed by 50 mg TID for 3 months; n = 16) or to control group (n = 12). At baseline and after 6 months all patients exercised supine cycle ergometry at 60 rpm starting at a 3-min period of low-level 25-W workload followed by 10-W increments in 1-minute stages to maximum tolerated levels.
Results: Both exercise time and peak ergometry workload were increased after 6 month of therapy in sildenafil group (+ 75 [95% CI 23 to 130] s, P = 0.008 and + 11 [95% CI 3 to 20] Watts, P = 0.013, respectively vs. baseline) but not in control group (−3 [95% CI 95% CI −39 to 33] s, and −1 [95% CI −7 to 6] Watts, respectively). At baseline, the exercise was associated with a prominent increase in PASP (estimated by TR velocity) in both groups but with only modest increase in PCWP (estimated by mitral E/é ratio; Figure). At 6 month stress test in sildenafil group the resting TR velocity was lower, although exercise TR velocity elevation was greater vs. the data at baseline stress test (Figure). The same dynamics were observed for mitral E/é ratio - lower resting values but greater exercise elevation (Figure). No changes in resting or peak exercise TR velocity or mitral E/é ratio were detected in control group.
Conclusion: In patients with HFpEF and predominantly Cpc-PH, 6-month therapy with sildenafil improved exercise capacity and was associated with resting PASP and PCWP decrease, but paradoxically with a significant increase in exercise PASP and PCWP, presumably reflecting the increased pulmonary blood flow due to improvements in RV contractile reserve and the restoration in LV preload during exercise.

P2139 Echocardiographic data

Parameters	Controls (n = 58)	Low NT-proBNP (n = 32)	p	Low NT-proBNP (n = 32)	High NT-proBNP (n = 35)	p
RWT	0.41 ± 0.04	0.44 ± 0.05	0.002	0.44 ±0.05	0.45 ± 0.07	0.593
LV EDVI (ml/m^2)	40.1 (36.0 - 44.5)	41.7 (37.3 - 47.2)	0.193	41.7 (37.3 - 47.2)	37 (30.7 - 43.9)	0.076
LV EF (%)	60.0 (58.0 - 63.0)	55.0 (54.0 - 58)	< 0.001	55.0 (54.0 - 58)	55.0 (52.0 - 58.0)	0.899
E' mean (cm/s)	8.89 ± 1.94	6.47 ± 1.18	< 0.001	6.47 ± 1.18	6.09 ±1.30	0.092
E/E' mean	8.83 ± 2.53	12.7 ± 3.26	< 0.001	12.7 ± 3.26	16.2 ± 6.18	0.009
LAVI max (ml/m^2)	26.2 ± 5.19	39.9 ± 8.34	< 0.001	39.9 ± 8.34	42.8 ± 12.8	0.277
LAVI min (ml/m^2)	11.6 ± 3.24	20.9 ± 4.86	< 0.001	20.9 ± 4.86	24.5 ± 8.61	0.041
LA global ef (%)	59.8 ± 4.87	49.1 ± 7.04	< 0.001	49.1 ± 7.04	44.2 ± 6.34	0.004
LA active ef (%)	39.3 ± 6.25	28.3 ± 7.49	< 0.001	28.3 ± 7.49	24.6 ± 6.52	0.035

RWT: Relative Wall Thickness. EDVI: End-diastolic Volume Index. EF: Ejection Fraction. E': peak early diastolic tissue velocity. E/E': peak early filling over early diastolic tissue velocities ratio. LAVI max, min: Left Atrium Volume Index maximal, minimal. ef: emptying fraction.

P2139

Plasma natriuretic peptides relate to distinct patterns of left ventricular dysfunction in chronic heart failure with preserved ejection fraction

E Elisa Dal Canto[1]; L Van Heerebeek[2]; K Kortekaas[2]; MT Waddingham[1]; WJ Paulus[1]
[1]VU University Medical Center, Physiology, Amsterdam, Netherlands; *[2]Hospital Onze Lieve Vrouwe Gasthuis, Cardiology, Amsterdam, Netherlands*

Funding Acknowledgements: CVON (Cardiovasculair Onderzoek Nederland), Dutch Heart Foundation, The Hague (RECONNECT, EARLY HFPEF).

Background: In HFpEF patients plasma levels of natriuretic peptides (NP) are frequently normal, and in several HFpEF trials outcomes differed between patients with low and high NP levels.
Purpose: To assess whether in chronic HFpEF low and high NP plasma levels underlie distinct cardiac structural and functional abnormalities.
Methods: Echocardiographic data of 67 stable HFpEF patients were derived from outpatient clinic visits. An age and gender matched control group was identified.
Results: Median NT-proBNP was 161 pg/ml with 35.8% of HFpEF patients below the diagnostic cut-off value of 125 pg/ml and 70.1% of HFpEF patients below the eligibility threshold used in several trials (<300 pg/ml). Compared to controls, HFpEF patients with below median NT-proBNP had left ventricular (LV) concentric remodeling, worse systolic function, slower relaxation and higher diastolic stiffness, which was evident from higher E/E' at comparable LV EDVI and from LA dilatation and dysfunction (Table). When HFpEF patients with below median NT-proBNP were compared to those with above median NT-proBNP, LV concentric remodeling, systolic function and relaxation were comparable but diastolic stiffness continued to deteriorate.
Conclusions: In patients with above median NT-proBNP, the halted progression of LV concentric remodeling, systolic dysfunction and slow relaxation suggests the continuing deterioration of stiffness to no longer result from cardiomyocyte dysfunction but from interstitial fibrosis. Unequal involvement of cardiomyocytes and interstitium could explain different outcome of trials in HFpEF patients with low and high NP.

P2140

Are radial artery flow mediation dilatation and shear rate the new imaging biomarkers in patients with stage B heart failure?

R Olszewski[1]; M Szubielski[2]; M Parol[3]; B Gambin[1]; W Secomski[1]; Z Trawinski[1]; A Nowicki[1]
[1]IPPT Polish Academy of Sciences, Department of Ultrasound, Warsaw, Poland; *[2]District Hospital, Cardiology, Siedlce, Poland*; *[3]District Hospital, Cardiology, Grodzisk Mazowiecki, Poland*

Funding Acknowledgements: NSC(Poland)Grant "Determination of factors of reactive radial artery response to hyperaemia in assessment of hypertension and coronary artery disease"

Background: There is growing interest in the application of non-invasive clinical method and tools to assess endothelial dysfunction as a new imaging biomarkers preceding heart failure. There are commercially available ultrasound scanners allowing measurements of the brachial artery flow mediation dilatation (FMD) and shear rate (SR) normalized FMD using 7.5-12 MHz linear array transducers; however the attainable precision in estimating the changes in artery dilation does not exceeds 0.2 mm, far beyond the required one. We are introducing a novel, high frequency scanning using a linear array 20 MHz imaging combined with 20 MHz pulsed Doppler, improving the axial resolution to be better than 0.1 mm. We expect that this approach to the measurements of FMD and SR in radial artery can help to predict early vascular disease.
Purpose: To evaluate the degree of radial artery FMD and FMD/SR after 5 minutes of reactive hyperaemia in healthy subjects and in patients with stage B heart failure (HF).
Methods: The studies were carried on 14 healthy volunteers (40-71 yr. old) and 14 patients (36-77 yr. old) with stage B heart failure due to coronary artery disease. A standard reactive hyperaemia protocol was employed in the right arm, followed by 3 min measurements of the subject's radial artery dilation and Doppler blood flow velocity measurements. FMD and SR calculations were performed offline. The FMD results were normalized using AUC of shear rate at the radial artery wall.
Results: In the healthy group the peak dilated radial artery diameter was in the range (1.97-3.57) mm, mean ± std was in the range 2.64 ± 0.43mm corresponding to a mean increase in overall radial artery diameter of FMD = 15 ± 4.8% (95% CI: 13.3-17.2%), at peak reactive hyperaemic states. The AUC shear rate calculated in time span from cuff release till peak dilation was equal 42730 ± 23630, median 37393 (95% CI: 33383-52078). In the patient's group the peak dilated radial artery diameter was in the range (2.37-3.27 mm), mean ± std was 2.85 ± 0.3mm corresponding to increase in overall radial artery diameter via FMD = 4.6 ± 4% (95% CI: 2.45-6.7%), at peak reactive hyperaemic states. The SR was equal 47761 ± 35871, median 42584, (95% CI: 26084-69438). The FMD/SR, for the healthy group was equal 5.365 ± 4.835·10-4, and in patient's group 1.3 ± 0.89·10-4.
Conclusions: In healthy volunteers the mean increase in radial artery diameter measured via FMD was 15 ± 4.8% while in patients with stage B heart failure FMD was much smaller and was 4.6 ± 4%. The SR normalized FMD, FMD/SR, was equal 5.365 ± 4.835·10-4 and 1.3 ± 0.89·10-4 for healthy volunteers and patients, respectively. Both parameters, FMD and FMD/SR showed highly significant univariate association with the occurrence of HF (P < 0.001). Radial artery flow mediation dilatation and shear rate should be considered as new imaging biomarkers in patients with stage B heart failure.

P2141

The retrospective analysis of chronic heart failure therapy, prior hospitalization for acute coronary syndrome in patients with atrial fibrillation

J Julia Dorofeeva[1]; EI Tarlovskaya[2]; SV Malhcikova[1]
[1]Kirov State Medical Academy, Internal medicine, Kirov, Russian Federation; *[2]Nizhny Novgorod State Medical Academy, Internal medicine, Nizhny Novgorod, Russian Federation*

Objective: To retrospectively evaluate the therapy of chronic heart failure (CHF) in patients with atrial fibrillation (AF) prior to hospitalization for acute coronary syndrome (ACS).
Materials and Methods: The analysis retrospectively included 163 patients with AF who were admitted to medical rehabilitation for ACS at the clinic of the Kirov Medical University from vascular centers. Criteria for inclusion - the passage of rehabilitation for ACS, the presence of AF. Exclusion criteria - absence of OP, prescription of ACS for more than 1 month. We have calculated M ± O, x2. Outpatient and inpatient patient cards were used. The average age of the patients was 64.9 ± 9.7 years. Of these, 55.8% of men and 44.2% of women.
Results: CHF before hospitalization had 133 (81.59%) patients (68 (51.13%) men and 65 (48.87%) women). Most CHF was combined with AF, ischemic heart disease and hypertension - 84 (63.16%) people. The average age of patients with CHF was 65.65 ± 9.8 years, the average length of the disease was 2.74 ± 2.8 years. XPS at the level I functional class (FC) had 42 (31.58%), II FC - 55 (41.35%), III FC - 36 (27.07%). No treatment was received at all for CHC 29 (21.8%) patients (I FC - 12 (28.57%), II FK-9 (16.36%), III FK-8 (22.22%)).Therapy with angiotensin-converting

enzyme (ACE inhibitors) / aldosterone receptor antagonists (APA) received a total of 57.9% of patients (I FC-23 (54.76%) patients, II-FC 30 (54.55%), III FC-24 66.67%)). Therapy with ß-adrenoblockers (BAB) / ivabradine at I FC 20 (47.62%) patients, although it was not shown to them, at II FK - 33 (60%), at III FK - 17 (47,22%). 15% of patients (I FC - none, II FC - 9 (16.36%) patients received therapy with mineral-corticoid receptor antagonists (AICM), although it was not shown to them, III FC - only 11 (30.56%) patients). Therapy with loop diuretics (PD) received in total 15 (11.3%) patients (I FC - none, II FK - 8 (14.55%) patients, although she was not shown them, III FC - only 7 (19,44 %) patients). Thus, out of 133 patients with CHF, therapy, corresponding to clinical recommendations received only 40 (30.08%) patients.

Conclusions: • In the group of patients with AF, hospitalized for ACS, during the previous hospitalization there was a very low quality of CHF therapy, especially III FC.

•Before the hospitalization, only 104 (78.2%) patients with CHF received treatment with CHF, and only 40 (30.08%) of them had rational therapy.

•Very rare was the use of AMPK (11 (30.56%) patients) and PD (7 (19.44%) patients) in patients with III FC of CHF.

P2142

Is loss of glycocalyx density associated with mortality in chronic heart failure?

PP Wadowski[1]; M Huelsmann[2]; IM Lang[2]; R Wurm[2]; J Pultar[1]; C Schoergenhofer[3]; C Weikert[1]; T Gremmel[1]; R Koppensteiner[1]; M Schwameis[3]; B Steinlechner[4]; B Jilma[3]

[1]Medical University of Vienna, Division of Angiology, Department of Internal Medicine II, Vienna, Austria; *[2]Medical University of Vienna, Division of Cardiology, Department of Internal Medicine II, Vienna, Austria*; *[3]Medical University of Vienna, Department of Clinical Pharmacology, Vienna, Austria*; *[4]Medical University of Vienna, Division of Cardiothoracic and Vascular Anaesthesia and Intensive Care, Vienna, Austria*

Funding Acknowledgements: The conduct of this study was in part supported by a grant from the Austrian Science Funds (FWF SFB 54-P04).

Background: Microcirculatory changes contribute to clinical symptoms and disease progression in chronic heart failure (CHF). We hypothesized that changes in cardiac microcirculation might also be reflected by a systemic reduction of capillaries and visualized by sublingual videomicroscopy. The aim was to study in vivo perfused and total capillary density and glycocalyx dimensions in patients with CHF vs. healthy controls.

Methods: Fifty-three patients with ischemic and non-ischemic cardiomyopathy and conservative treatment were compared to thirty-five healthy age-matched subjects in a prospective cross-sectional study. Sublingual microcirculation was visualized using a Sidestream Darkfield videomicroscope. Perfused (functional) and total capillary densities were compared between patients and controls. A reduced glycocalyx thickness was measured by an increased perfused boundary region (PBR).

Results: Median functional and perfused total capillary densities were 31% and 46% respectively lower in patients with cardiomyopathy (both $p < 0.001$). Dimensions of the glycocalyx were marginally lower in CHF patients than in healthy controls (< 7% difference). Loss of glycocalyx was significantly associated with overall death after a mean follow up time of 27 months (PBR: 2.05 vs. 1.86µm, $p = 0.006$). Furthermore, PBR correlated significantly with inflammation markers (fibrinogen: $r = 0.54$; C-reactive protein: $r = 0.36$), platelet counts ($r = 0.38$), and inversely with measures of liver/renal function such as bilirubin (r=-0.39) and albumin (r=-0.30) or estimated glomerular filtration rate (r=-0.34) in CHF patients.

Conclusion: CHF patients have got a markedly lower perfused and total capillary density in sublingual microvasculature when compared to controls. In addition, decreased glycocalyx thickness is related to poor overall survival.

P2143

Soluble interleukin-1 receptor-like 1 (ST2) and left ventricular remodeling after ST-segment elevation myocardial infarction: A cardiac magnetic resonance study

J Gonzalez D' Gregorio[1]; G Minana[1]; J Nunez[1]; A Bayes-Genis[2]; E Revuelta[2]; E Nunez[1]; MP Lopez-Lereu[3]; JV Monmeneu[3]; FJ Chorro[1]; J Lupon[2]; E Valero[1]; S Garcia-Blas[1]; C Rios[1]; J Gavara[1]; V Bodi[1]

[1]University Hospital Clinic of Valencia, Cardiology Department, INCLIVA. Medicine Department, University of Valencia., Valencia, Spain; *[2]Germans Trias i Pujol Hospital, Cardiology Department and Heart Failure Unit, Badalona (Barcelona), Spain*; *[3]ERESA, Valencia, Spain*

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Background: The association of soluble interleukin-1 receptor-like 1 (ST2), with left ventricular (LV) remodeling is unclear in unselected patients with a first STEMI.

Objetive: The aim of this work was to assess the relationship between ST2 a marker of inflammation and (LV) remodeling, by cardiac magnetic resonance (CMR) imaging 6 months after a STEMI.

Methods: We prospectively evaluated 109 patients with a first STEMI treated with primary percutaneous coronary intervention who had ST2 assessed within 24 h. All patients underwent CMR imaging 1 week and 6 month after STEMI. The associations between ST2, LV diastolic and systolic volumes, and LV ejection fraction (LVEF) were evaluated by linear mixed models.

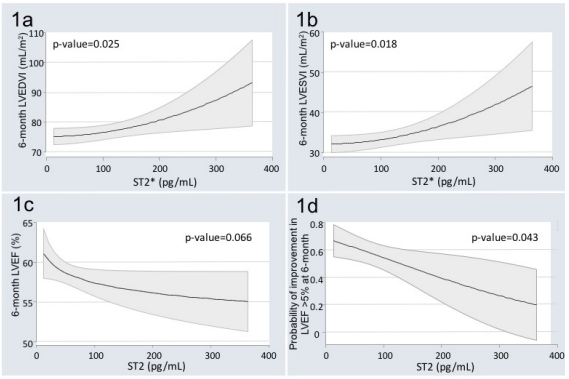
Results: The mean age was 59 ± 12 years, 85 patients (78%) were male, and 13 (11.9%) had a LVEF = 40%. The median (IQR) of ST2 was 55.3 (38.7-94.1) pg/mL. After comprehensive adjustment, ST2 was positively associated with increasing 6-month LV volume indices ($p = 0.025$ and $p = 0.018$ for diastolic and systolic volumes, respectively, Fig. 1a, 1b) and inversely associated with the 6-month LVEF (Fig. 1c)($p = 0.06$). The effect of ST2 on the endpoints was greater in patients with a larger infarct size, extensive microvascular obstruction, and a LVEF = 40% at 1-week.

Conclusions: In patients with a first STEMI treated with primary percutaneous coronary intervention, soluble ST2 predicted the changes in LV volumes and LVEF at 6 months. Future studies must assess whether targeting interleukin-1 leads to lower ST2 levels and less LV remodeling.

Table 1.

	$Q1_{ST2}$ (13.7-38.7 pg/mL) (n = 28)	$Q2_{ST2}$ (38.9-55.3 pg/mL) (n = 27)	$Q3_{ST2}$ (57.9-94.1 pg/mL) (n = 27)	$Q4_{ST2}$ (98.7-363.7) pg/mL) (n = 27)	p-value for trend
Age, years	58 ± 13	55 ± 13	61 ± 12	62 ± 13	0.114
Male, n (%)	23 (82.1)	23 (85.2)	20 (74.1)	19 (70.4)	0.194
Hypertension, n (%)	9 (32.1)	15 (55.6)	14 (51.8)	19 (70.4)	0.009
Diabetes Mellitus, n (%)	2 (7.1)	6 (22.2)	11 (40.7)	5 (18.5)	0.133
GRACE score	120 ± 30	121 ± 28	140 ± 34	153 ± 37	<0.001
TIMI risk score*	1 (0-3)	1 (1-3)	3 (2-5)	3 (2-4)	<0.001
Peak hsTnT, ng/mL*	599 (235-1723)	3160 (1645-3919)	2898 (2065-4090)	5619 (3341-8134)	<0.001
ST2, pg/mL	28.6 ± 8.1	46.6 ± 6.0	74.8 ± 11.4	170.3 ± 80	<0.001
NT-proBNP, pg/mL*	108.2 (32.3-245.9)	110.2 (39.9-402.2)	193.1 (86.5-497.9)	404.5 (181.7-744.1)	<0.001

GRACE: Global Registry of Acute Coronary Events; TIMI: Thrombolysis In Myocardial Infarction; hsTnT: high-sensibility troponin T; NT-proBNP: amino-terminal pro-brain natriuretic peptide. Values for continuous variables are expressed as mean ± standard deviation unless otherwise specified.*Values expressed as median (interquartile range).



Effect of ST2 in LV volumes and EF

Chronic Heart Failure - Epidemiology, Prognosis, Outcome

P2144

Socio-economic factors and outcomes in heart failure: Insights from the ASIAN-HF registry.

WT Tay[1]; THK Teng[1]; J Tromp[1]; JJL Yap[2]; MR Macdonald[3]; C Chandramouli[1]; E Geelhoed[4]; AM Richards[5]; IS Anand[6]; CSP Lam[7]
[1]National Heart Centre Singapore, National Heart Research Institute, Singapore, Singapore; *[2]National Heart Centre Singapore, Singapore, Singapore*; *[3]Changi General Hospital, Singapore, Singapore*; *[4]The University of Western Australia, School of Allied Health, Perth, Australia*; *[5]National University Health System, Cardiovascular Research Institute, Singapore, Singapore*; *[6]University of Minnesota, Veteran Affairs Medical Center, Minneapolis, United States of America*; *[7]University Medical Center Groningen, Duke-NUS Medical School, National Heart Centre Singapore, Singapore*

On behalf of: ASIAN-HF Investigators
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Background: Epidemiological evidence in Western nations suggests socio-economic deprivation is associated with poorer health outcomes. However, there is a paucity of data from Asia.
Aim: We examined the association of household income and educational status with quality of life (QoL) and 1-year all-cause mortality in patients with heart failure (HF) from 11 regions in Asia recruited in the prospective, multi-national ASIAN-HF registry.
Methods: Household income (in US$) was grouped as < 1000, 1000-2999, 3000-4999 and >5000. Educational status was grouped as no formal or primary only, secondary, pre-university and degree or higher education. Health-related QoL was assessed using the Kansas City Cardiomyopathy Questionnaire. Multivariable regression models, incorporating adjustment for comorbidities and pharmacotherapy, were used to examine the association of socio-economic factors with QoL and mortality.
Results: Among 5598 Asian patients (mean age: 61.5 ± 13.4 years, 27% women) with HF, 55.4% and 19.4% were in the two lowest monthly household income categories. One-third of the cohort had no formal or only primary education and another third had received secondary education. Lower household income was related to lower educational status. Patients in the lowest income category or no/primary only education were likely to be older, have more severe HF (NYHA Class III/IV), and more comorbidities (i.e. CKD, anaemia, hypertension, CAD and diabetes) but less likely to receive evidence-based HF medications.
Household income and educational status were not correlated with overall QoL and symptom burden/frequency. No/primary only education was however, associated with poorer self-efficacy and greater physical limitation domains (5-15 points lower adjusted mean scores) of QoL, compared to degree-holders or those with other higher education, in univariable and multivariable models.
454 (8.1%) of the cohort had died at one year. Crude hazard ratios (HR) were 1.96 (95% CI 1.10-3.49) and HR 1.75 (95% CI 1.31-2.36) in those with the lowest (>$1000) vs. highest (<$5000) income category and no/primary only vs. degree or higher educational status, respectively. Those with both low educational status (no/primary only) and low household income (>$1000) had 47% increased hazards of 1-year mortality, as compared to secondary or higher education and household income=$1000 - a difference that remained significant even after multivariable adjustment.
Conclusions: These first prospective multinational data across Asia show that socio-economic factors (household income and educational status) are related to outcomes in heart failure. Low education status negatively impacted patients' self-care behaviour, whereas excess mortality was observed in those with both less education and low household income.

P2145

Patient-reported outcomes in patients with heart failure - associated with demographics?

AA Anne Ankerstjerne Rasmussen[1]; H Wiggers[1]; SK Berg[2]; TB Rasmussen[3]; B Borregaard[4]; L Thrysoee[5]; CB Thorup[6]; RE Mols[1]; SH Larsen[1]; SP Johnsen[7]
[1]Aarhus University Hospital, Department of Cardiology, Aarhus, Denmark; *[2]Rigshospitalet - Copenhagen University Hospital, Department of Cardiology and Department of Cardiothoracic Surgery, Copenhagen, Denmark*; *[3]Herlev and Gentofte University Hospital, Department of Cardiology, Gentofte, Denmark*; *[4]Odense University Hospital, Department of Cardiothoracic and Vascular Surgery , Odense, Denmark*; *[5]Odense University Hospital, Department of Cardiology, Odense, Denmark*; *[6]Aalborg University Hospital, Heart and Lung Clinic and Clinical Nursing Research Unit, Aalborg, Denmark*; *[7]Aalborg University, Department of Clinical Medicine , Aalborg, Denmark*

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Background
A range of clinical and sociodemographic prognostic factors are well-established in heart failure (HF), while a substantial need for clarifying the prognostic significance of self-reported information from the patients.
Patient-reported outcomes (PRO) data reflects the patient's subjective assessment of health status and quantifies the patient's perspective on the disease, anxiety and depression, symptoms and impact on everyday life.
Purpose: To study the association between demographic patient characteristics and PRO in a Danish population of patients with HF.
Methods: A cross-sectional cohort study based on the nationwide DenHeart Questionnaire Survey. Patients with a HF diagnosis, completing the DenHeart Questionnaire at discharge from one of the five heart centres in Denmark in the study period from April 2013 to April 2014, were included. Anxiety and depression was assessed by the Hospital Anxiety and Depression Scale (HADS), with a cut-off at = 8 points, indicating symptoms of anxiety and depression. Health-related quality of life was assessed by using HeartQol, where a global score < 2 points, is defined as a low quality of life. The Charlson Comorbidity Index categorised comorbidity: none (0 conditions), moderate (1-2 conditions) and high (= 3 conditions). Questionnaire data was linked to The Danish Civil Registration System, The Danish National Patient Registry and medical records. The statistical analysis included chi-squared tests and multivariable logistic regression analysis
Results: A total of 1.506 patients with HF with a mean age of 66.2 ± 12.2 years, 74.2% males, and 30.8% living alone, were included. In total 73.6% had an ejection fraction (EF) < 40% and 62.2% >1 comorbid condition. Symptoms of anxiety and depression was reported by 34.3% and 25.2% of the patients, respectively, while 70.5% suffered from low health-related quality of life. Regression analysis identified female gender (adjusted OR: 1.5 95% CI: 1.2-2.0), and a high comorbidity level (adjusted OR: 1.7, 95% CI: 1.2-2.3) to be associated with symptoms of anxiety. The same risk factors were associated with symptoms of depression: female gender (adjusted OR: 1.5, 95% CI: 1.2-2.0), a moderate comorbidity level (adjusted OR: 1.4, 95% CI: 1.1-1.9) and a high comorbidity level (adjusted OR: 1.9, 95% CI: 1.4-2.8). Finally, being female (adjusted OR: 1.4, 95% CI: 1.0-1.8), living alone (adjusted OR: 1.3, 95% CI: 1.0-1.7), an EF < 40% (adjusted OR: 1.4, 95% CI: 1.1-1.9), a moderate comorbidity level (adjusted OR: 1.5, 95% CI: 1.2-2.0) and a high comorbidity level (adjusted OR: 2.9, 95% CI: 2.0-4.2) was associated with low quality of life.
Conclusion: The patients reported symtoms of anxiety and depression and low health-related quality of life. Further efforts are warranted to clarify the potential additional prognostic information that PRO may represent. This may potential identify vulnerable patients with HF, who could benefit from a closer contact to the healthcare system.

P2146

Cardiologists perspectives on discussing prognosis with heart failure patients

MHL Van Der Wal[1]; L Hjelmfors[1]; A Stromberg[2]; T Jaarsma[1]
[1]Faculty of Medical and Health Sciences, Department of Social and Welfare Studies, Linköping, Sweden; *[2]Linkoping University, Department of Medical and Health Sciences , Linkoping, Sweden*

Purpose: Recent Heart Failure (HF) ESC guidelines recommend that HF patients should be invited to discuss prognosis and end-of-life. However, it is unknown what the cardiologists' attitudes are regarding discussing this with their patients. Therefore, the purpose of this study was to describe the cardiologists' attitudes on discussing prognosis with HF patients with focus on barriers and how difficult they experience these conversations.
Methods: A total of 125 HF cardiologists in the Netherlands were invited by email to participate. The questionnaire used was adapted from a previously validated questionnaire developed for HF nurses. The cardiologist were asked to fill in a 10-item questionnaire about communicating prognosis, including experienced barriers in these communications. They also were asked to select a time in the HF trajectory when they would discuss prognosis for the first time with the patient. Finally they were asked to rate their experienced difficulty with discussing prognosis on a scale ranging from 1 (not difficult at all) to 10 (very difficult).
Results: A total of 43 cardiologists (response rate 34%) filled in the questionnaire (mean age 51 ± 9; 23% women). Most of the cardiologist (95%) stated that discussions about prognosis should be initiated by the patients own cardiologist although 72% also reported that another cardiologist could discuss this with the patient in case of a hospitalization, or the nurse at the HF clinic (58%). Although the mean reported difficulty in discussing prognosis was rather low (mean 3,7 ± 2), about a quarter of the cardiologists rated a 6 or higher. With regard to timing of the discussion of prognosis, half of (49%) of the cardiologists stated that prognosis should be discussed at time of diagnosis, although 23% found the first period of decompensated HF or HF hospitalization the best time to discuss it with the patient. Sixteen percent suggested that they only would discuss it in case of a serious deterioration of the HF condition. The most reported barrier to discuss prognosis were cognitive

P2146 Effect of cardiovascular risk factors

	CV risk factor	Impact of CV risk factor	P	Effect size women vs men	P for effect in women	P for effect in men	P for inter-action
GLPS	Obesity	+0.7%	<0.001	+0.9% vs. +0.7%	<0.01	<0.01	0.69
Hypertension	+0.3%	ns	+0.7% vs. -0.1%	<0.01	ns	0.004	
Dyslipidemia	+0.3%	<0.001	+1.2% vs. +0.3%	<0.001	ns	0.03	
Systolic SR	Obesity	+0.04 s-1	<0.001	+0.06 s-1 vs. +0.01 s-1	<0.001	ns	0.047
Hypertension	+0.03 s-1	<0.01	+0.06 s-1 vs. +0.02 s-1	<0.001	ns	0.02	
Dyslipidemia	+0.03 s-1	<0.05	+0.05 s-1 vs. +0.01 s-1	<0.01	ns	0.07	
Early diastolic SR	Obesity	-0.12 s-1	<0.001	-0.14 s-1 vs. -0.12 s-1	<0.001	<0.001	0.72
Hypertension	-0.72 s-1	<0.001	-0.24 s-1 vs. -0.10 s-1	<0.001	<0.001	<0.001	
Dyslipidemia	-0.12 s-1	<0.001	-0.19 s-1 vs. -0.2 s-1	<0.001	ns	0.001	
Late dia-stolic SR	Hypertension	+0.09 s-1	<0.001	+0.11 s-1 vs. +0.06 s-1	<0.001	<0.001	0.02

Effect of cardiovascular (CV) risk factors on global longitudinal peak systolic strain (GLPS), systolic, early diastolic, and late diastolic strain rate (SR). ns = not significant.

problems of the patient (56%), too little time to discuss the subject (53%) and that the patient was not ready for it (53%). Other important reasons that made it more difficult were the unpredictability of the disease (50%) and fear that the patient would be worried or lose hope (50%).
Conclusion: Most cardiologists did not find it very difficult to discuss prognosis with their patients and suggest to discuss it when the diagnosis is assessed. Barriers to discuss prognosis were related to organization (lack of time) or condition of the patients (cognitive problems, not being ready). Most of the cardiologists reported that the own cardiologist should discuss prognosis with the patient, although also other health care providers (cardiologist on the ward, HF nurse) could discuss this. Therefor a multidisciplinary team approach seems important to improve discussing prognosis with HF patients.

P2147

Impact of cardiovascular risk factors on systolic and diastolic myocardial deformation Results from the population-based STAAB cohort study

C Morbach[1]; B Walter[1]; M Breunig[1]; G Gelbrich[2]; T Tiffe[2]; M Wagner[2]; PU Heuschmann[2]; S Stoerk[1]
[1]University Hospital Wuerzburg, Comprehensive Heart Failure Center and Dept. of Medicine I, Wuerzburg, Germany; *[2]University of Wuerzburg, Institute of Clinical Epidemiology and Biometry and Comprehensive Heart Failure Center, Wuerzburg, Germany*

Funding Acknowledgements: German Ministry of Education and Research (BMBF 01EO1004 and 01EO1504)

Background: Hypertension, smoking, obesity, dyslipidemia, and diabetes mellitus impact adversely on cardiovascular health and are related to heart failure (HF).
Purpose: We determined the impact of these cardiovascular risk factors (CVRF) on myocardial deformation assessed by echocardiography.
Methods: The Characteristics and Course of Heart Failure STAges A/B and Determinants of Progression (STAAB) cohort study recruited a representative sample of the population of Würzburg, Germany, aged 30-79 years and reporting no previous history of HF. Participants underwent detailed cardiovascular phenotyping and transthoracic echocardiography (Vivid S6, GE). Segmental and global longitudinal peak systolic strain (GLPS), systolic (sSR), early (edSR) and late diastolic strain rates (ldSR) were derived from 2D speckle tracking analysis.
RESULTS In 1219 of 1818 participants (49% male, mean age 54 ± 12 years) strain analysis could be performed. In a linear model, dyslipidemia, obesity, and hypertension but not diabetes mellitus and smoking showed a significant association with myocardial deformation (table).
CONCLUSION We observed sex-specific alterations of different aspects of myocardial deformation by CVRF. The female myocardium might be more vulnerable to hypertension and dyslipidemia regarding both systolic and active diastolic deformation. Late diastolic SR increased in individuals with hypertension - most likely in response to impaired early diastolic function. Obesity was the single CVRF exhibiting the most consistent adverse impact on systolic and diastolic deformation in both sexes.

P2148

Coronary artery bypass surgery versus percutaneous coronary intervention in patients with ischemic cardiomyopathy. Long term outcome depends on severity of heart failure.

C Christian Roth[1]; M Schneider[1]; D Dalos[1]; C Gangl[1]; R Berger[1]
[1]Medical University of Vienna, Department of Internal Medicine II, Division of Cardiology, Vienna, Austria

Aims: Registries and a meta-analysis suggested a similar survival benefit from percutaneous coronary intervention (PCI) compared to coronary artery bypass graft surgery (CABG) over medical therapy alone for treatment of ischemic cardiomyopathy. The severity of heart failure may impact the long-term results of these different revascularisation strategies.
Methods and Results: Patients with moderate to severe left ventricular systolic dysfunction and multivessel disease who underwent either PCI with drug-eluting stents (DES) or CABG were selected from the catheter laboratory database of the Medical University of Vienna. The primary outcome was long-term all-cause death. Among 398 patients (340 PCI, 58 CABG) the mode of revascularisation did not contribute to the prediction of death (univariate analysis - p = 0.336; Kaplan-Meier analysis - p = 0,442 during a median observation period of 1,495 (819/2,458) days), whereas NT-proBNP was the strongest predictor of long-term all-cause death. In patients with advanced heart failure (NTproBNP > median 3042pg/ml, n = 199) the mode of revascularisation was an independent predictor of death. In the Kaplan-Meier analysis patients with CABG had a better long-term survival compared to patients with PCI (p = 0.035).
Conclusions: Among patients with ischemic cardiomyopathy, PCI with DES had comparable long-term survival compared with CABG. However, patients with advanced heart failure may benefit from CABG compared to PCI.

P2149

Does NYHA class predict health-related quality of life?

A Gallagher[1]; R Lucas[2]; MR Cowie[1]
[1]Imperial College London, London, United Kingdom; *[2]Royal Brompton Hospital, London, United Kingdom*

Background: Improving quality of life is a primary aim of heart failure management. Evaluation of health-related QoL (HR-QoL) is recommended in guidelines, however, advice on implementation is lacking. Despite the use of validated HR-QoL instruments in clinical trials, their use in routine practice is yet to be widely adopted. Conversely, functional assessment using New York Heart Association (NYHA) classification is standard in the monitoring and treatment pathways of heart failure patients.
Purpose: To investigate the acceptability and feasibility of using validated HR-QoL instruments in heart failure outpatient clinics, and to examine the clinical predictors of HR-QoL.
Methods: 163 patients attending two specialist heart failure clinics, between May 2015 and 2017, were invited to complete three HR-QoL assessments: the Minnesota Living with Heart Failure questionnaire (MLHFQ); the EuroQoL 5D-3L (EQ-5D-3L); and the Kansas City Cardiomyopathy questionnaire (KCCQ). Data on the patient demographics, co-morbidities, NYHA class, plasma BNP (B-type natriuretic peptide), renal function and echocardiographic parameters were recorded.
Results: 94% of patients were willing to participate. The EQ-5D-3L questionnaire had all questions answered by 92%, compared to 86% for the MLHFQ and 49% for the KCCQ. 32% of patients requested assistance in completing the

questionnaires. There was no association between age, gender, body mass index (BMI), left ventricular ejection fraction (LVEF), plasma BNP or renal function with HR-QoL. NYHA class significantly correlated with each of the QoL assessment tools (MLHFQ r = 0.59; KCCQ r = -0.61; EQ-5D-3L r = -0.44, all p < 0.01). However, there was a wide spread of HR-QoL outcome scores for each NYHA class (Figure 1).

Conclusion: Although NYHA class correlated significantly with HR-QoL scores, in each class there was high variability in the HR-QoL scores between individual patients. NYHA classification is a focused functional assessment made from the perspective of the clinician as opposed to the patient, with consequent drawbacks. Therefore, the incorporation of validated methods to assess health-related QoL into clinical practice is required. This study confirms the acceptability and feasibility of using validated HR-QoL instruments in heart failure clinics and highlights the limitations of NHYA classification.

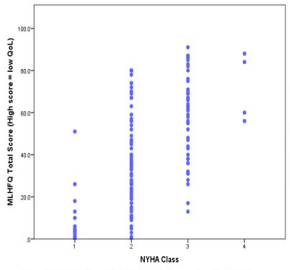

Figure 1: Distribution of the MLHFQ Total scores in each NYHA class

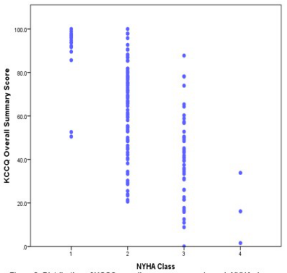

Figure 2: Distribution of KCCQ overall summary scores in each NYHA class

P2150

Heart failure prevalence in general population - interim report of the Screening Of adult urBan pOpulation To diAgnose Heart Failure (SOBOTA-HF) study

D Omersa[1]; J Farkas[2]; A Zupan Meznar[3]; N Sedlar[4]; M Lainscak[2]
[1]General Hospital Jesenice, Department of Internal Medicine, Jesenice, Slovenia; *[2]General Hospital Murska Sobota, Department of Research and Education, Murska Sobota, Slovenia*; *[3]General Hospital Celje, Department of Cardiology, Celje, Slovenia*; *[4]National Institute of Public Health, Ljubljana, Slovenia*

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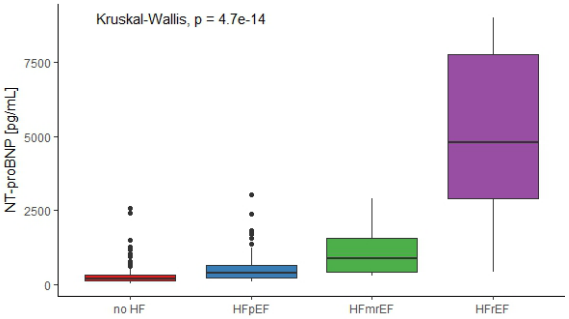
Background: The estimated heart failure (HF) prevalence of 1-2% in general population is based on studies that primarily used clinical criteria and many of them were conducted in specific populations. In view of continuous ageing of the population and diagnostic algorithm that is now based on natriuretic peptides and echocardiography, prevalence estimates are higher but were not investigated in contemporary general population.

Purpose: The purpose of this study was to assess the HF prevalence in general population aged 55 years or more.

Methods: SOBOTA-HF study is an ongoing cross sectional epidemiological study in city residents aged 55 years or more (N = 1282, 29% of the city population). In this interim report we present the data from a representative sample of residents, who were invited for screening with NT-proBNP. Those with NT-proBNP >= 125 pg/mL were invited for a detailed diagnostic visit with echocardiography, history and physical examination and electrocardiogram. HF diagnosis was based on 2016 European Society of Cardiology guidelines to calculate the HF prevalence.

Results: A total of 702 participants (response rate of 55%) completed the screening visit. Of those, 266 (38%) had NT-proBNP = 125 pg/mL and were invited for diagnostic visit. HF diagnosis was established in 83 participants with a prevalence of 11.4% in the study population. After an extrapolation to the whole population, an estimated HF prevalence was 4.6% (with the assumption that the HF prevalence in people < 55 years is 0%). Of those with HF, 8.5% had HF with reduced ejection fraction, 7.2% had HF with mid-range ejection fraction and 84.3% had HF with preserved EF. Between the participants without HF and HF groups, there were significant differences in the values of NT-proBNP (Figure).

Conclusion: The prevalence of HF in residents aged 55 years or more is 11.4% and 4.6% in all residents, mainly with preserved EF.



P2151

Prognostic value of ventilation equivalent of carbon dioxide slope in overweight heart failure patients

A Antonio Valentim Goncalves[1]; R M Soares[1]; T Pereira-Da-Silva[1]; R Ilhao Moreira[1]; J Feliciano[1]; P Rio[1]; A Abreu[1]; S Aguiar Rosa[1]; T Mendonca[1]; M Coutinho Cruz[1]; R Cruz Ferreira[1]
[1]Hospital de Santa Marta, Lisbon, Portugal

Introduction: Pulmonary function and ventilation mechanics are not normal in overweight patients, leading to a decreased hypercapnic ventilatory response which would lower the VE/VCO2 slope but worsen prognosis.

Purpose: The aim of this study was to compare the prognostic ability of the VE/VCO2 slope and pVO2 between normal and overweight heart failure (HF) patients.

Methods: Patients followed in NYHA class II-III with LVEF = 40%, underwent a prospective evaluation including a CPET. All patients were followed for 5 years and the combined endpoint was death and urgent heart transplantation.

The VE/VCO2 slope and pVO2 were analysed as potential predictors of the combined endpoint in 1, 3 and 5 years (Cox regression) and their predictive power was compared (area under the curve (AUC)) in the subgroups with body mass index (BMI) of 18.5-24.9kg/m2 (G1) and = 25kg/m2 (G2).

Results: Of the 270 enrolled patients (males 75.9%; mean BMI 26.93 ± 4.21kg/m2; mean NYHA 2.21 ± 0.46), G2 group were older (50.55 ± 14.28 vs 55.23 ± 10.42; p = 0.006), with higher LVEF (25.55 ± 6.93 vs 28.28 ± 7.41; p = 0.004) and higher HFSS (8.43 ± 0.57 vs 8.78 ± 0.94; p = 0.004).

There were 88 major events during the 5 years (G1 = 38.0% vs G2 = 29.8%; p = 0.170). The discriminative power of VE/VCO2 slope and pVO2 in G1 and G2 are presented in the Table.

The VE/VCO2 slope had at least as good AUC values as pVO2 in both groups. The comparison of VE/VCO2 slope between G1 and G2 revealed a significant lower predictive power at 3 and 5 years for G2 patients (p = 0.022 and p = 0.044, respectively).

Conclusion: Despite VE/VCO2 slope provides a discriminative power at least as good as pVO2 for predicting adverse events in both normal and overweight HF patients, a significant lower predictive power was found in overweight patients in long-term outcomes.

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Outcome V_E/V_{CO2} slope	All	A) BMI 18.5-24.9 kg/m^2	B) BMI ≥25 kg/m^2	Comparison of A-B AUCs (p-value)			
HR; 95% CI	AUC	HR; 95% CI	AUC	HR; 95% CI	AUC		
1 year	1.145; 1.108-1.182	0.890	1.108; 1.063-1.155	0.848	1.180; 1.133-1.228	0.921	0.357
3 years	1.141; 1-114-1.169	0.841	1.126; 1.089-1.165	0.921	1.172; 1.121-1.225	0.787	0.022
5 years	1.145; 1.119-1.172	0.829	1.128; 1.092-1.165	0.898	1.223; 1.142-1.310	0.787	0.044
Outcome pVO_2	All	A) BMI 18.5-24.9 kg/m^2	B) BMI ≥25 kg/m^2	Comparison of A-B AUCs (p-value)			
HR; 95% CI	AUC	HR; 95% CI	AUC	HR; 95% CI	AUC		
1 year	0.728; 0.656-0.807	0.847	0.751; 0.654-0.861	0.802	0.709; 0.605-0.830	0.854	0.816
3 years	0.793; 0.745-0.845	0.793	0.802; 0.731-0.879	0.805	0.790; 0.726-0.861	0.786	0.788
5 years	0.801; 0.759-0.847	0.791	0.811; 0.747-0.881	0.844	0.797; 0.741-0.858	0.787	0.911

P2152

Prognostic value of random urine sodium in predicting outcomes of patients with acute decompensated heart failure

M J Jhessica Pecson[1]; MC Torres[1]
[1]*Philippine Heart Center, Adult Cardiology, Quezon City, Philippines*

Background: Heart failure is an urgent public health need being the leading cause of hospitalization and an important cause of morbidity and mortality in the world.1 The science of prognostication attempts to identify patient's clinical and biological characteristics that are associated with poor outcome. Risk prediction in patients admitted with acute decompensated heart failure remains a challenge hence this study was conducted to determine association between urine sodium (Na+) level of patients admitted for acute decompensation of heart failure and outcome.
Method: All patients >19 years old admitted at a heart center for acute decompensation of heart failure with normal creatinine level at admission and with consent to participate were included in the study. Random urine sodium level was determined during first 24 hours of hospitalization. Patients were then followed up and clinical outcomes noted.
Results: Study included 150 patients which were grouped into three groups. First group included 31 patients with low urine Na+ <30 mmol/L, 48 patients in the second group with normal urine Na+ 31-90 mmol/L and 71 patients in the third group with high urine Na+ >90 mmol/L. Baseline characteristics of the three groups were similar. The primary composite outcome of death occurred in 42 patients (28%): 13 patients (42%) in the 1st group, 11 patients (23%) in the 2nd group and 18 patients (25%) in the 3rd group which was statistically significant (p = 0.002) (Table 1).
Conclusion This prospective cohort study showed significant prognostic value of random urine sodium on cardiovascular mortality on patients with acute decompensated heart failure. Low urine sodium level (uNa+ < 30 mmol/L) is associated with poor outcome

Association of urine sodium to outcome

Parameters	Low Urine Na+ (< 30 mmol/L) n = 31	Normal Urine Na_+ (31-90 mmol/L) n = 48	High Urine Na+ (>90 mmol/L) n = 71	P value
Frequency (%); Mean + SD				
Death	13 (42)	11 (23)	18 (25)	0.002
Readmission	13 (42)	19 (40)	25 (35)	0.889

P2153

Can cardiac biomarkers improve the diagnostic value of a clinical base model in diagnostically naive patients with suspected heart failure?

C Morbach[1]; S Demirbas[1]; D Oder[2]; V Holzendorf[3]; C Prettin[3]; S Stoerk[1]; G Ertl[1]; C Angermann[1]
[1]*University Hospital Wuerzburg, Comprehensive Heart Failure Center and Dept. of Medicine I, Wuerzburg, Germany*; [2]*Department of Internal Medicine I / Center of Cardiovascular Medicine, Würzburg, Germany*; [3]*Clinical Trial Center, Leipzig, Germany*

Background: Up to date, little is known about the prognostic significance of modern cardiac biomarkers in diagnostically naïve patients who present to their general practitioner (GP) with signs and symptoms potentially indicative of heart failure (HF).
Methods: N-terminal B-type natriuretic peptide (NT-proBNP), mid-regional pro-atrial NP (MR-proANP), mid-regional pro-adrenomedullin (MR-proADM), high sensitive C-reactive protein (hsCRP), tumor necrosis factor alpha (TNF a), and copeptin were determined from stored (-80°) blood of participants of the Handheld-BNP study, diagnostically naïve individuals who attended their GP with suspected HF.
The prognostic significance of individual biomarkers was compared with that of a base model consisting of age at baseline (years), sex, body mass index ((= vs >30kg/m2), renal failure (glomerular filtration rate = vs < 60ml/min./1.73m2), anaemia (haemoglobin = vs < 12mg/dL in females and = vs < 13mg/dL in males), arterial hypertension (systolic blood pressure >140mmHg and diastolic blood pressure >90mmHg or on antihypertensive drugs), diabetes mellitus (history or on antidiabetic drugs), New York Heart Association (NYHA) classes III-IV, vascular disease (stroke, peripheral artery disease or myocardial infarction), and atrial fibrillation. Further the prognostic value of a multimarker model with all biomarkers ± the base model was tested.
Results: 854/917 (93.1%) individuals (68 ± 12 years, 63% female) qualified for the present analysis. 15.8% died during the observation period of 72.2 (68.5-72.2) months. The base model alone predicted all-cause death with an area under the curve (AUC) of 0.797 which was higher than AUCs for each biomarker or a combination of all biomarkers (AUC= 0.584-0.755, and 0.754, respectively). Combination of the base model with individual biomarkers improved the AUC (e.g. addition of MR-proANP AUC = 0.809). Mortality risk was best predicted by a combination of the base model and all biomarkers (AUC 0.815).
Conclusion: Diagnostically naïve patients who present to their GP with signs and symptoms potentially indicative of heart failure have a higher mortality risk compared to the same age group of the general population (6.6%, Federal Statistical Office). The base model, which is easy to evaluate by a GP, predicted the 5-year mortality risk more accurately than each biomarker or the combination of all biomarkers. Nevertheless, addition of the biomarkers to the base model positively impacted on prognostic value and mortality risk was best predicted by a combination of the base model and all biomarkers.

P2154

Predictors of mid-term rehospitalization and mortality rates in Bulgarian patients with heart failure and preserved ejection fraction: a single-center study

R Pancheva[1]; N Runev[1]; E Manov[1]; B Stoimenov[1]; D Vassilev[2]
[1]*University Hospital Alexandrovska, Cardiology Clinic, Department of Propaedeutics of Internal Diseases , Sofia, Bulgaria*; [2]*University Hospital Alexandrovska, Department Cardiology, Sofia, Bulgaria*

Background: Chronic heart failure (CHF) is a major cause of death and recurrent rehospitalization. Hospitalized HF patients are becoming a significant economic burden. About half of the people who develop HF die within 5 years of diagnosis in spite of current optimal medical therapy. Moreover, recent epidemiological studies have demonstrated that nearly 50% of all HF patients have preserved left ventricular ejection fraction (HFpEF), with survival rates similar to those of patients with reduced EF.
Purpose: We aimed to analyze the reasons, predictors and rates of mortality and rehospitalization of patients with HFpEF in the Bulgarian population.
Methods: An observational study of patients with decompensated HFpEF, admitted at our Department between January 2012 and June 2013, was conducted. Among the risk factors, co-morbidities, clinical, echocardiographic and hemodynamic indicators, predictors of their mortality and rehospitalization rates were investigated.
esults: A total of 680 patients, mean age 67.2 ± 11.3 years, were studied. The demographic characteristics were as follows: 95.9% had arterial hypertension (AH)

(1.5% I grade; 70.1% II grade; 24.4% III grade); 23% type 2 diabetes mellitus (DM); 41.5% suffered from coronary artery disease (CAD), of whom 11.0% with previous myocardial infarction (MI); 27.9% had valvular heart disease (VHD); 57.5% atrial fibrillation (AF) and 43.7% elevated pulmonary artery systolic pressure (PASP) (<40 mmHg). In the follow-up period with average duration of 5.1 years, 178 patients (26.2%) died. For independent predictors of the 5.1-year mortality in our HFpEF group, the following were found: age>78 years, previous MI, mitral valve disease (MVD) and combined mitral and aortic valve disease (AVD), anemia, left atrium (LA) parasternal diameter >42 mm, LA length >57 mm, PASP >45 mmHg, permanent AF and CHA2DS2VASc >3 points.
In the clinical follow-up period with average duration of 1.2 years, 78 patients (11.5%) experienced rehospitalization because of an exacerbation of congestive HF. Using a multivariate logistic regression analysis, the following independent predictors of rehospitalization were found: prosthetic VHD (OR 4.58; 95% CI, 2.18-9.62; $p < 0.01$), HF NYHA classes III and IV (OR 7.90; 95% CI, 1,10-56.86; $p < 0.05$), LA diameter >43 mm (OR 1.64; 95% CI, 1.0-2.67; $p < 0.05$), LA length >54 mm (OR 1.87; 95% CI, 1.10-3.21; $p < 0.05$), and paroxysmal AF (OR 3.38; 95% CI, 1.95-5.86; $p < 0.01$).
Conclusion: Because of the lack of national registry of the HF population in Bulgaria, we performed this single-center study of patients with HFpEF. The analysis has revealed that the 5.1-year mortality rate is predicted by the advanced age (<78 years), presence of MVD and combined MVD + AVD, history of MI, anemia, as well as LA enlargement with AF and pulmonary hypertension. The mean 1.2-year rehospitalization rate has been found to be highly dependent on prosthetic VHD, NYHA III and IV, and increased LA size with paroxysmal AF.

P2155
Analysis of the China Heart Failure Surgery Registry Study (China-HFSR):from 2012 to 2017

H Hanwei Tang[1]; J Hou[1]; S Hu[1]
[1]*Fuwai Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China People's Republic of*

On behalf of: China Heart Failure Surgery Registry Study Collabrative Group
Funding Acknowledgements: National Key Reserch Project (2016YFC1300900)

Background
The cardiac surgery in heart failure patients in China is growing, but data on these patients have been limited.
Objective
To clarify the real-world etiology, clinical characteristics and real-world treatment patterns of Chinese HF surgery patients.
Methods: We used the China Heart Failure Surgery Registry Study(China-HFSR) database to obtain the demographic and clinical characteristics and treatment patterns of Chinese HFf surgery patients.
Results: From January 2012 to June 2017, data on 13 665 patients have been received from 94 participating centre. The median age was 59.2, and 26.9% were women. The most frequently performed operation was isolated coronary artery bypass graft (CABG) which was received in 47.8% patients, while the isolated valve surgery was 27.1% and CABG combined with valve surgery was 6.6%.Median length of stay (LOS) was 23 days and in-hospital mortality was 4.1%, with the highest mortality in north-east region (7.7%) and the lowest in south-west region. Perioperative implantaion of intra-aortic balloon pump (IABP) was in 6.9% patients, and the use of extracorporeal membrane oxygenation (ECMO) was 6.9%. The postoperation ß-blockers was used in 42% patients while the use of angiotensin-converting enzyme (ACE) inhibitor or angiotensin receptor blockers was 23%.
Conclusions: The China-HSFR has described the real-world clinical characteristic of Chinese HF surgery patients. Currently ,there is a relatively small amount of heart failure surgery and perioperative extracorporal life-assistant device use in China, with nonadherent to HF medications use and regional variations in outcomes. Therefore, there is a demand for quality-of-care improvement.

P2156
Guideline-recommended drug therapy in patients with chronic heart failure

G Gerald Gredinger[1]; C Trischak[1]; S Wieser[1]; S Reitter-Pfoertner[1]
[1]*Wiener Gebietskrankenkasse, Competence Center Integrierte Versorgung, Vienna, Austria*

Background: Chronic heart failure is associated with frequent hospital admissions as well as high mortality. The implementation of guideline-recommended drug therapy was shown to reduce both, hospital admission rates and mortality. Nevertheless, guideline-recommended drugs often remain underused in clinical practice.
Purpose: Evaluation of guideline-conform treatment and its impact on hospital admission and mortality in our patient population.
Methods: We used data from the 13 bigger Austrian health insurance funds and identified 19,314 hospitalized patients (79.1 years ± 11.5, 44.8 % men) for whom a discharge diagnosis of chronic heart failure has been reported between January 1, 2015 and December 31, 2015. For these identified patients we retrieved information on prescribed medication for one year after the first discharge from our records. Multivariate Logistic Regression was performed to explore the relationship between drug therapy, demographic characteristics, hospital readmission rates and mortality.
Results: Overall, 27.1 % of the patients were readmitted to hospital due to heart failure within 1 year; 33.7 % died within 1 year. Regarding guideline-conform treatment, 55.4 % of the patients were prescribed angiotensin-convertin-enzyme inhibitors (ACE-I) or angiotensin-receptor blockers (ARB), 53.22 % had beta-blockers, 35.2 % aldosterone-antagonists and 56.0 % diuretics. Multivariable variable logistic regression analysis showed that the prescription of ACE-I/ARB in combination with beta-blockers significantly lowers the mortality risk. In the readmission context no significant results could be detected.
Conclusion: It can be concluded that a combination of ACE-I/ARB with beta-blockers has a beneficial impact on mortality. Unfortunately, this therapy remains underutilised in our population.

P2157
Rapid pharmacological therapy optimisation in newly diagnosed severe left ventricular systolic dysfunction through seamless heart failure care:Effects on left ventricular function and 1-year mortality

C Chee Lim[1]; T Hunt[1]; K Hann[1]; A Baker[1]; L Jenkins[1]; L Hardy[1]; M Dewhurst[1]
[1]*North Tees and Hartlepool NHS Trust, Stockton-on-Tees, United Kingdom*

Background :
Delays in achieving optimised pharmacological therapy (OPT) for left ventricular systolic dysfunction (LVSD) lead to increased mortality. Patients with severe LVSD have worse outcomes than those with milder dysfunction. There are sparse data examining the beneficial effects of rapid achievement of OPT on LVSD and outcomes. Integrated heart failure (HF) services are recommended in international guidance to improve patient experience and efficiency in care delivery, and we have recently moved to an integrated model.
Purpose: The aim of this study was to assess whether an integrated heart failure service enabled rapid achievement of OPT in patients with severe LVSD and how this impacted upon improvements in left ventricular function on repeat imaging and mortality at 1 year.
METHODOLOGY :
We performed retrospective analysis of consecutive patients with newly-diagnosed severe LVSD (EF = 35%) over a six-month period after HF service integration (HF specialist nurses providing working across both primary and secondary care). Data was obtained from our local HF specialist nurse patient database and corroborated through data submitted to the national HF database. Time from first diagnosis (initial echocardiogram) to repeat imaging was calculated, subtracting 3 months from this to calculate time to OPT (repeat imaging recommended 3 months post OPT). Mortality data at 1 year was recorded. Factors influencing time to OPT, improvement in LVSD and outcome were assessed.
Results: 38 patients had newly diagnosed severe LVSD, of which 27 had repeat imaging. Mean age was 69(range 34-98), 61%(23) male. Mean time from diagnosis to OPT was 2.5 months for in-patients and 4.3 months for out-patients. 20/27 (74%) showed improvement in LVSD from severe to at least moderate on repeat imaging. 1 year mortality was 10.5%. Factors reducing time to OPT include being in-patient at diagnosis, no requirement of dosette box and use of perindopril versus ramipril. Factors increasing chances of LV improvement include non-ischaemic aetiology, higher medication dose achieved, lower Charlson co-morbidity score and narrow QRS. Factors increasing chances of mortality include number of hospital admissions, inability to tolerate target dose 'triple therapy' medication and higher Charlson score. reason for not having repeat imaging include patient choice, multiple comorbidities and poor prognosis.
Conclusion: An integrated HF service contributes to the rapid achievement of OPT. The prevalence of LV improvement in this modern service is significantly higher than historic data in the literature, and the 1 year mortality rate much lower.

Chronic Heart Failure - Diagnostic Methods

P2158
Complications in endomyocardial biopsy - a single center experience

CDJ Christophe Denis Josef Capelle[1]; F Duca[1]; C Binder[1]; C Zotter-Tufaro[1]; C Nitsche[1]; AA Kammerlander[1]; S Aschauer[1]; L Schachner[1]; B Oeztuerk[1]; C Dona[1]; J Mascherbauer[1]; D Bonderman[1]
[1]*Medical University of Vienna, Internal Medicine II, Division of Cardiology, Vienna, Austria*

Background: According to current literature endomyocardial biopsy (EMB) is a relatively safe procedure when performed by experienced physicians. Previous studies investigating EMB-related complications have included relatively young and healthy patient populations. However, EMB is often necessary in clinically compromised patients in order to establish a correct diagnosis (e.g. cardiac amyloidosis versus heart failure with preserved ejection fraction). Whether EMB is safe in an elderly, clinically compromised patient population is not known.
Purpose: The present study aimed to assess the frequency and severity of EMB-associated complications in an elderly, clinically compromised patient population.
Methods: Consecutive patients who underwent EMB at the Division of Cardiology at the Medical University of Vienna were analyzed for the present study. Clinical as well as invasive hemodynamic parameters were assessed at the time of EMB.
Results: Between May 2010 and September 2017, 106 patients were analyzed for our study. The study population consisted of 44 (41.5%) female and 62 (58.5%) male patients. Median age was 67.0 years [Interquartile range (IQR): 55.0 - 74.0] and median N-terminal prohormone of brain natriuretic peptide (NT-proBNP) was 1725 pg/mL (IQR: 572 - 4239). Mean pulmonary arterial pressure was 30.5mmHg (IQR: 24.0 - 38.0). The vast majority of EMBs were performed with left heart catheterization via femoral access [n = 96 (90.6%)]. Further EMBs were acquired during surgery [n = 8 (7.5%)] or right heart catheterization using a jugular access [n = 2 (1.9%)].
In total, 23 (21.7%) EMB-associated complications occurred. The most common complication was pericardial effusion [n = 12 (11.3%)] followed by stroke/transient ischemic attack [n = 5 (4.7%)], vascular or nerval damage at site of puncture [n = 4 (3.8%)], death [n = 1 (0.9%)], and contrast agent induced renal failure [n = 1 (0.9%)] (Figure 1).
Patients who experienced complications had higher NT-proBNP levels as compared to patients without [2838 pg/mL (IQR: 783 - 9065) versus 1473 pg/mL (IQR: 433 - 4049)]. However, this was only borderline significant (p = 0.065). No further differences regarding clinical or invasive hemodynamic parameters were detected between patients with and without complications.
Conclusion: A significant number of patients experienced EMB-related complications in our patient cohort. Patients with complications showed a trend towards higher NT-proBNP levels. Therefore, we should be aware of a possibly greater rate of complications and question the necessity for EMB in clinically compromised patients.
Figure legend.
Figure 1.
Pie chart showing endomyocardial biopsy related complications (n = 23) in relation to the study cohort (n = 106).

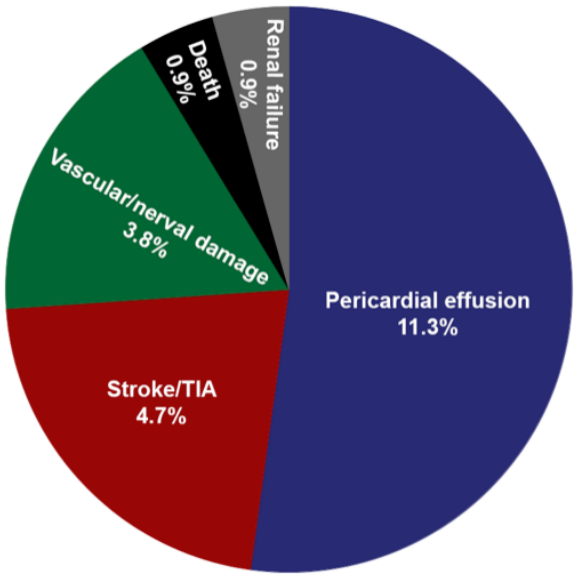


Figure 1

P2159
Obesity-related reduction in NT-proBNP levels in healthy individuals is greater in women compared to men

N Navin Suthahar[1]; WC Meijers[1]; JE Ho[2]; RT Gansevoort[1]; AA Voors[1]; P Van Der Meer[1]; SJ Bakker[1]; S Heymans[3]; V Van Empel[3]; P Van Der Harst[1]; DJ Van Veldhuisen[1]; RA De Boer[1]
[1]University Medical Center Groningen, Cardiology, Groningen, Netherlands; *[2]Massachusetts General Hospital, Cardiovascular Research Center, Boston, United States of America*; *[3]Maastricht University Medical Centre (MUMC), Maastricht, Netherlands*

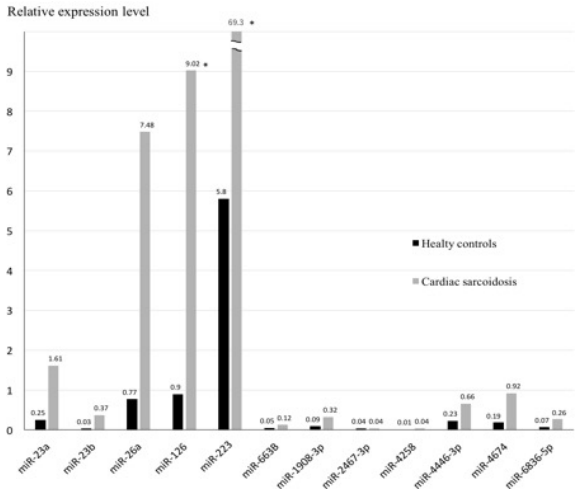
Funding Acknowledgements: CVON DOSIS, grant 2014-40; CVON SHE-PREDICTS-HF, grant 2017-21; CVON RED-CVD, grant 2017-11; NWO VIDI, grant 917.13.350

Background: N-terminal pro-B-type natriuretic peptide (NT-proBNP) is an established biomarker for diagnosis and risk stratification of cardiovascular diseases. It is known that NT-proBNP levels increase with age, and are inversely related to obesity. Whether the obesity association varies by sex remains unclear. We investigated sex-specific associations of obesity and NT-proBNP levels in a large community-based cohort.
Methods: We measured NT-proBNP in 7608 participants (3824 women) from the Prevention of Renal and Vascular End-stage Disease (PREVEND) cohort (free of heart failure), and studied its relationship with obesity-associated parameters in the overall population, and in males and females separately, accounting for various age categories.
Results: NT-proBNP levels were significantly higher in females (50.7pg/mL, 28.4-86.8; median, interquartile-range) than in males (23.7pg/mL, 10.0-53.6; P < 0.001). NT-proBNP was lower in heavier individuals - but this could largely be explained by the fact that females have a lower body weight whilst having higher NT-proBNP levels. NT-proBNP levels displayed a "U-shaped" relationship with increasing waist circumference (WC) and were not associated with body-mass index (BMI) in the overall population; sex-stratification significantly altered these relationships. Age is an important confounder and increasing age is associated with higher NT-proBNP levels in males than in females (P < 0.001). In multivariable analyses, the inverse association of NT-proBNP levels and obesity was modified by sex. Specifically, NT-proBNP levels were lower with increasing waist circumference (Pinteraction < 0.001) as well as increasing BMI (Pinteraction = 0.002) and weight (Pinteraction = 0.040) among women compared with men.
Conclusions: Obesity-associated reduction in NT-proBNP has a strong sex-related component, and NT-proBNP levels decline more in obese females than in obese males. Age-associated increase in NT-proBNP is greater in males than in females. Sex and age should be considered while interpreting NT-proBNP in obese individuals.

P2160
Serum microRNA-126 and -223 as new generation biomarkers for cardiac sarcoidosis

W Wakaya Fujiwara[1]; Y Kato[1]; M Hayashi[1]; Y Sugishita[1]; S Okumura[1]; M Yoshinaga[1]; T Ishiguro[1]; R Yamada[1]; S Ueda[1]; M Harada[2]; H Haruse[2]; J Ishii[2]; Y Ozaki[2]; H Izawa[1]
[1]Fujita Health University, Banbuntane Hotokukai Hospital, Nagoya, Japan; *[2]Fujita Health University, Toyoake, Japan*

Background: Sarcoidosis is a multisystem inflammatory disorder of unknown etiology with a wide range of manifestations in a variety of organs. Although cardiac sarcoidosis is associated with poor prognosis, diagnosis of the disease is challenging and the sensitivity and specificity of diagnostic modalities are limited. This study was performed to evaluate the potential of Serum micro RNAs (miRNAs) as diagnostic biomarkers for cardiac sarcoidosis.
Methods and Results: We performed genome-wide expression profiling for 2565 miRNAs (Human-miRNA ver.21) using peripheral blood samples from 5 patients with cardiac sarcoidosis (61 ± 9 years) and 3 healthy controls (54 ± 7 years). From this screening study, we selected 12 miRNAs that were significantly related to cardiac sarcoidosis. Next, we performed real-time Polymerase chain reaction (PCR) on blood samples from 15 new patients with cardiac sarcoidosis and 4 healthy controls to quantify the expression of these 12 miRNAs. In the screening study, 12 miRNAs were differentially expressed (p < 0.01) in all 5 patients with cardiac sarcoidosis, showing greater fold-change values (< 4 or < 0.25) compared with the expression in the 3 healthy controls. Analysis of the real-time PCR for blood samples from the other 15 patients and 4 controls using Mann-Whitney U tests revealed that the expression



Figure

of miR-126 and miR-223 was significantly higher in the patients than in the healthy individuals.

Conclusions: The results demonstrated the potential of serum miR-126 and miR-223 as new-generation diagnostic biomarkers for cardiac sarcoidosis.

P2161

Analysis of NT-proBNP baseline levels in apollo as a predictor of survival in hereditary transthyretin-mediated (hATTR) amyloidosis

MS Slama[1]; S Solomon[2]; D Adams[3]; T Coelho[4]; T Damy[5]; G Merlini[6]; M Maurer[7]; AM Partisano[8]; J Chen[8]; V Karsten[8]; J Vest[8]; O Suhr[9]; A Kristen[10]
[1]Service de cardiologie - Hospital Antoine - Beclere , Clamart, France; *[2]Brigham and Women's Hospital, Boston, United States of America*; *[3]National Reference Center for FAP (NNERF)/ APHP/ INSERM U 1195/ CHU Bicêtre, Le Kremlin-Bicêtre, France*; *[4]Unidade Clinica de Paramiloidose, Centro Hospitalar De Porto, Porto, Portugal*; *[5]Universite Paris-Est Creteil Val De Marne , Paris, France*; *[6]IRCCS Policlinico San Matteo Hospital , Pavia, Italy*; *[7]HCM Center at New York-Presbyterian Hospital/Columbia University Medical Center, New York, United States of America*; *[8]Alnylam Pharmaceuticals , Cambridge, United States of America*; *[9]Umea University Hospital, Umea, Sweden*; *[10]Heidelberg Universtiy Hospital , Heidelberg, Germany*

Funding Acknowledgements: Alnylam Pharmaceuticals

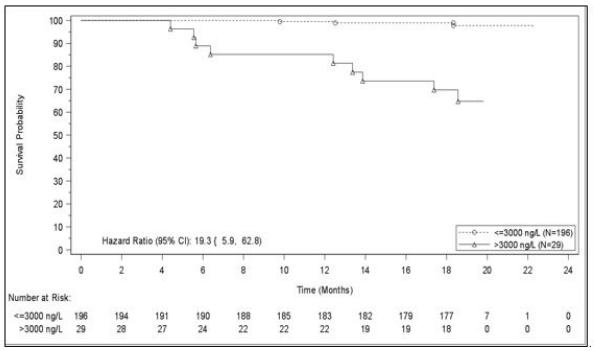
Background/Introduction: Hereditary transthretin-mediated (hATTR) amyloidosis is a multi-systemic, heterogeneous, fatal disease resulting in multi-organ TTR amyloid deposition. Clinical manifestations include sensorimotor and autonomic neuropathy, gastrointestinal symptoms, as well as cardiomyopathy, a major cause of death. N-terminal pro-brain natriuretic peptide (NT-proBNP), a cardiac biomarker, has shown prognostic value in cardiac diseases and has been clinically validated as a biomarker. Clinical studies in patients with light chain (AL) amyloidosis have shown NT-proBNP to be predictive of clinical outcome and survival in patients with cardiac involvement, thus suggesting its use as a surrogate endpoint for treatment efficacy. A recent analysis supports the proposition that NT-proBNP levels are also predictive for mortality for both hATTR and wild-type ATTR amyloidosis where survival in patients with serum NT-proBNP levels of >3000ng/L was associated with poorer survival compared to patients with NT-proBNP < 3000ng/L. Furthermore, a recent study in 27 hATTR amyloidosis patients demonstrated that NT-proBNP is a marker for cardiac involvement.

Purpose: To determine the predictive value of baseline NT-proBNP on survival in patients enrolled in the APOLLO study.

Methods: APOLLO was a Phase 3, randomized (2:1), double-blind study of patisiran 0.3mg/kg or placebo IV q3W in patients with hATTR amyloidosis patients with polyneuropathy (NCT01960348). The majority of patients likely had cardiac involvement on the basis of prespecified criteria: left ventricular (LV) wall thickness = 13mm and absence of aortic valve disease or hypertension. APOLLO enrolled 225 patients: mean age 61 years, 57% non-V30M mutation, NT-proBNP geometric mean 531 ng/L (range: 25, 16500). To assess the prognostic significance of baseline factors on survival, univariate and multivariate Cox regression analyses were conducted. NT-proBNP was evaluated as a continuous variable following logarithmic transformation as well as a binary variable using a cut off value of 3000 ng/mL.

Results: The median survival follow-up duration was 18.7 months. Of 13 deaths in total, 6 (8%) and 7 (5%) were observed in the placebo and patisiran arms, respectively. NT-proBNP was the key significant factor predictive of survival based on univariate and multivariate analyses. The risk of death increased with higher baseline NT-proBNP (hazard ratio = 2.9 [95% CI: 1.8, 4.8, p-value = 8.7x10-7] per unit increment in log(NT-proBNP). Patients with NT-proBNP > 3000 ng/L (n = 29) had a 19.3-fold [95% CI 5.9, 62.8, p-value = 8.7x10-7] increased risk for mortality compared with those below 3000 ng/L (n = 196) (Figure 1).

Figure 1: Survival by Baseline NT-proBNP Threshold (mITT)



Conclusion(s): Based on the data from the APOLLO study, baseline NT-proBNP serum levels in hATTR amyloidosis patients are predictive of survival. These data underscore the importance of diagnosing and potentially treating patients early in the course of the disease.

P2162

Albumin-to-globulin ratio as an independent predictor of mortality in chronic heart failure

J T Niedziela[1]; B Hudzik[2]; B Szygula-Jurkiewicz[1]; J Nowak[1]; L Polonski[1]; M Gasior[1]; P Rozentryt[3]
[1]Medical University of Silesia, SMDZ in Zabrze, 3rd Department of Cardiology, Silesian Centre for Heart Disease in Zabrze, Katowice, Poland; *[2]Medical University of Silesia, Department of Nutrition-related Disease Prevention, School of Public Health in Bytom, Katowice, Poland*; *[3]Medical University of Silesia, Department of Social Medicine and Prevention, School of Public Health in Bytom, Katowice, Poland*

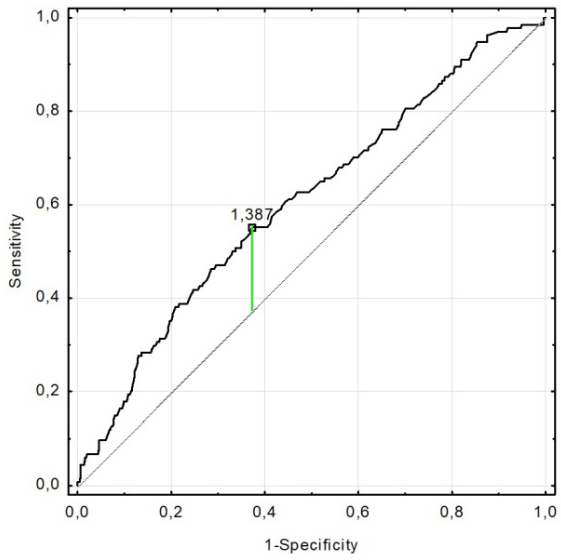
Background: Albumin-to-globulin ratio (AGR) is considered to be a marker of impaired prognosis. Low AGR is associated with poor prognosis in oncology patients and in general population. There are only sparse studies of AGR in cardiovascular diseases. AGR is related to worse survival after non-ST segment elevation myocardial infarction or stroke.

Purpose: We determined the predictive value of AGR in patients with heart failure with reduced ejection fraction (HFrEF) in one-year follow-up.

Methods: The study included 999 patients with HFrEF. Patients with infection, fever, trauma or urgent hospitalization in the last 3 months were excluded. Malnutrition or body wasting were also considered as exclusion criteria. AGR was calculated using formula AGR = Albumin/(Total serum protein-Albumin). Quartiles (Q) of AGR were defined as Q1 < 1.25, Q2 = 1.25 and < 1.48, Q3 = 1.48 and < 1. 75 and Q4 = 1.75. One-year mortality between AGR quartiles was compared using log-rank test. Multivariate survival analysis in Cox's regression model was applied with Q1 as a reference. Receiver operating characteristic (ROC) analysis was also performed.

Multivariate survival analysis

Parameter	HR	95% CI	p
Age [years] per 1 year increase	1.03	(1.01-1.05)	0.006
Serum sodium [mEq/L] per 1 mEq/L increase	0.95	(0.91-0.99)	0.02
NT-proBNP [pg/ml] per 1000 pg/ml increase	1.07	(1.03-1.12)	0.0008
peak VO2 [ml/kg/min] per 1 ml/kg/min increase	0.89	(0.85-0.93)	0.000001
LVEF [%] per 1% increase	0.95	(0.92-0.98)	0.001
AGR per 0.1 decrease	1.07	(1.01-1.13)	0.01



ROC analysis - AGR in 12-month mortality

Results: AGR found to be an independent risk factor for one-year mortality with 7% increase of risk of death for each 0.1 AGR decrease (Table). ROC analysis revealed moderate diagnostic value of AGR in predicting one-year mortality with cut-off < 1.38 and area under curve (AUC) 0.61 (0.58-0.64), p = 0.0001 (PPV 17.7, NPV 90.4) (Figure).
Conclusion: AGR had a moderate prognostic value and remained an independent predictor of one-year mortality in HFrEF patients.

P2163

Serum parathyroid hormone levels predict treatment failure in acute decompensated heart failure

H Altay[1]; F Ozkalayci[1]; S Pehlivanoglu[1]
[1]*Baskent University Istanbul Hospital , Cardiology, Istanbul, Turkey*

Background: Treatment failure is not uncommon in patients with acute decompansated heart failure (ADHF), due to very heterogenous patient population regarding cardiac pathology and existing comorbidities, and limited effective treatment modalities. Also predictors of treatment failure is not well defined in this patient population. Increased paratahyroid hormone (PTH) level is associated with advanced heart failure which forms most of difficult to treat ADHF patients.
Purpose: In this study we aimed to investigate the predictors of treatment failure and also investigate whether the assessment of serum PTH could enable us to identify patients likely to develop treatment failure during inhospital treatment of ADHF.
Method: Thirty three consecutive patients who were hospitalized with ADHF were enrolled as a part of prospective non-randomised study. Baseline patient demographic and clinical characteristics including serum levels of PTH and amino-terminal pro-B-type natriuretic peptide (NT-proBNP) were measured during 24 hours of admission. All patients were given standarised treatment including intraveneous continuous furasemide infusion, along with inotrope-inodilator and vasodilator drugs according to prespesified criteria regarding left ventricular (preserved vs low EF) and renal function (serum creatinine level), hemodynamic status (BP). "Treatment resistance" (TR) was defined according to clinical criteria; hemodynamic detoriation, or inadequate decongestion or diuresis at the end of 72 hours of treatment. Baseline characteristics were analysed in order to investigate the predictors of TR in this population.
Results: 10 out of 33 patients (30,3%) were found to have treatment resistance (TR+) and 23 (69,7%) had favorably responded to the treatment (TR -). Elevated mean levels of PTH were found in TR+ patients (129,9 ± 30 vs 88,9 ± 39 pg/ml; (p = 0,006). Patients who developed < 30% reduction in NT-proBNP were found to have higher PTH level compared to patients developed >30% reduction (127,52 ± 47,95 vs 88,40 ± 31,93 pg/ml, p = 0,028). In univariate analysis, blood urea nitrogen (BUN), creatinine (cr), presence of left bundle branch block (LBBB) on electrocardiogram and PTH were found to be predictors of TR+. In multivariate logistic regression analysis, PTH level (hazard ratio 1,045 , 95% confidence interval 1,009-1,084) p = 0.015) and LBBB (hazard ratio 12,410, 95% confidence interval 1,0-154,1, p = 0,045) were associated with presence of TR+. In receiver operator characteristics curve analysis, the optimal cut-off value of PTH to predict presence of TR+ was >119 pg/ml, with 80,0% sensitivity and 82,61% specificity.
Conclusion: An elevated admission PTH level, could identify patients hospitalized with ADHF likely to experience to have "treatment resistance". Thereby early implementation of alternative pharmacologic or non-pharmacologic decongestive therapies can be considered in these patients.

P2164

Prognostic role of cardiac troponin in acute heart failure

JP Jose Pedro Sousa[1]; M Madeira[1]; L Reis[1]; C Negrier[1]; L Goncalves[1]
[1]*Centro Hospitalar e Universitário de Coimbra - Hospital Geral, Cardiology, Coimbra, Portugal*

Introduction: Troponins I and T (cTnI e cTnT) are well-established biomarkers of cardiac injury. Testing for either of the two has long been a core component of both diagnosis and prognosis of acute myocardial infarction. However, their value in heart failure (HF) is not without controversy, particularly when not measured using the new high sensitivity assays.
Purpose: To determine the short term prognostic significance of non-high sensitivity cTnI at hospital admission in the setting of acute HF.
Methods: Retrospective single-center study comprising patients consecutively admitted into a cardiac intensive care unit, during six years, presenting with de novo or decompensated acute HF. Demographic, clinical, laboratory, echocardiographic and prognostic data were evaluated. Follow-up (FU) was performed targeting hospital readmission for acute HF and all-cause mortality. All statistical analysis was performed using SPSS version 23 (IBM Corp., Armonk, NY, USA).
Results: 264 patients were included. Mean age was 70 ± 14 years and 22% were female. Median FU was 10 months. In-hospital mortality was 15%, while readmission for HF and death in FU occurred in 46.7% and 42% of patients, respectively. Median troponin was 0.07ng/mL. No difference was found between cTnI levels in males and females and there was no significant correlation between cTnI and age. Ischemic etiology was not found to influence cTnI, whereas acute cardiogenic pulmonary edema (p < 0.001) and cardiogenic shock (p 0.027) were associated with higher troponin levels. Correlation between cTnI and both serum creatinine and NT-proBNP, at admission and discharge, was statistically significant but negligible (p < 0.003 / rho 0.13-0.16 for creatinine and p < 0.001 / rho 0.208-0.209 for NT-proBNP). Furthermore, left ventricular ejection fraction, measured using echocardiography, at admission, was not associated with cTnI. Higher serum troponin levels were found in those who died during hospitalization (p 0.024), but not in patients who were readmitted for HF or died during FU.
Conclusions: Non-high sensitivity cTnI at admission is a biomarker of severity in acute HF, with higher levels predicting acute cardiogenic pulmonary edema, cardiogenic shock and mortality during hospitalization. However, it seems to be of no value for FU.

P2165

Exploring the role of lung ultrasound in the diagnostic process of heart failure in primary care

L Conangla[1]; M Domingo[1]; J Lupon[2]; A Wilke[1]; G Junca[3]; G Volpicelli[4]; X Tejedor[5]; A Mas[1]; P Toran[1]; G Pera[1]; JM Verdu[1]; L Evangelista[1]; P Moliner[3]; M De Antonio[3]; A Bayes-Genis[2]
[1]*Primary Care Research Institute (IDIAP), Barcelona, Spain*; [2]*Germans Trias i Pujol University Hospital, Heart Failure Clinic, Badalona, Spain*; [3]*Germans Trias i Pujol University Hospital, Cardiology Service, Badalona, Spain*; [4]*San Luigi Gonzaga Hospital, Emergency Department, Turin, Italy*; [5]*Germans Trias i Pujol University Hospital, Biochemistry and Hematology Service, Badalona, Spain*

Funding Acknowledgements: La Marató de TV3 (PI201510.10), Primary Healthcare University Research Institute IDIAP-Jordi Gol, Catalan Society of Family and Community Medicine

Background: Detection of B-lines at lung ultrasound (LUS) is emerging in recent years as a new complementary tool in the diagnostic process for heart failure (HF). However, there are no data on the application of LUS in the first diagnosis of HF in primary care (PC).
Purpose: To explore if detection of pulmonary congestion by LUS may improve the efficiency of the diagnostic process in outpatients with first suspicion of HF.
Methods: Consecutive patients referred by their PC physician to NTproBNP test for suspected HF were included. We performed all the standard tests, including LUS with a pocket device, and echocardiography. LUS was applied by examining 6 chest areas per side, including 2 anterior (A), 2 lateral (L) and 2 posterior (P). Each area was considered positive when = 30% of the corresponding scan showed B-lines. We applied 4 different criteria of positivity for pulmonary congestion (on both sides): C1= 2 positive out of 4 AL areas (as recommended by the International Consensus in acute dyspnoea); C2 = 2 positive out of 6 ALP; C3 = 3 positive out of 12 ALP (involving both hemithorax); C4 = sum of B-lines' percentage of 12 ALP (= 30% affectation in each hemithorax). We measured the accuracy of these criteria

in predicting the final diagnosis of HF adjudicated by a cardiologist blinded to LUS results who had access to echocardiography and NTproBNP data.
Results: 211 patients were studied (66.8% women; median 75.8 years [IQR 69-83]), 55.6% already under diuretic treatment. LUS was positive in 7 (C1), 19 (C2), 37 (C3) and 45 (C4) patients. HF diagnosis was confirmed in 52 patients (24.6%), mean LVEF 59.3%.
Conclusions: In our PC setting, LUS showed low sensitivity for HF but excellent specificity, depending on the used criteria. Our patients are mainly scarcely symptomatic and already treated at home. For these reasons, a possible role of LUS may be to confirm the disease, while it is insufficient to rule-out it. Integration with clinical evaluation and other tests may be a promising strategy, as well as defining criteria for patients in the community.

Pulmonary congestion criteria by LUS

	Sensitivity	Specificity	PPV	NPV	Accuracy	AUC
C1 = 8 areas (2 per hemithorax)	0.12	0.99	0.86	0.77	0.78	0.55 (0.46-0.65)
C2 = 12 areas (2 per hemithorax)	0.29	0.97	0.79	0.80	0.80	0.63 (0.54-0.72)
C3 = 12 areas (3 involving both hemithorax)	0.44	0.91	0.62	0.83	0.80	0.68 (0.59-0.78)
C4 = 12 areas (≥ 30% per hemithorax)	0.54	0.88	0.62	0.86	0.81	0.72 (0.62-0.80)

P2166

Right atrial mechanics in chronic thromboembolic pulmonary hypertension: the right measure?

P Patricia Alves[1]; AV Marinho[1]; C Domingues[1]; J Milner[1]; JA Ferreira[1]; R Baptista[1]; G Castro[1]
[1]*University Hospitals of Coimbra, Cardiology, Coimbra, Portugal*

Background: Regardless of etiology, right ventricular (RV) dysfunction is considered the major determinant of morbidity and mortality in pulmonary hypertension (PH).
Purpose: To assess RV function and right atrium (RA) mechanics through 2-dimensional speckle-tracking echocardiography (2D-STE) in different groups of PH.
Methods: We included all 91 PH incident cases followed in our center in the previous 5 years, group 1 (pulmonary arterial hypertension - PAH) (n = 63) and group 4 (chronic thromboembolic PH - CTEPH) (n = 28). RV global longitudinal strain (RVLS) and RA mechanics were assessed through 2D-STE. Global atrial strain and atrial strain rate during systole (RA ?sys and SRs), early diastole (RA?e, SRe), and late diastole (RA?a, SRa) were measured, corresponding to RA reservoir, conduit and contractile functions, respectively. These parameters were correlated to clinical, analytical and right heart catheterization (RHC) data.
Results: Mean age was 48 ± 19 years for PAH and 59.7 ± 16 years for CTEPH; 62% were women. Mean tricuspid annular plan systolic excursion (TAPSE) and tricuspid regurgitation velocity (TRV) did not vary between groups. RVLS values were numerically better in CTEPH (-13 ± 4% vs -10 ± 9%, p = 0.170). RA mechanics was globally and statistically superior in CTEPH patients (table 1). In the global cohort, BNP values (r2 = 0.53, p = 0.003) and RHC-derived cardiac index (CI) (r2 = 0.51, p = 0.039) at admission were correlated to RA ?sys, but not to RVLS. In CTEPH patients, BNP values were only moderately correlated with RV diameter (r2 = 0.33, p = 0.005), TAPSE (r2 = 0.42, p = 0.003) and RA volume (r2 = 0.50, p <0.001), but were strongly correlated with RVLS (r2 = 0.57, p= 0.018), RA ?sys (r2 = 0.67, p = 0.027) and RA?a (r2 = 0.59, p = 0.004). A similar pattern of correlation was seen for CI [TAPSE (r2= 0.3, p = 0.02), RVLS (r2 = 0.56, p = 0.041), RA ?sys (r2 = 0.64, p = 0.036) and RA?a (r2 = 0.58, p = 0.004)]. Pulmonary vascular resistance (PVR) was only associated to RA?a (r2 = 0.56, p = 0.007) and mean pulmonary artery pressure (mPAP) to RA?e (r2 = 0.72, p = 0.012).
Conclusions: : 2D-STE derived RVLS and RA mechanics demonstrated stronger correlations with established prognostic factors in CTEPH, as BNP or RHC-derived indexes, than currently used morphological parameters, as TAPSE or cavity dimensions.

	CTEPH	PAH	P value
RA ?sys (reservoir)	15.0±4.2	12.4±4.1	0.011
RA ?e (conduit)	7.5±3.8	5.2±3.6	0.009
SRs	0.8±0.4	0.6±0.3	0.04
SRa	-1.3±0.6	-0.8±0.4	<0.001

P2167

The role of cardiac index assessed by echocardiography in the predicion of mortality and morbidity in heart failure

B Szabo[1]; E Marosi[1]; K Vargova[1]; N Nyolczas[2]
[1]*University Hospital Örebro, Heart-Lung Clinic, Örebro, Sweden*; [2]*State Health Centre, Budapest, Hungary*

Background: Echocardiography is a basic diagnostic method and provides important data in the diagnosis of heart failure (HF). Left ventricular ejection fraction (LVEF) is the most frequently used parameter despite high intra- and interobserver variability. Cardiac index (CI) is referred in the literature as a potential alternative for LVEF despite limited evidence, mainly extrapolated from trials with invasive CI-measurement. Thus, further research is needed to define its role in clinical practice.
Purpose: To assess and compare the predictive accuracy of LVEF and echocardiographically assessed CI in HF patients.
Methods: A retrospective cohort study was performed in patients hospitalized for acute HF between 2010-2016 at the Heart-Lung Clinic of University Hospital Örebro. Patients were eligible regardless of LVEF if they had an echocardiography after the first HF-admission in the study period, if stored images were available for the assessment of CI, and if they had no significant aortic valve disease or hypertrophic obstructive cardiomyopathy. LVEF was collected from initial echocardiography reports and CI measured retrospectively according to current echocardiographic recommendations. Cox proportional hazards models were created to predict cardiovascular (CV) death or first HF-readmission using LVEF or CI and adjusted for traditional risk factors, identifying independent risk factors and providing associated relative risks (RR). Prognostic accuracy was assessed by c-index and compared by unpaired t-test.
Results: 334 patients were included in the study (age: 75.8 ± 10.0 years, male: 65.3%, ischemic etiology: 49.4%, diabetes: 31.7%, atrial fibrillation: 42.8%, GFR: 55.8 ± 25.2ml/min/1.73m^2, COPD: 14.1%, heart rate: 78.0 ± 17.8/min, LVEF: 35.7 ± 14.7%, CI: 2.17 ± 0.73l/min/m^2). 58.7% had HF with reduced LVEF (HFrEF). Patients were on ACE-inhibitor/ARB in 86.5%, betablocker in 86.8%, mineralocorticoid antagonist in 45.8%, diuretics in 84.7%. 10.2% had cardiac resynchronization therapy and 9.9% had an implantable defibrillator). Neither LVEF nor CI had any association with CV death, neither in the overall cohort, nor in HFrEF or non-HFrEF patients. CI was an independent predictor of HF-readmission in HFrEF patients (RR: 0.653 /0.428-0.998/, p = 0.049) as well as in the non-HFrEF group (RR: 0.634 /0.416-0.967/, p = 0.034) while LVEF was not predictive for HF-readmission. Both LVEF and CI-based Cox-models had moderate prognostic accuracy for HF-readmission in the overall cohort, with a slight but statistically significant benefit for CI (c-index: 0.675 vs 0.690, p <0.001).
Conclusion: Neither LVEF nor CI proved to be predictive of CV death in this real-life elderly cohort of HF patients. CI provides a slight improvement of the prediction of HF-readmission compared to LVEF. Our results suggest that CI provides additional information on disease severity and may be an important new tool in the assessment of HF patients regardless of LVEF.

P2168

Evaluation of right ventricular function in advanced heart failure: gated blood-pool SPECT ventriculography

T Tereza Havlenova[1]; M Tupy[1]; L Mlateckova[1]; M Buncova[1]; J Ters[1]; J Kidery[1]; I Netuka[1]; J Kautzner[1]; V Melenovsky[1]
[1]*Institute for Clinical and Experimental Medicine (IKEM), Prague, Czech Republic*

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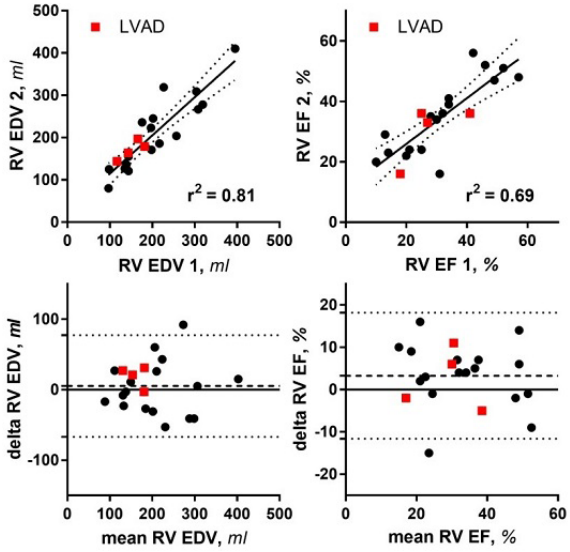
Background: Accurate estimation of right ventricular (RV) function and volumes plays a critical role in management of advanced heart failure (HF) patients. However, it's often challenging, especially in subjects with left ventricular assist device (LVAD).
Purpose: In present study, we aimed to assess the performance of quantitative 3-dimensional gated blood-pool single photon emission computed tomography (SPECT) imaging of the RV employing a novel high-resolution SPECT camera (D-SPECT).
Methods: A total of 21 advanced HF patients were enrolled (age 61 ± 11 years, 76% males, body mass index 28 ± 4 kg/m2, LV EF 28 ± 16%, 4 patients after LVAD

HeartMate III implantation). All subjects received intravenous injection of stannous pyrophosphate (Technescan PYP) followed after 30 minutes by intravenous administration of 740 MBq 99mTc isotope to in-vivo label the erythrocytes (radiation dose was 5-6 mSv). After that, the hearts were imaged by D-SPECT camera (Spectrum Dynamics, Israel) with Cadmium-Zinc-Telluride detector. Volume analyses of 3D reconstructed ventricles were conducted using semiautomatic plug-in software (QBS Cedars-Sinai, USA). To measure reproducibility, both data acquisition and analysis were performed twice in all study subjects.



Results: The ventricles were successfully imaged even in subjects after LVAD implantation; however, in 2 LVAD patients the device caused intermittent interference with surface ECG gating, requiring manual ECG cable repositioning. The acquisition time was uniformly set for 8 minutes. In data processing, no (in 2/3 of patients) or minimal manual intervention was necessary. The figure below shows that the RV end-diastolic volume (EDV) and ejection fraction (EF) correlated well between the 2 consecutive measurements (R2: 0.69-0.81). In Bland-Altman plots, both measures displayed only minimal bias and acceptable confidence limits. Reproducibility was comparable in both LVAD and non-LVAD groups.
Conclusion: This study provides evidence that the gated blood-pool SPECT ventriculography is fast and reproducible tool in evaluation of RV function even in advanced HF patients with serious RV remodelling or after LVAD surgery.

P2169

Role of stress test echocardiography in the evaluation of myocardial function in hypertensive patients.

F A Federico Angelo Immordino[1]; S Tumminello[1]; G Evola[1]; S Novo[1]
[1]*University Hospital Paolo Giaccone, Department of emergency, Division of Cardiology, Palermo, Italy*

Introduction: There are few data assessing the role of stress echocardiography (echo) in the evaluation of myocardial function in hypertension. Therefore, it should be useful to study if mild dyspnoea or fatigue during exercise may be a prelude of diastolic dysfunction in hypertensive patients without signs or with subclinical cardiac dysfunction at rest.
Purpose: To evaluate the role of stress echo to identify early changes in cardiac function, PAPs, filling and systemic pressure as a possible cause of exercise dyspnoea and as marker of incoming diastolic dysfunction.
Methods: We enrolled 70 hypertensive patients (BP > 140/90 mmHg or under antihypertensive treatment) without history of major cardiovascular events and with EF > 55%. Patients reported to be symptomatic for mild dyspnoea during moderate physical activity. Sixty-eight patients have already been under pharmacological treatment. Each patient performed a supine bike stress echo following the standard protocol (increase of 25 Watt each 2 minutes). All the tests were performed until maximal heart rate or symptoms. We acquired data at baseline and at peak of exercise. Patients were finally divided in 2 groups according to E/e' ratio at peak (G1 E/e' ratio >14; G2 E/e' ratio < 14).
Results: No significant differences were shown between the groups concerning age, gender, blood pressure (BP), history of smoking, diabetes or hyperlipidaemia nor in the classes of drugs used (P > 0,05). At baseline were shown difference in DBP (G1 = 80,8 mmHg ± 7,4; G2 = 70,5 mmHg ± 11; P < 0,04); PAPs (G1 = 29,5 mmHg [23,5-33]; G2 = 24 mmHg [20-29]; P < 0,01); e' (G1 = 0.06 [0,04-0,07]; G2 = 0,08 [0,07-0,1]; P < 0,001); E/e'(G1 = 11,86 [11,18-13,99]; G2 = 7,33 [5,8-8,9]; P < 0,001). At exercise peak G1 patients have higher SBP (204,3 mmHg ± 17,3; P < 0,0001), DBP (90,2 mmHg ± 9,8; P = 0,01), PAPs (46,12 mmHg ± 8,84; P = 0,0001), TR velocity (3,24 m/s ± 0,38; P < 0,0001) and e' (0,07 [0,05-0,08]; P < 0,0001) showing several differences compared to patients still in range during the test, potential risk of evolution to the hypertensive cardiomyopathy and diastolic dysfunction. Moreover G1 patients have higher increases in ?PAPs (P = 0,002), ?TR velocity (P = 0,03), and ?SBP (P < 0,001). In multiple regression analysis the increase in PAPs seems to be dependent from ?E/e' ratio (P = 0,007) and heart rate (?HR) (P = 0, 04).
Conclusions: The stress echo seems to be a valid test to detect patients with subclinical signs of hypertensive cardiomyopathy and/or diastolic dysfunction, enabling an early diagnose and, in the end, a better management. The increase in filling pressure due to the cardiac dysfunction during exercise may explain the symptoms of these patients.

P2170

Features of myocardial dissynchrony in patients with chronic heart failure and atrial fibrillation

T Tatyana Troyanova-Shchutskaia[1]; A Kurlianskaya[1]; T Asmalouskaya[1]; T Denisevich[1]; O Shatova[1]
[1]*Republican Scientific and Practical Centre of Cardiology, Minsk, Belarus*

Background: Myocardial dissynchrony (MD) is one of the important causes of chronic heart failure (CHF) contributing to the progression of the disease.
Purpose: to explore MD in patients with CHF NYHA III, permanent atrial fibrillation (AF) vs. sinus rhythm (SR).
Methods: The study included 29 patients with SR and 50 patients with AF. Initially the groups did not differ in sex, age, and parameters of echocardiography. Determination of myocardial dissynchrony was performed in all cases.
Results: Presystolic aortic delay in group with QRS 130-149ms was 161 (140; 168)ms in patients with AF and 118 (90; 155)ms with SR (p = 0,021). In group with QRS = 150 ms and AF it was 211 (183; 223)ms and in patients with SR - 119 (104; 154)ms (p <0,001). Presystolic delay on pulmonary artery valve was higher in patients with SR. Interventricular delay (IVD) was higher in patients with SR and QRS 130-149 ms - 65 (55; 78)ms vs. 56 (33; 58)ms (p = 0,063). In group with QRS = 150 ms IVD was higher in patients with AF (86 (69; 95)ms vs. 63 (45; 74)ms, p = 0,002). Table demonstrates parameters of intraventricular dissynchrony.

P2169 Intraventricular myocardial dissynchrony

Delay, ms	QRS 130-149 ms	P	QRS≥150 ms	P		
Atrial fibrillation	Sinus rhythm	Atrial fibrillation	Sinus rhythm			
Septal lateral	72 (41; 85)	72 (43; 121)	0.629	92 (51; 143)	87 (44; 115)	0.344
Septal posterior	63 (46; 84)	79 (57; 116)	0.081	36 (15; 78)	70 (20; 140)	0.164
Maximal basal	107 (87; 151)	125 (115; 145)	0.244	109 (64; 154)	140 (124; 162)	0.148
Basal dely index	49 (40; 77)	63 (52; 73)	0.120	77 (52; 87)	67 (50; 74)	0.273
All segments standart deviation	146 (117; 198)	174 (149; 209)	0.292	212 (195; 222)	178 (160; 222)	0.093
All segments standart deviation	64 (47; 76)	71 (58; 78)	0.211	80 (74; 87)	63 (53; 82)	0.146
Basal septal lateral	100 (60; 160)	85 (40; 100)	0.607	90 (65; 165)	80 (60; 120)	0.169
Basal antero-inferior	110 (60; 160)	100 (80; 200)	0.532	106 (85; 140)	100 (80; 150)	0.796
Medium septal lateral	100 (80; 180)	98 (80; 120)	0.912	145 (120; 185)	100 (50; 140)	0.016
Medium antero-inferior	110 (50; 160)	125 (80; 160)	0.573	140 (95; 210)	130 (90; 140)	0.366
basal antero-septal infero-lateral	90 (40; 160)	100 (40; 140)	0.607	85 (35; 135)	90 (70; 140)	0.772
Medium antero-septal infero-lateral	110 (60; 160)	115 (70; 180)	0.769	100 (70; 175)	120 (90; 200)	0.518

Conclusions: The features of mechanical myocardial dissynchrony were revealed in patients with AF versus SR. In patients with AF the severity of mechanical dissynchrony depends on the width of the QRS complex: presystolic aortic delay, IVD and all segments maximum delay were higher in patients with wide QRS. The frequency and duration of presystolic aortic delay in patients with AF was significantly greater than in persons with sinus rhythm.

P2171

Thoracic Bioreactance in clinical practice - Test-retest reliability in patients with hypertension, heart failure with preserved ejection fraction and healthy controls

H-D Duengen[1]; MT Coll Barroso[2]; MT Hoppe[2]; T Krahn[3]; F Kramer[4]; E Tahirovic[1]; A Busjahn[5]; S Beckmann[1]; C Kiefer[6]; T Mondritzki[3]; M Karoff[2]; P Boehme[4]; W Dinh[4]
[1]Charité University Hospital, Department of Cardiology, DZHK Partner Site Berlin, Berlin, Germany; *[2]Klinik Königsfeld der LVA-Westfalen Ennepetal, University of Witten/Herdecke, Department of Rehabilitation Sciences, Witten, Germany*; *[3]Bayer AG, Drug Discovery, Pharmaceuticals, Therapeutic Research Groups, Wuppertal, Germany*; *[4]Bayer Pharma, Drug Discovery, Pharmaceuticals, Clinical Sciences, Experimental Medicine, Wuppertal, Germany*; *[5]Health Twist, Berlin, Germany*; *[6]Helios Clinic Wuppertal, Department of Cardiology, Wuppertal, Germany*

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Purpose: Thoracic bioreactance (TB), a noninvasive method for hemodynamic measurement, shows good test-retest reliability in healthy adults under research conditions. Here we evaluate the test-retest reliability of TB in healthy adults, subjects with hypertension (HT) and heart failure with preserved ejection fraction (HFpEF) under routine conditions.
Methods: 75 sublects (25 healthy, 26 HFpEF, 24 HT) performed a symptom-limited graded cycling test on two different days separated by one week. Cardiorespiratory (power output, VO2peak) and hemodynamic parameters (heart rate, stroke volume, cardiac output, mean arterial pressure, cardiac power output) were measured at rest and continuously up to maximum exercise using a breath-by-breath gas-analyzer and bioreactance cardiograph.
Results: There was no systematic bias in all parameters under all conditions (effect size: 0.03-0.6). We found that all noninvasively measured hemodynamic parameters showed acceptable test-retest-reliability (intraclass correlation coefficient: 0.53-0.98; typical error: 0.3-1.8). The key value derived from TB, cardiac output (CO) showed a satisfying reliability in all groups at rest and during maximum exercise (healthy: intraclass correlation coefficient: 0.80-0.85; effect size: 0.9-1.1, HT: 0.66-0.91, effect size: .14, typical error: 1.37, HFpEF: 0.19-0.76, effect size: 0,14, typical error: 1,79). Moreover, peak cardiac power output showed a superior reliability (intraclass correlation coefficient: 0.80-0.85; effect size: 0.9-1.1) then the underlying physiological single parameters (intraclass correlation coefficient: 0.59-0.98; effect size: 0.3-1.8) and was found to be independent to traditional cardiopulmonary exercise parameters.
Conclusion: Our findings suggest that TB might be suitable method to noninvasively monitoring hemodynamic status in clinical practice in heart failure patients.

P2172

Novel method with a microwave radar for a non-contact monitoring of jugular venous pulse: clinical implication for heart failure practice

M Masaaki Hoshiga[1]; K Sakane[1]; N Ishizaka[1]; S Suzuki[2]
[1]Osaka Medical College, Cardiology, Osaka, Japan; *[2]Kansai University, Department of Mechanical Engineering, Osaka, Japan*

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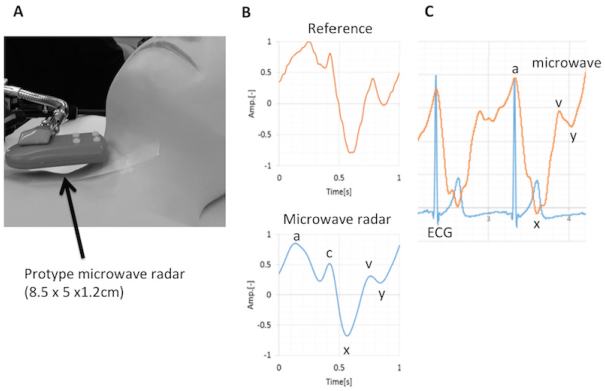
Background: The jugular venous pulse (JVP) provides a window of the right heart and its assessment is important in patients with heart failure. Very recently, impact of right ventricular distensibility, detected as the prominent 'Y' decent of JVP, has been suggested on HFpEF (Harada et al. Heart and Vessels, 2017). However, the conventional method to monitor JVP waveform such as pulse transducer requires skill and is not frequently used.
Purpose: We herein propose a novel method using a microwave radar, which has been recently applied to a non-contact vital sign monitoring, for JVP assessment. The aim of this study is to evaluate this new method for a non-contact monitoring of JVP in cardiology patient simulator and healthy volunteer.
Methods: A microwave radar system consists of three of an antenna (Figure A), A/D converter, and PC. We recorded JVP waveform in Cardiology Patient Stimulator "K" known as "Ichiro" (Kyoto KAGAKU Co. Ltd) and 10 healthy subjects (20-24 y.o. male) using a pulse transducer (TY-501, FUKUDA DENSHI) as a reference and a microwave radar.
Results: JVP waveform determined by a microwave radar showed normal wave patterns with 3 waves (a,c,v) and 2 descents (x, y), identical with reference (Figure B). Simultaneous recording of ECG and JVP waveform by a microwave revealed that "x" is deeper than "y" in all the 10 healthy subjects (Figure C). The amplitude of each waveform measured by microwave radar correlated significantly with that measured by pulse transducer (r = 0.65). Conclusion: The proposed method seems to be promising for a non-contact JVP monitoring and useful in the clinical setting, especially heart failure practice.



Microwave Radar for JVP Monitoring

Chronic Heart Failure - Treatment

P2173

Comparison of therapeutic effects between urapidil and nitroglycerin for treatment of acute heart failure with hypertension and atrial fibrillation in elderly patients

Q Qi Hua[1]; ZICHEN Wang[1]
[1]Xuan Wu Hospital, Capital Medical University, cardiology, Beijing, China People's Republic of

Background and objective: Acute heart failure (AHF) is a complex clinical syndrome and frequently complicated by hypertension and atrial fibrillation (AF). The aim of this study was to evaluate whether urapidil provides additional therapeutic benefits compared to nitroglycerin (NG) in the treatment of AHF with hypertension and AF in elderly patients.
Methods: 58 elderly patients from 10 hospitals were randomized into 2 groups. Control group (n = 30) were treated with NG, while other group (n = 28) were treated with urapidil. We monitored systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels and carry out echocardiogram before and 24 h, 48 h, 72 h and 7 d after treatment with either NG or urapidil. Lipid profile, liver and kidney function, blood glucose levels in nitroglycerin and urapidil groups were examined before and 24 h, 48 h, and 7 d after treatment.
Results: Patients receiving urapidil had lower SBP than that in NG group ($P < 0.05$). Compared with NG group, patients in urapidil group showed increased LVEF ($P < 0.05$), CO, SV and CI ($P < 0.05$), but no significant differences in LVEDD and EDV. NT-proBNP was decreased following the treatment of urapidil or nitroglycerin, and the difference of NT-proBNP level was significant between the two groups ($P < 0.01$) at 7 d. Urapidil had trend to decrease blood glucose after 7 d.
Conclusions: Urapidil demonstrated better efficacy and fewer side effects than nitroglycerin on lowering and stabilizing systolic BP, attenuating cardiac afterload and improving cardiac function.

P2174

Obstacles to mineralocorticoid receptor antagonists in a community based heart failure population

H Norberg[1]; A Anna Jonsson[2]; E Berghdal[2]; K Lindmark[2]
[1]Umea University, Department of Pharmacology and Clinical Neuroscience, Umea, Sweden; *[2]Umea University, Department of Public Health and Clinical medicine, Umea, Sweden*

Funding Acknowledgements: This work was supported by the Heart Foundation of Northern Sweden.

Background: The cornerstones of heart failure (HF) treatment consist of angiotensin converting- enzyme inhibitors (ACE-I) or Angiotensin-receptor blockers (ARB), beta blockers and MRA. Previous studies and national assessments indicate an under-treatment of MRA in heart failure with reduced ejection fraction (HFrEF).

Purpose: In order to offer our patients the best available HF treatment and to reduce morbidity, mortality, health care costs and patient suffering, we want to investigate the reasons why MRA is not used to full extent.
Methods: A community based heart failure population in Sweden was studied. Approximately 90 variables were collected and medical records were scrutinized to identify reasons for not prescribing MRA.

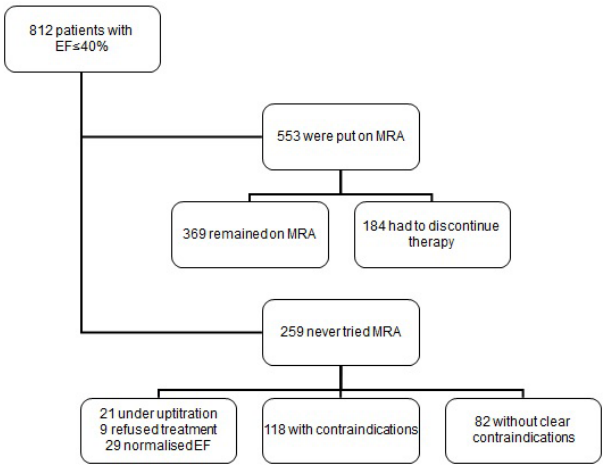


Figure 1

Results: Of 2029 patients, 812 had EF = 40 %. 553 patients (68%) tried MRA at some point but 184 (33%) of these discontinued therapy. There were 259 patients that never tried MRA, of which 177 had a listed explanation or contraindication. 82 patients, 10% of the total HFrEF population, had no clear contraindications. They were older, had less HF hospitalizations and less treatment with ACE-I/ARB and beta blockers and fewer patients reached standard therapy target doses compared to patients on MRA ($p < 0,05$). 26 of the 82 patients (32%) did not have any follow up at the cardiology clinic. Contraindications to MRA were renal dysfunction (93 patients), hypotension (28 patients) and hyperkalemia (25 patients). Only six patients had hyperkalemia without renal dysfunction. Of the patients with renal dysfunction, 66 (72%) had an estimated glomerular filtration rate (eGFR) > 30 ml/min.
Conclusions: The reasons why MRA are underutilized were mainly because of contraindications. However, the data indicate that the physicians are overly cautious about adverse effects with MRA in patients with moderately reduced kidney function. We propose education on the risk-benefit ratio of moderate renal dysfunction and minor hyperkalemia vs the risks of not receiving complete heart failure treatment. We believe that we could reach a higher degree of MRA usage with better and regular monitoring of these patients. There seems to be a 10% avoidable undertreatment with MRA, especially for elderly patients that are admitted to hospital for other reasons than HF. The fact that these patients had lower doses of basic heart failure therapy could be a partial explanation to why these patients did not receive treatment with MRA, but in previous MRA studies not all patients received maximum doses of ACE inhibitor/ARB but there was still a survival benefit in the MRA-arm. Furthermore, the data suggests that patients with heart failure would benefit from routine follow up at a cardiology clinic.

P2175

Prognostic value of diuretic dose in stable chronic heart failure

L Lupi[1]; E Rocco[1]; I Papa[1]; R D'ortona[1]; G Arabia[1]; M Piazzani[1]; L Branca[1]; M Metra[1]; S Nodari[1]
[1]*University of Brescia, Department of Clinical and Surgical Specialities, Cardiology section , Brescia, Italy*

Background: High daily diuretic dose (DDD) in chronic heart failure (HF) patients is related to cardiac and renal dysfunction but its relationship with outcomes in this population is still not completely understood
Purpose: To evaluate the prognostic implications of DDD in patients with chronic HF
Methods: We conducted a retrospective analysis of patients (pts) with HF and reduced Left Ventricular Ejection Fraction (LVEF < 45%) followed at our outpatient HF Clinic. Inclusion criteria were optimized therapy and clinical stability (neither events nor therapeutic changes) in the previous three months. We evaluated clinical, laboratory, echocardiographic and therapeutic parameters. Hypervolemic or euvolemic status was defined according to the Framingham Score, calculated by assigning a score of 0,5 or 1 for each of the following signs or symptoms: orthopnea, paroxysmal nocturnal dyspnea, reduction in exercise tolerance, resting sinus tachycardia, increased jugular venous pressure, hepatojugular reflex positive, third heart sound, basal crackles, hepatomegaly, peripheral oedema; a score = 2 indicates a state of hypervolemia. DDD was considered as continuous and categorical variable (ROC analysis was perfomed to identify optimal cut off of DDD for prognosis). The composite endpoint considered was all cause death (ACD) and hospitalization for Heart Failure (HHF) or cardiovascular causes (HCV).
Results: A total of 570 pts (mean age 67 ± 12 years, 84% male) were included. Almost all of the pts received guideline-recommended therapy for HF. After a mean follow-up of 43 ± 14 months, the composite endpoint occurred in 255 pts (54%). At Univariate analysis advanced age, dyspnea at rest or for minumum effort, atrial fibrillation, higer heart rate, a state of congestion evidenced by echocardiography or by a Framingham Score = 2, furosemide DDD, lower level of haemoglobin, glomerular filtration rate and serum sodium, lower LVEF and higher degree of mitral regurgitation were significantly corralated with the occurrence of the composite endpoint ACD + HHF + HCV. In the multivariate model only LVEF (HR 0.97; CI 0.94-0.99; p = 0.029), DDD (HR 1.002; CI 1.005-1.004; p = 0.011) and Framingham Score (HR 2.58; CI 1.52-4.39; p < 0.001) were independently associated with adverse events. The ROC analysis identified a furosemide DDD of 87 mg as optimal cut-off to predict the development of events (AUC 0.65, sensitivity 47%, specificity 78%). A DDD > 87 mg was associated with adverse prognosis only in the subgroup of euvolemic patients (Framingham Score < 2) (HR 1.49; CI 1.08-2.07)
Conclusions: In pts with chronic stable HF, DDD is associated with adverse outcome, expecially in euvolemic pts. In hypervolemic pts high DDD are likely to be indirect marker of the severity of the disease. The goal of diuretic therapy is to ensure the persistence of hemodynamic stability and DDD should be adjusted periodically in oder to avoid decompesated HF but also excessive diuretic dosage.

P2176

Two-years outcome of patients with heart failure and severe left ventricular dysfunction treated with ivabradine and low doses of beta-blocker

FM Melillo[1]; C Godino[1]; A Sisinni[2]; A Salerno[1]; A Cappelletti[1]; G Fragasso[1]; A Margonato[1]
[1]*San Raffaele Hospital of Milan (IRCCS), Milan, Italy*; [2]*University Vita-Salute San Raffaele, Milan, Italy*

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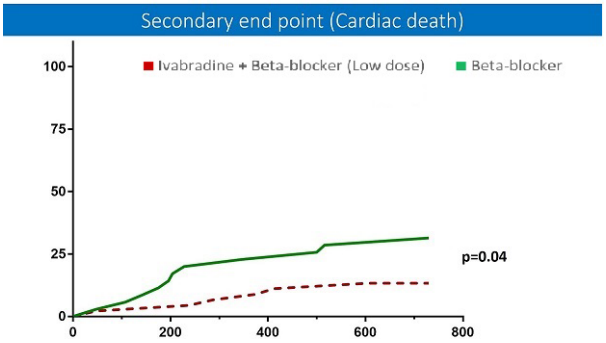
Background: Uptitrating beta-blockers (BB) to target dose is threatening in patients with heart failure (HF) and markedly depressed left ventricular function. No data are available in patients with intolerance or poor BB tolerability in whom ivabradine is used to achieve heart rate reduction alone or in addition with low BB doses.
Methods: In this single-centre observational study we included patients with chronic HF (stable from = 2 months) and markedly depressed EF (= 30%) referred to our Heart Failure Unit from August 2010 to December 2015. Patients with acute HF and transient causes of EF depression were excluded. BB used were bisoprolol, nebivolol and carvedilol. Low BB dose corresponded to less than 25% of the BB target dose. Among patients included in the registry, two sub-cohorts were considered for the present analysis, according to ivabradine and BB use: group 1) patients treated with high BB dose (<25% of BB target dose) alone; group 2) patients treated with ivabradine and low BB dose. Primary end-point was the combination of hospital admission for acute HF and cardiac death at 1 and 2 years.
Results: A total of 145 patients were included in the registry during the index period. For the present analysis 105 patients (45 pts group 1 and 60 pts group 2) were eligible. Mean BB dose was 45% of the target dose in group 1 and 7% in group 2 (p = 0.0001). Most baseline clinical characteristics were well balanced between the two groups: age (71.8 ± 9.1 vs 69.3 ± 12.3 years), EF (26.0 ± 5.5 % vs 25.0 ± 5.5 %), LVEDV (216.4 ± 55.4 vs 202.8 ± 53.9 ml), TAPSE (17.8 ± 0.9 vs 8.2 ± 0.9 mm), severe mitral regurgitation (26.7% vs 28.3%), history of myocardial infarction (44.4 vs 48.3%), creatinine clearance (57.9 ± 25.6 vs 62.4 ± 32.3 ml/min), loop diuretics dose (90.1 ± 88.1 vs 92.3 ± 90.7 mg/die). Patients in group 2 had less concomitant use of ACE inhibitor or angiotensin receptor blocker (61% vs 80%, p = 0.04), due to inadequate tolerability. In terms of primary endpoint, there was any difference between groups at 1-year (40.0 vs 33.0%, p = ns) and 2-years (54.3 vs 48.9%, p = ns) follow-up. Conversely, a statistically significant difference was detected in terms of cardiac death at both 1-year and 2-years (20.0 vs 5.9% and 31.4 vs 13.3%, p = 0.04 and p = 0.05 respectively). The rate of hospital admission for acute heart failure were similar (32.5 vs 27.5%) at 1 year and (42.9 vs 40.0%) at 2 years.
Conclusion: In this study population including patients with advanced HF and poor BB tolerability, we observed no beneficial effects of uptitrating BB compared to adding ivabradine to low BB doses.



Kaplan-meier analysis of cardiac death

P2177

Effectiveness of Sacubitril/Valsartan in real-life practice: experience of a single center

JN Joana Neiva[1]; IGO Gomez-Otero[2]; AVR Varela-Roman[2]; MMG Moure Gonzalez[2]; ASB Seoane Blanco[2]; JRGJ Gonzalez-Juanatey[2]
[1]Hospital de Vila Franca de Xira, Cardiology, Vila Franca de Xira, Portugal; *[2]University Hospital of Santiago de Compostela, Centro de Investigación Biomédica en Red de Enfermedades Cardiovasculares (CIBERCV), Santiago de Compostela, Spain*

Introduction: Sacubitril/valsartan (SV) reduced mortality and hospitalizations in the PARADIGM-HF trial as compared to enalapril in patients (P) with chronic heart failure with reduced ejection fraction (HFrEF). ESC guidelines currently recommend SV for P with ongoing symptomatic HFrEF, despite first line medical therapy.
Purpose: Evaluate effectiveness of SV, regarding impact on functional capacity and on HF related outcomes and healthcare resource utilization.
Methods: Retrospective and descriptive study extended to all P on SV in a specialized HF unit in a single center since October 2016. Demographics, medical history, concomitant treatment and final dose were analyzed. Clinical parameters such as functional class of New York Heart Association (NYHA) and N-terminal pro-B-type natriuretic peptide (NT-proBNP) were assessed at each evaluation. Outcomes assessed were: HF hospitalization, non-elective hospitalization for any reason; death for any cause; cardiovascular (CV) death and emergency department (ED) visits due to decompensated HF. Descriptive statistics and Kaplan-Meier curve were used for analysis.
Results: Within a population of 106P (79% male; 68,2+10,7 years; 45,3% ischemic etiology; mean left ventricular ejection fraction (LVEF) 29,5%), 75,5% had NYHA II and 23,6% NYHA III at baseline. Mean baseline NT-proBNP was 2415pg/mL. 99,1% of P were on ACEI/ARB, 98,1% with beta-blockers and 89,6% on MRA. 52,8% had implantable cardioverter defibrillator and 31,1% cardiac resynchronization therapy system. The mean follow-up time was 194 days (4 - 421). Up-titration to maximum dose was achieved in 45,3%. 41,5%P had subjective improvement in symptoms and quality of life. NYHA class improved in 35,5%P (2P upgraded two classes); in 25,3%P it occurred early on first month. NT-proBNP did not significantly change (2415 vs 2104pg/mL). The mortality rate was 2,8% - all 3P had sudden death, HF hospitalization occurred in 2,8% (3P), hospitalization for all reasons in 6,6% (42,8% for non CV etiologies) and 2,8% (3P) had ED visits due to acute HF. Of 13P who obtained repeated LVEF measurement, 8 (61,5%) had improved LVEF (increase of 8,3%).
Conclusion: Our data suggests that SV is effectiveness in real-life. The overall outcomes rates were lower when compared to PARADIGM-HF trial, however our mean follow-up period was significantly shorter and our population is monitored closely in an HF specialized consultation.

P2178

Non-response predictors to physical rehabilitation in heart failure patients

VL Galenko[1]; TA Lelyavina[1]; MY Sitnikova[1]
[1]North-west state medical university, Saint-Petersburg, Russian Federation

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Introduction: In the world practice, physical training is widely used in CHF patients. But in most cases, is not taken into account the influence of the initial clinical status of patients (gender, age, CHF NYHA, peak oxygen uptake, comorbidity) on the results of physical rehabilitation.

Purpose: To reveal the most significant predictors of inadequate response to physical rehabilitation in CHF patients, selected on the basis of achievement the lactate threshold during CPET.

Methods: 90 patients, CHF NYHA II-III were randomized into two groups - primary (aerobic training) and control (standard treatment of CHF). Main group - 77 patients, mean age 52 ± 12,5 years, body mass index (BMI) 25,3 ± 5,4 kg/m2, among them 55 patients (72%) had III CHF functional class and 22 patients (28%) - II CHF functional class. The control group - 13 patients, age 51 ± 13,4 years, BMI was 25,4 ± 5.2 kg/m2, 12 patients had III CHF functional class, 1 patient - II. The original estimated results of physical examination, laboratory parameters, comorbidity. CPET, quality of life (QOL), exercise tolerance (ET) was assessed at baseline and after 1,3,6 months of follow-up. The CPET served on tredmile using hardware. Echocardiography (EchoCG) were performed at baseline and after 6 months. The data were statistically processed using software package "Statistika, 9.0".
Results: In the main group after 6 months of training EF increased by 8.7 ± 0.5% and End-diastolic volume decreased by 6 ± 2.0 ml from baseline, QOL was changed by 17.5 ± 8 points (significant regression of symptoms), ET increased by 9.5 ± 1 points and VO2 peak increased by 4.4 ml/min/kg. In the control group showed an increase EF 4 ± 1,1%, End-diastolic volume decreased by 68 ± 14,8 ml, the change of QOL 14 ± 7,22 points, the increase in ET at 1.5 points, VO2 peak decreased by 1,7 ml/min/kg. Revealed a strong positive correlation between the initial values of VO2 peak and EF (rEF = 0,4, p), and between baseline levels of sodium, hemoglobin and the of physical rehabilitation efficiency (rNa= 0,41, p,0,05; rHb = 0,45, p <0,05). There was a positive impact of the initial content of red blood cells (rEr = 0,6, p = 0.03), sodium (rNa = 0,4, p = 0.05), LV EF (r = 0.5, p = 0.05) and level VE at the peak of exercise load (r = 0.5,p = 0.01) on training efficiency. BNP level and a long history of CHF had a negative effect on the result of physical training (rBNP=-0,7, p = 0.05; rCHF=-0,6, p = 0.05). Significant differences in training performance between patients II and III functional class were not received.
Conclusion: Aerobic physical exercise in CHF patients, selected on the basis of lactate threshold achievement during the CPET, is effective in improving values of CPET, EchoCG, QOL and increasing exercise tolerance. Age, BNP and uric acid levels, CHF duration can be considered as most significant predictors of inadequate response to physical rehabilitation in CHF patients.

P2179

Telemedicine support to patients with heart failure at their self-management at home

M Pusnik-Vrckovnik[1]; C Slemenik-Pusnik[1]; D Rudel[2]; S Pusnik[3]; Z Balorda[2]; M Epsek-Lenart[1]; J Lavre[1]
[1]Slovenj Gradec General Hospital, Internal medicine, Slovenj Gradec, Slovenia; *[2]MKS Electronic Systems Ltd., Ljubljana, Slovenia*; *[3]Healthcare Centre Ravne, Ravne na Koroskem, Slovenia*

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Introduction: - In several scientific publications authors suggest that telemedicine (TeleMed) support to patients with long-term conditions is potentially useful tool for those patients who are likely to benefit from frequent and regular monitoring by health care providers. Some studies have already confirmed that TeleMed can be an effective add-on tool also in self-management of heart failure (HF) at home.
Purpose: - This study aimed at analyzing potential impact of TeleMed support to HF patients at their self-management at home when provided in addition to the standard care.
Methods - A TeleMed support was provided to a group of 130 HF patients (intervention group) for a minimum of 12 months. The median age of the patients was 72 years, 65% were male. The patients measured daily their blood pressure (BP), heart rate (HR), body weight and oxygenation. Data were immediately transferred to a telemedicine monitoring. In case of exceeding the personally set values the patients were called and advised on changing their lifestyle, nutrition, physical activity or to change the prescribed medication. The comparative group (N = 201) was the intervention group itself with 71 additional patients in the period of one year prior to the patients' inclusion into the TeleMed service. In the observed period patients in both groups received equal standard support through the existing long-term HF care programme. For the control period data on BP and HR for the patients involved in were obtained from a hospital HF register. To assess potential effects of TeleMed support LVEF ultrasound measurements and clinical marker proBNP were measured at three milestones: one year before the enrollment of patients into the TeleMed programme (-1y), at the enrollment (0y), and then after 12 months (+1y). Data on BP, HR, LVEF and proBNP were statistically analysed using descriptive statistics. Changes in average values of the measured values at milestones (-1y, 0y and +1y) were compared.
Results - After the observed 12 months period of using TeleMed support the average values of BP and HR did not changed with statistically significance neither in the intervention nor in the control group, but the intervention group changed its characteristics. Some patients moved from the high level BP (above 140/90 mmHg) to the normal BP level group (below 140/90 mmHg). Number of patients with normal BP measurements was 36% higher after 12 months of TeleMed support. Number of patients with normal heart rate measurements was 64% higher after 12 months of TeleMed support. The average LVEF increased from 41,6% to 44,7% (improvement

by 7,5%). The ProBNP clinical marker was reduced from 2.780 pg/ml to 1.795 pg/ml (improvement by 35%).
Conclusion –TeleMed support to HF patients at their self-management at home provided in addition to the standard care positively influenced the patients' health conditions. This was confirmed by the periodic external ultra sound and laboratory measurements.

P2180
Physical rehabilitation efficiency in heart failure patients

VL Victoria Galenko[1]; TA Lelyavina[1]; MY Sitnikova[1]
[1]*North-west state medical university, Saint-Petersburg, Russian Federation*

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Introduction: In the world practice, the selection of CHF patients physical training intensity is based on anaerobic threshold achievement during cardiorespiratory test (CPET). But the majority of patients with severe HF are not able to achieve it, that requires the use of certain indicators in the appointment of physical training. This alternative indicator can be lactate threshold, which achieved by every HF patient during the CPET.
Purpose: To evaluate aerobic physical training efficiency in CHF patients, selected on the basis of achievement the lactate threshold during CPET.
Methods: 90 patients, CHF NYHA II-III were randomized into two groups - primary (aerobic training) and control (standard treatment of CHF). Main group - 77 patients, mean age 52 ± 12,5 years, body mass index (BMI) 25,3 ± 5,4 kg/m2, among them 55 patients (72%) had CHF NYHA III, 22 patients (28%) - II. Control group - 13 patients, age 51 ± 13,4 years, BMI was 25,4 ± 5.2 kg/m2, 12 patients had CHF NYHA III, 1 patient - II. The original estimated results of physical examination, laboratory parameters, comorbidity. CPET, quality of life (QOL), exercise tolerance (ET) was assessed at baseline and after 1,3,6 months of follow-up. The CPET served on tredmile using hardware. Echocardiography (EchoCG) was performed at baseline and after 6 months. The data were statistically processed using software package "Statistika, 9.0".
Results: Main group - after 6 months of training EF increased by 8.7 ± 0.5% and End-diastolic volume decreased by 6 ± 2.0 ml from baseline, QOL was changed by 17.5 ± 8 points (significant regression of symptoms), ET increased by 9.5 ± 1 points and VO2 peak increased by 4.4 ml/min/kg. Control group - EF increased by 4 ± 1,1%, End-diastolic volume decreased by 68 ± 14,8 ml, QOL changed 14 ± 7,22 points, ET increased at 1.5 points, VO2 peak decreased by 1,7 ml/min/kg. Revealed a strong positive correlation between the initial values of VO2 peak and EF (rEF = 0,4, p), and between baseline levels of sodium, hemoglobin and the of physical rehabilitation efficiency (rNa= 0,41, p,0,05; rHb = 0,45, p <0,05). There was a positive impact of the initial content of red blood cells (rEr = 0,6, p = 0.03), sodium (rNa = 0,4, p = 0.05), LV EF (r = 0.5, p = 0.05) and VE level at the peak of exercise load (r = 0.5,p = 0.01) on training efficiency. BNP level and a long history of CHF had a negative effect on the result of physical training (rBNP=-0,7, p = 0.05; rCHF=-0,6, p = 0.05). The most significant impact on physical training efficiency of CHF NYHA III patients had a CHF duration (rCHF =-0,4, p = 0,05). Significant differences in training performance between patients CHF NYHA II and III were not received.
Conclusion: Aerobic physical exercise in CHF patients, selected on the basis of lactate threshold achievement during the CPET, is effective in improving values of CPET, EchoCG, QOL and increasing exercise tolerance.

P2181
Devices for objective assessment of physical activity in patients with heart failure: a systematic review

M Martha Kyriakou[1]; L Klompstra[2]; T Jaarsma[2]; N Middleton[1]; M Piepoli[3]; E Lambrinou[1]
[1]*Cyprus University of Technology, Limassol, Cyprus*; [2]*Linkoping University, Linkoping, Sweden*; [3]*Cardiology Unit, Guglielmo da Saliceto Hospital, Piacenza, Italy*

Devices for objective assessment of physical activity in patients with heart failure: A systematic review
Introduction
Heart Failure (HF) is associated with severe impairment of exercise capacity and reduced exercise tolerance, functional ability and health-related quality of life (HR-QoL). Low levels of physical activity (PA) are a sensitive indicator of poor prognostic outcomes in HF. Currently, most interventional studies assess PA subjectively and not objectively.
Aim of the study: To identify all intervention studies which used objective tools to assess PA of patients with HF. It was also examined whether changes in PA were associated with exercise capacity, health related- quality of life (HR-QoL) and psychological status
Methods: A systematic search of PubMed, CINAHL, Scopus and Web of Science was performed to identify studies which assessed the functional status in patients with HF using accelerometry, published in the English language. The search was conducted in September and October 2017 and the following terms were used: ("accelerometer" OR accelerometry OR "motion sensor" OR "activity monitor") AND ("heart failure"). Two researchers independently reviewed the results and a third one adjudicated, in case of lack of consensus. The Cochrane tool was used to assess the risk of bias of each study. Meta-analytic methods were used to extract, graphically display and explore data, but not to estimate an overall effect due to the small number of studies.
Results: Eight intervention studies (5 randomized control trials) were identified. A large heterogeneity was observed regarding the intervention period, the way chosen to measure the outcomes and the intervention as such (e.g. complexity and intensity). All studies measured the primary outcome: physical activity. Secondary outcomes, (i.e exercise capacity, HR-QoL and psychological status) were measured in seven, three and four studies, respectively. Heterogeneity in study estimates was also confirmed by a forest plot.
Conclusions: Heterogeneity among the few studies extracted suggests that more and better designed studies which assess physical activity with the use of objective measures are needed.

P2182
Restoration of sinus rhythm as a predictor of effectiveness of crt in patients with severe heart failure and persistent atrial fibrillation

D Lebedev[1]; M Lebedeva[1]; S Popov[1]
[1]*Cardiology Research Institute, Tomsk National Research Medical Center of RAS, Tomsk, Russian Federation*

Objective: To evaluate the effect of sinus rhythm restoration on the effectiveness of cardiac resynchronization therapy in patients with severe heart failure and persistent atrial fibrillation. Materials and Methods. The study included 150 patients (76 women) with mean age of 47.7 ± 10.9 years, Chronical Heart Failure (CHF) NYHA functional class III, dilated cardiomyopathy (DCM), and persistent atrial fibrillation (AF). The width of the QRS complex varied from 146 to 240 ms (mean 183 ± 32 ms); left ventricular ejection fraction (LVEF) was 30.1 ± 3.8%; and End-diastolic volume (EDV) was 272.4 ± 49.8 mL. The 6-min walk distance was 247.8 ± 57.3 m. Optimal drug therapy for CHF was ineffective for a period of three to six months. CRT-devices were implanted in all patients. A follow-up examination in the presence of biventricular stimulation was performed at 36 months.
Results: An analysis of CRT results at 36 months showed that sinus rhythm spontaneously restoration in 115 patients (76.7%) who had pre-treatment AF and ineffective antiarrhythmic therapy. In this group of patients, three-year follow-up showed that EF increased by 18% from 29.0 ± 3.8% to 42.5 ± 4.2% (p <0.0001); EDV decreased by 48 mL from 215.9 ± 58.1 to 177.1 ± 26.6 mL (p <0.0005). AF persisted in 35 patients (23.3 %) for 36 months after beginning of CRT. In these patients, three-year follow-up showed that LVEF increased by 9% from 29.0 ± 3.8% to 38.7 ± 2.1%; EDV decreased by 15 mL from 215.9 ± 58.1 to 200.7 ± 39.1 mL (p <0.0005).
Conclusion: Our study demonstrated that achieving sinus rhythm provided a stable increase in EF and a decrease in EDV during the entire period of CRT in patients with DCM and severe heart failure. Therefore, achieving sinus rhythm should be considered an important task in this category of patients.

P2183
Changes in quality of life in patients with chronic heart failure after cardiac resynchronization therapy

GS Pushkarev[1]; AD Sapozhnikova[1]; YA Fisher[1]; AM Soldatova[1]; TN Enina[1]; VA Kuznetsov[1]
[1]*Tyumen Cardiology Research Center, Tomsk National Research Medical Center, Russian Academy of Scienc, Tomsk, Russian Federation*

Background: Chronic heart failure (CHF) is a serious medical problem associated with high rates of mortality and low quality of life in patients. Cardiac resynchronization therapy (CRT) is one of promising new methods for heart failure treatment. Thus, the study on assessment of quality of life in patients with CHF after CRT is a vital and pressing issue.
Purpose: To assess the quality of life (QoL) changes in patients with CHF one year after CRT.
Methods: The study included 82 patients (68 males and 14 females) aged from 30 to 74 (mean age 55.8 ± 9.2 years) who underwent implantation of a biventricular cardiac pacemaker for CRT. The SF-36 questionnaire was used to measure QoL. The results of the questionnaire were represented as scores over the eight subscales: physical functioning (PF), role-physical functioning (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role-emotional (RE), and mental health perceptions (MH). The QoL assessment was performed before and one year

after CRT. Student's paired t-test was applied in statistical analysis for comparing normally distributed values, while the Wilcoxon nonparametric test was used when the sample data were not normally distributed.
Results: Patients with CHF one year following CRT had significantly higher rates of improvement in PF QoL (PF before CRT 46.28 ± 26.16; PF one year after CRT 53.05 ± 27.65 p = 0.023). The statistical tendency towards QoL improvement was revealed: VT (VT before CRT 47.07 ± 20.12, VT after CRT 51.83 ± 20.07, p = 0.081), SF (SF before ??? 61.58 ± 25.06, SF after CRT 67.07 ± 24.57, p = 0.088). No significant differences were found in paired comparisons of other QoL indicators.
Conclusion: Significant increase in PF index and statistical tendency towards increase in VT and SF were detected in patients with CHF one year following CRT.

P2184

Transcranial doppler findings in heart failure patients with ventricular assist devices

NK Doan[1]; V Rosta[1]; BA Bruckner[1]; AB Lumsden[1]; Z Garami[1]
[1]The Methodist Hospital, DeBakey Heart and Vascular Center, Houston, United States of America

Introduction: Left ventricular assistance device (LVAD) implantation is a "live saving" approach for patients (pts) with heart failure waiting for cardiac transplantation, although cerebral vascular events continue to be frequent sequelae. Transcranial Doppler (TCD) is a novel method for studying cerebral hemodynamics and embolization in these patients.
Methods: The Methodist LVAD TCD diagnostic protocol examined major intracranial arteries in 19 segments. TCD data and embolic signals were interpreted using previously published and validated TCD criteria. TCD results were then correlated to clinical, laboratory and imaging findings.
Results: Thirty-three patients (19 Male, 14 Female; average age: 53.4 years) underwent LVAD placement. Fourty-seven TCD studies were performed (10 pts had multiple tests) on LVAD recipients (35 HeartMate, 4 DeBakey, 4 Thoratec, 1 Novacor, 1 Ventracor, 1 Biomedicus, 1 Levitronic) an average of 202 days (range: 1-840 days) after implantation. Only one patient did not have an adequate acoustic window for the transtemporal examination. There were 4 neurological events during the observation period [3 TIA in 2 pts (1 DeBakey, 1 HeartMate) and 1 stroke (DeBakey)]. We detected 33.2 microembolic signals/minute in 2 of the 3 TIA and in 1 pt under deep sedation. After therapeutic dose adjustment of heparin, microembolic signals were no longer detectable in 3 of 6 pts. Contrast echocardiography shortly before TCD may have contributed to false microembolic signal detection in 2 cases. Bilateral severe middle cerebral artery stenosis was detected in the stroke patient and contributed to her seizures and death. By detecting oscillating flow patterns in 2 pts, we could confirm a brain death diagnosis.
Conclusions: TCD can be used to guide anticoagulation therapy and the replacement of older, embolizing LVADs. Eliminating emboli might prolong symptom-free periods for our patients.

P2185

Applying virtual reality to increase physical activity in Left Ventricular Assist Device (LVAD) supported patients: Is it feasible?

B Ben Avraham[1]; T Jaarsma[2]; S Donnenhirsh[1]; L Klompstra[2]; I Mats[1]; V Yaari[1]; M Abu-Hazeira[1]; D Golub[1]; A Stromberg[2]; T Ben Gal[1]
[1]Rabin Medical Center, Sackler faculty of Medicine, Tel Aviv University, Heart Failure Unit, Cardiology Department, Petah Tikva, Israel; [2] Linköping University, Division of Nursing, Department of Social and Welfare Studies, Linköping, Sweden

Background: Rehabilitation of patients after LVAD implantation is of major importance but seldom applied. The usefulness of physical training in an out-patient setting is limited mainly by transportation issues but also by the huge variability of the post operative physical condition and the need for specialized staff for training and managing of the LVAD supported patients. Virtual reality applications (exergaming) might provide encouragement to increase physical activity and give the opportunity to play at home at the time and level that are most suitable for the individual patient. However, the feasibility of applying this new form of exercise for LVAD supported patients is not known.
Purpose: The aim of the study is to evaluate the feasibility and patient experience of a virtual reality exergame to encourage physical activity in LVAD supported patients.
Methods: A feasibility study is performed with previously used standardized observations and questionnaires to evaluate practical application and experiences of patients. After introducing the virtual reality exergame during a regular LVAD clinic visit, the computer-game was installed at the patient's home. Patients were instructed to play the game for 40 minutes 4 times a week. Feasibility and patient experiences are assessed after 1 month of exergaming at home. The interview guide includes questions about frequency of exergaming, enjoyment, barriers for exergaming, experiences and symptoms (e.g. pain) and LVAD specific practical challenges (e.g. if the controller bag interferes with the physical activity). Descriptive statistics and content analysis are used to present and analyze the data.
Results: Preliminary results show that patients supported with an LVAD can be instructed to play exergames as a mode of physical activity at home. The computer-game was installed at the patient's home by a dedicated instructor. Patients manage to play the exergame and first results show that they enjoy exercising with an exergame. In total, 10 patients are included in this feasibility study and currently followed. Additional data are collected and will be presented during the conference.
Conclusion: Applying virtual reality exergaming in LVAD supported patients seems feasible and is encouraging physical activity in those patients. Our study will enable us to assess the usability of such promising modern technology in engaging LVAD patients in regular physical activity thus improving their physical fitness and prognosis.

P2186

Evaluating community health practitioners perspective of the heart failure pathway

E Lennon[1]; R Kernan[1]; J Gallagher[2]; M Walshe[2]; JP Reily[3]; C Keane[2]; M Ledwidge[2]; PR Kalra[4]; MR Cowie[3]; K Mc Donald[2]
[1]University College Dublin, Dublin, Ireland; *[2]Heart Failure Unit, Dublin, Ireland*; *[3]Imperial College London, London, United Kingdom*; *[4]Portsmouth Hospitals NHS Trust, Portsmouth, United Kingdom*

Funding Acknowledgements: Enterprise Ireland

Background: There is growing interest in building community capacity to manage Heart Failure (HF). As well as patient/caregiver engagement, the Community Pharmacist (CP) and General Practitioner (GP) play a central role in the community care of HF. As part of a care-pathway mapping programme for HF, we aimed to describe GP/CP perspectives and identify areas for development.
Purpose:/Method
We administered an internally validated questionnaire to eighty CPs and GPs of consecutive consenting HF patients admitted with an acute decompensation. These patients were participating in a prospective care-pathway mapping project in the Heart Failure Unit of a large teaching hospital. Questionnaires were conducted by post. The responses were then analyzed. Response rates were 57.5% (46) and 40% (32) of GPs and CPs respectively.
Results: In terms of enablers of better community HF care, 93%(43) of GPs felt that they could improve diagnosis and management of HF in the community if they had routine access to Natriuretic Peptide testing and the support of same-day HF services. Eighty-five percent (39) stated that if they had access to Echocardiography they would be better enabled to screen for heart failure. A further perceived barrier to optimal HF care within the community amongst 83% (38) of GPs was the patient's own lack of HF education and understanding of their diagnosis. Furthermore, 67% (31) of GPs felt that there should be an increase in the number of outpatient HF clinics.
Almost half of CPs, 45%(14) did not have access to information regarding the patient's diagnosis of HF, requiring confirmation before medicines management. Prescription changes were needed in half of cases (16) and just under half of pharmacists reported spending 30-60 minutes seeking information from medical and healthcare professionals regarding HF issues. Changes related to discharge prescription errors, omitted regular medications, inappropriate medications and incorrect dosages. Conversely, 45% (14) of CPs reported no access t the hospital team regarding medication queries yet, almost half of CPs (16) reported that GPs did not have adequate information regarding the HF plan. Most 72%(23) of CPs felt that it should be standard of care for teams making a medication change on a HF patient's script, to communicate this change and reason for it to the community pharmacist.
Conclusion: These results describe significant gaps in the community HF care pathway amongst healthcare professionals with the most frequent HF patient contact. Most of the barriers relate to information flows, care coordination and access to diagnostics with negative consequences on community care management and resources. Identifying areas for targeted improvement along each stage of this pathway will improve outcomes, efficiencies and the experience of care for HF patients.

P2187

Heart Failure Virtual Consult; A tool for delivering specialist opinion but also transferring knowledge to community practitioners

C Keane[1]; J Gallagher[1]; M Hammond[1]; P Campbell[1]; M Ledwidge[1]; K Mcdonald[1]
[1]St Vincent's University Hospital, Heart Failure Unit, Dublin, Ireland

Funding Acknowledgements: Health Service Executive Ireland

Heart failure (HF) is a highly prevalent disease, affecting the elderly in particular. Early diagnosis of HF is important so that treatment can be initiated on time in order to delay disease progression to overt HF. In Europe, most patients with HF first present in primary care. At present HF diagnosis and treatment is often inadequate in primary care and General Practitioner (GP) confidence of managing HF can be low. The increasing prevalence rates for HF means a greater role for primary care in disease management. The Heart Failure Virtual Clinic (HFVC) provides access for GPs to specialist opinion and thus assists with the management of patients in the community. Importantly the HFVC also facilitates GP empowerment and education by providing support within the community thus reducing the need for secondary/tertiary care referrals. The HFVC is distinct from other eHealth initiatives as it has a dual function, it is not only a system to provide an appropriate health care intervention but also acts as a system for knowledge dissemination, dispersing knowledge and improving GP confidence levels.
The established HFVC (ongoing for 36 months) has recently expanded its geographical reach. In a 9 month period 75 GPs engaged with the service. There were 160 individual patient referrals received and 270 patient appointments in total, 72 virtual clinics took place. Two hundred and thirty CME credits were awarded, with some GPs attending, not to present cases, but to observe the 10 minute CME presentation at the beginning of each session and the anonymised cases presented by their GP colleagues. For patients travel saved was 15,781km (particularly important for this frail, elderly population). If the HFVC were not available then68.75 % of these patients would have been referred to Cardiology Outpatients or Emergency Departments. Another 26.25% of patients would have had unsupervised intervention such as echocardiogram or medication titration. Five per cent would not have been referred anywhere. In relation to knowledge and confidence 83% of GPs said the HFVC had impacted their ability to identify HF patients to a high degree, 80% said due to participation in the HFVC they are now very competent in their ability to treat HF patients and manage side effects.
This expansion of the HFVC demonstrates the potential for such a model in terms of bridging the gap and increasing expertise across primary, secondary and tertiary care, while upskilling community based clinicians. It clearly has the potential to benefit the patient as well as the system.

P2188

Optimizing standards of care of heart failure in general practice. Results of the OSCAR-HF pilot study.

M Miek Smeets[1]; B Aertgeerts[1]; S Janssens[2]; J Penders[3]; J Vercammen[4]; W Mullens[4]; B Vaes[1]
[1]KU Leuven, Department of public health and primary care, Leuven, Belgium; *[2]Gasthuisberg University Hospital, Department of Cardiovascular diseases, Leuven, Belgium*; *[3]Hospital Oost-Limburg (ZOL), Departement of Clinical Biology, Genk, Belgium*; *[4]Hospital Oost-Limburg (ZOL), Departement of Cardiology, Genk, Belgium*

On behalf of: OSCAR-HF study group
Funding Acknowledgements: Unconditional grant of Novartis to finance the HF nurses and data manager working in region Leuven. Cobas h232 devices are provided by Roche.

Background Heart failure (HF) imposes a burden for patients and health economics. General practitioners (GPs) are confronted with the broadest range of HF management. The European Society of Cardiology (ESC) guidelines recommend implementation of multidisciplinary disease management programs to optimize quality of HF care. However, until now, HF care in Belgium is not organized as such.
Purpose: We implemented a multifaceted intervention to support GPs in the implementation of evidence-based HF guidelines.
Methods: The OSCAR-HF pilot study is a non-randomized, non-controlled prospective observational trial (6 months follow-up). The multifaceted intervention consisted of an audit and feedback method to detect previously unrecognized patients with HF in the electronic health record (EHR) and to increase awareness for proactive HF management, an NT-proBNP point-of-care test (Cobas h232) to improve detection and adequate diagnosis of patients with HF and a specialist HF nurse to assist GPs in the education of patients, optimization of treatment and follow-up after hospitalization. All patients aged 40 years and older with a confirmed diagnosis of HF by their GP based on the clinical audit were eligible for participation.
Preliminary results Eight general practices (51 GPs) participated; four in region Leuven, four in region Limburg. The study started in the first practice on 1/1/2017 and ended in the last practice on 30/11/2017. By searching on a registered diagnosis of HF in the EHR 333 patients (prevalence 1.8%) were identified. After the extended clinical audit, GPs confirmed the HF diagnosis in 538 patients, our study population (prevalence 3.0%). The mean age of our study population was high (78 ± 11) and 50% (n = 269) were men. In the past 5 years 457 patients (85%) underwent an echocardiography. Based on the echocardiography results in the EHR 20% (n = 105) were classified as HF with reduced ejection fraction (HFrEF) patients (EF < 40), 13% (n = 71) as HF with mid-range EF (HFmrEF; EF 40-50) and 53% (n = 285) as HF with preserved EF (HFpEF; EF>50). The remaining 77 patients (14%) were not classifiable. Out of 105 HFrEF patients 92 (88%) were treated with a B-blocker and 88 (84%) with renin-angiotensin-aldosterone system (RAAS) blockade. However, target doses were only reached in 15% of HFrEF patients (n = 16) for B-blockade and 36% (n = 38) for RAAS-blockade. Practices were encouraged to objectify uncertain HF diagnoses, increase awareness for new HF diagnoses and optimize care. To support them in these goals an NT-proBNP POC test and support by a specialist HF nurse were offered to each practice. As a results, during the study course, GPs performed 395 NT-proBNP POC tests and the HF nurses did 60 interventions. Data analysis is ongoing and will be finalized april 2018.

P2189

An integrated chronic heart failure and palliative care approach. Is this the way forward?

M Al Barjas[1]; J Roy[2]; F Hodson[2]; P Hansford[2]; S Karwatowski[3]; R George[2]
[1]King's College Hospital, London, United Kingdom; *[2]St Christopher's, Palliative Care, Kent, United Kingdom*; *[3]Princess Royal University Hospital, Farnborough, United Kingdom*

Aim: A pilot study to assess the benefits of integrating chronic heart failure care with palliative care for patients in NYHA class III and IV.
Heart Failure is a chronic illness and cause of death despite the many advances in pharmacological, device based and surgical therapies. People living with long term conditions such as heart failure require an integrated approach to their care with a robust care pathway to meet their needs, from diagnosis through to end of life care. A series of target GP practices encompassing a range of different 'styles' / approaches to managing HF patients and different demographic and deprivation profiles has been identified
A growing consensus has emerged in the literature that confirms the need to extend multidisciplinary management beyond the early targets of reducing heart failure-related mortality and morbidity.
Criteria for patients inclusion:
a. Have been reviewed by the cardiology / heart failure team AND have a confirmed diagnosis of heart failure
b. Know they have a diagnosis of heart failure and can engage in the process of managing their care
c. Agree to the referral
All referrals were discussed in a joint meeting of the heart failure and palliative care teams.
Results: 37 patients were included in the study.
Age - Median 85 yrs (46-100) , Gender - 56% male, ethnicity - 86% White
1 patient 15% risk dying in 1 year; other 7 had 37-60% risk dying that year
MAGGIC average score (SD) 31 (5.8). 4 patients scores < 25
Anxiety scores ranged from 0 to 13 (median 8) with an average of 7 (± 3.9)
Depression scores ranged from 0 to 15 (median 8) with an average of 8 (± 4.2)
−25 patients contacted within 7 days of referral
−9 within 7-14 days of referral
−3 contacted >14 days (wrong contact info, admitted to hospital day after referral, awaiting cardiology review before accepted onto pilot). 5 haven't been contacted yet (awaiting further cardiac information).
−27 patients were seen in under 7 working days
−5 within 7-14 days
−4 > 14 days. One patient requested to be contacted in one month and is awaiting first assessment; one patient died before being seen and 5 are waiting cardiology assessment prior to acceptance on the pilot.
Patients' needs were:
Pain / Symptom Control 45 (87%), carer Support 17 (33%), psychological / Emotional Support 12 (23%) social / financial 4 (8%), rehabilitation 3 (6%) and terminal Care 2 (4%)
8 patients died at the following locations:
•5 died at a local hospital.
•1 died in the hospice.
•1 died at home with family present
•1 died in a Nursing Home
average length of care was 38.4 (± 20.7) days
•30/35 patients with decision not to resuscitate
•5/35 patients remain for resuscitation.
Discussion and conclusion:
•Patient population is older, frail, with comorbidities.
•The pilot study demonstrate significant improvements in palliative care outcome score. MAGGIC score did not predict referral or clinical outcomes in this cohort

P2190

Psychological interventions to improve psychological outcomes in patients with heart failure: a systematic literature review

N Sedlar[1]; M Lainscak[2]; J Farkas[3]
[1]*National Institute of Public Health, Ljubljana, Slovenia*; [2]*General Hospital Murska Sobota, Department of Internal Medicine, Murska Sobota, Slovenia*; [3]*General Hospital Murska Sobota, Department of Research, Murska Sobota, Slovenia*

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Background: A growing body of evidence supports the association between psychological symptoms and adverse outcomes in patients with heart failure. As a consequence, the importance of psychological interventions, aiming to assist with the disease adjustment and general well-being improvements (ie. reducing depression, improving quality of life) has been emphasized in the recent years.
Aims. To review literature on psychological interventions in patients with heart failure and identify most commonly used psychological intervention features.
Methods: PRISMA guidelines were used to search major health databases (PubMed, Scopus, ScienceDirect, PsycInfo) for randomized controlled trials evaluating psychological interventions in patients with heart failure. Interventions were analyzed based on their success in producing a significant change ($p < 0.05$) in outcomes, in the hypothesized direction; outcome measures included total or cardiac-related mortality, cardiac morbidity, depression, anxiety, health-related quality of life. The reviewers examined intervention features such as setting, format, duration, interventionist, as well as psychological components and education strategies.
Results: We identified 15 studies that were included in the review. Interventions used different approaches, including cognitive behavioral therapy, motivational interview, supportive counselling/psychoeducation, stress management and mindfullness-based therapy. Thirteen studies reported on depression and HRQOL, nine on anxiety and four on total or cardiac-related mortality/morbidity. Positive outcomes were obtained in less than half of the studies reporting on the outcomes; six studies reported significantly ($p < 0.05$) improved HRQOL, five reduced depressive symptoms, four reduced anxiety symptoms and one reduced mortality/morbidity in the intervention group compared to the control group. Most interventions were hospital- or home-based, delivered by nurse, using one-on-one format and less than six months in duration. Guidance on successful behaviour change, self-awareness/self-monitoring, emotional support/client led discussion, cognitive challenge/cognitive restructuring techniques and homework exercises were most commonly used psychological components. Most frequently used educational strategies included mutually-agreed goal-setting, situational problem-solving, lecture-based teaching, feedback and use of diaries.
Conclusion: Due to the heterogeneity of published studies, individualized nature of psychological interventions and various outcome measures our study highlights the need for further exploration regarding most effective types of psychological intervention and their benefits.

P2191

Overweight/obesity paradox in Acute Coronary Syndrome prognosis; not a truth for each heart failure phenotype. Results from Hellenic Heart Failure study.

C Christina Chrysohoou[1]; M Kouvari[2]; P Aggelopoulos[1]; I Haritou Kotsopoulou[1]; H Kosyfa[1]; E Tsiamis[1]; C Pitsavos[1]; D Tousoulis[1]
[1]*University of Athens, Athens, Greece*; [2]*Harokopio University, Nutrition Science - Dietetics, Athens, Greece*

Background/Introduction: Weight management is arguably recommended in the primary prevention of chronic diseases; yet this is not the case in the treatment spectrum of diseases like heart failure, usually, characterized by a high catabolic state. In such cases, overweight/obese subjects are to have a survival advantage. However, to what extent this is a truth for all raises many doubts.
Purpose: to evaluate the role of body mass index (BMI) in coronary patients prognosis with established heart failure and to investigate potential interactions with left ventricle performance.
Methods: in 2006-2009, 1,000 consecutive patients, hospitalized at a Cardiologic Clinic in Athens with ACS diagnosis were enrolled in the study. In 2016, 10y follow-up (after intermediate follow up in 1 month, 1 & 2 years) was performed (75% participation rate). Overweight was defined as 25 = BMI = 29.9 kg/m2 while obesity as BMI>29.9 kg/m2. Heart failure phenotype was defined according to baseline EF; heart failure with reduced EF (i.e. <40%) (HFrEF), preserved EF (i.e = 50%) (HFpEF) and mid range EF (i.e. 40-49%) (HFmrEF).
Results: BMI status and ACS prognosis followed a J-shape association. Ranking from normalweight to overweight and to obese subjects, the aforementioned association was evident in case of in hospital mortality (7%, 4% and 5%, $p = 0.09$), 2y ACS prognosis (50%, 32% and 36%, $p = 0.009$) and 10y ACS prognosis (65%, 52% and 58%, $p = 0.03$); fatal/non fatal ACS events within the decade were 65%, 52% and 58% ($p = 0.009$). Focusing on long term prognosis (i.e. 10y), multivariate logistic regression analysis, revealed that overweight patients had significantly better ACS prognosis compared with their normalweight counterparts (OR = 0.45, 95%CI (0.23, 0.90)), whilst obese patients did not have significant differences compared with the reference group. Significant interactions were observed between left ventricle performance (i.e. ejection fraction) and BMI on 10y ACS prognosis (p for interaction <0.001). With heart phenotype as strata, the aforementioned association remained significant only in HFrEF patients (OR = 0.35, 95%CI (0.13, 0.89)). HFmrEF and HFpEF patients did no reach significance. Conclusion: overweight paradox was highlighted in 10y ACS prognosis of heart failure patients. However, certain prerequisites were indicatively stated, with the aforementioned association being more evident in heart failure patients with the highest catabolic state (i.e. HFrEF); yet not being the case in patients with better left ventricle performance.

P2192

Safety profile of novel angiotensin II type-1 receptor neprilysin inhibitor lcz696 (sacubitril/valsartan) - a collaborative summary from clinical trials

A Z Barano[1]; E N Putri[2]; M F Addai[3]; M Abduh[4]; D Ilmasari[5]
[1]*Bergerak Badau Hospital, Kapuas Hulu, Indonesia*; [2]*Hermina Hospital, Bekasi, Indonesia*; [3]*Johar Baru Primary Health Care, Jakarta, Indonesia*; [4]*Dr. M. Yunus General Hospital, Bengkulu, Indonesia*; [5]*Hardjolukito Central Air Force Hospital, Yogyakarta, Indonesia*

Background: LCZ696 (Sacubitril/Valsartan) is a first-in-class inhibitor of the angiotensin II type-1 receptor and neprilysin.
Purpose: We aim to evaluate the safety profile of novel medication, LCZ696 (Sacubitril/Valsartan).
Methods: Pubmed database were searched for Clinical Trials of LCZ696 (Sacubitril/Valsartan). We required the trials to report adverse events (AEs) of the medication. The data was compiled in IBM SPSS Ver 21. Continuous data were reported in number of samples (n) and percentage (%).
Results: Twelve clinical trials were included with a total of 14,447 patients. The majority of patients were suffering from hypertension and heart failure. Numbers of reported serious AEs 0.27% (39), Discontinuation 1.41% (203), and death 0.007% (1, caused by acute myocardial infarct). Total numbers of AEs were 19.57% (2827). Cardiovascular and Respiratory AEs were the most common AEs, respectively 9.07% (1310) and 8.6% (1242). Numbers of reported AEs (< 1% for each AE) were contributed by Neurology, Gastrointestinal, Skin, Locomotor, Renal and urinary tract, Hypersensitivity and autoimmune, psychology problem. Based on AEs, Hypotension 8.95% (1293), Cough 6.77% (978), and Nasopharyngitis 1.052% (152) were the most reported AEs, while other AEs (< 1% for each AE) were dizziness, URTI, headache, angioedema, diarrhea, hematuria, pharyngitis, etc. The reported laboratory result changes were 13.878% (2005). Electrolyte and renal function were the most reported changes related with laboratory results, respectively 11.05% (1596) and 2.5% (362). The other reported laboratory changes (< 1% for each changes) were changes in liver function, lipid profile, uric acid, and blood glucose level. The most commonly reported electrolyte profile changes were Increase in potassium level 10.65% (1539), followed by other (< 1% for each changes) reported decrease potassium level, increase sodium level, and decrease sodium level. The most commonly reported changes in renal function were increase in creatinine level 2.39% (345), and other (< 1% for each changes) changes were increase in blood urea nitrogen level.

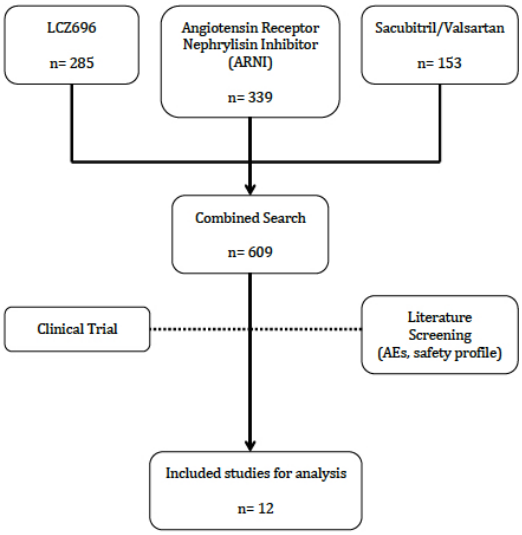

Figure 1. Flow diagram of systematic literature searching

Systematic Literature Searching

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Biological Process	Protein	% Change from Baseline to Day 14	% Change from Baseline to Day 30	% Change from Baseline to Day 60	% Change from Baseline to Day 90	Adjusted P Value (False Discovery Rate)
Acute-Phase and Inflammatory Response	C-Reactive Protein	202.4	48.5	-20.6	-42.6	4.0E-12
	Lipopolysaccharide-binding protein	48.5	22.6	-2.9	-5.9	5.0E-10
	Protein S100-A9	163.2	95.9	30.2	14.8	9.8E-10
	Alpha-1-acid glycoprotein 1	92.9	67.3	13.7	-6.9	5.6E-09
	Alpha-1-acid glycoprotein 2	71.0	45.2	2.5	-10.3	2.6E-07
Regulator of Proteolysis	Gelsolin	-16.5	9.0	20.5	47.8	2.8E-11
	Phosphatidylinositol-glycan-specific phospholipase D	-29.3	-5.0	5.2	16.9	4.3E-11
Complement Activation	Ig gamma-4 chain C region	-12.4	33.7	58.9	41.1	2.1E-05
	Alpha-2-macroglobulin	-35.7	-25.3	-10.8	-8.6	1.3E-05
Platelet Degranulation	Galectin-3-binding protein	-9.8	-14.2	-24.8	-29.9	1.8E-06
Cardiac remodeling	Peptidase inhibitor 16	4.4	42.5	71.6	75.7	9.6E-11
Collagen Fibril Formation	Lumican	-3.2	14.6	37.0	57.4	1.1E-10

Conclusions: According to the studies, the most common AEs of LCZ696 (Sacubitril/Valsartan) are hypotension, nasopharyngitis, cough, increase potassium level, and increase creatinine level. LCZ696 (sacubitril/valsartan) is a relatively safe medication for hypertension and heart failure.

P2193

Quantifying changes in the plasma proteome over time following left ventricular assist device implantation

C Aquilante[1]; A Brieke[1]; K Fritz[1]; L Saba[1]; K Deininger[1]; P Harris[1]; K Brown[2]; L Wolfe[2]; R Page[1]; J Cleveland Jr[1]; J Lindenfeld[3]
[1]University of Colorado, Aurora, United States of America; *[2]Colorado State University, Fort Collins, United States of America*; *[3]Vanderbilt University, Nashville, United States of America*

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Background: Left ventricular assist devices (LVADs) exert high shear stress on blood components. However, the impact of LVADs on the entire complement of circulating proteins, i.e., the plasma proteome, is unknown.
Purpose: We used discovery-based, quantitative proteomics to evaluate changes in the abundance of plasma proteins following LVAD implantation.
Methods: We enrolled patients undergoing HeartMate II LVAD implantation. Whole blood was collected prior to LVAD implant (baseline), and at days 14, 30, 60, and 90 post-implant. We used Tandem Mass Tag (TMT) labeling of peptides and LC-MS/MS analysis for relative quantification of plasma protein abundance. Data were analyzed using a mixed model to estimate protein level differences.
Results: The study included 18 LVAD recipients (14 men; 14 Caucasian; mean age = 57 ± 14 yrs). 280 total proteins were identified. After adjustment for multiple comparisons, 14 plasma proteins changed significantly over time (table). Acute-phase and inflammatory proteins (e.g., C-reactive protein) increased immediately following LVAD implant and then subsequently decreased relative to baseline. Conversely, proteins regulating proteolysis (e.g., gelsolin) and complement activation (e.g., Ig gamma-4 chain C region) decreased after implant and then increased over time. Time-dependent changes in other proteins are shown in the table.
Conclusion: Proteomic analysis yields insight into the changes in underlying biological processes following LVAD implantation. Additional studies evaluating associations between the identified plasma proteins and LVAD-related clinical outcomes are warranted.

P2194

Failure to achieve guideline directed beta blockade early post hospitalization

C Carsten Jungbauer[1]; LS Maier[1]; K Emoto[2]; MJ Mirro[3]
[1]University Hospital Regensburg, Cardiology, Regensburg, Germany; *[2]Zoll Medical Corporation, Pittsburgh, United States of America*; *[3] Parkview Health System, Fort Wayne, United States of America*

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Introduction: Guidelines for the treatment of heart failure (HF) recommend the titration of beta-blockers (BB) to a target dosage shown to be effective in clinical trials. The benefit of beta-blockers is associated with heart rate (HR) control, with a target resting HR < 70 bpm.
Purpose: To assess the ability to achieve guideline-directed BB usage in the early post hospitalization period in patients (pts) indicated for wearable cardioverter defibrillator (WCD) use.
Methods: The WCD platform allows continuous recoding of HR. To assess the adequacy of BB, HR's were evaluated at rest (nighttime: midnight-7am; daytime: 7am-midnight), during normal daily activities, and during a 6 minute walk test (6MWT). HR's during normal daily activity (ADL) were collected from WCD pts that wore the WCD for = 5 weeks (n = 1449) between 2015 and 2017. Activity of daily living episodes were defined as a contiguous period (= 60 secs) where the device accelerometer records a = 60 milligravity (mG) mean amplitude deviation, and median peak HR/week was calculated. Peak HRs at the end of a six minute walk test (6MWT) are reported as median HR per patient (n = 115 pts).
Results: First, 684,922 activity episodes from 1449 pts were analyzed. Resting HRs averaged 69 bpm and increased to 94 bpm during ADL at the last week of WCD use. 43% of pts had an average daytime resting HR = 70 bpm at the last week of WCD use. During ADL, in 14% of pts HR exceeded = 110 bpm, and 6% exceeded = 120 bpm. HR during the 6MWTs averaged 90 bpm (range: 45-151), and exceeded 110 bpm in 9% of pts. When comparing individual peak HR during the first week of WCD use to the last week, there was no difference. Graph below demonstrates HR after median of 73 and 90 days of use for the two groups.
Conclusion: In the early post hospital discharge period 43% of pts do not meet target HR control, indicating they are not effectively managed with BB. Remote HR monitoring during WCD use may help physicians to adequately titrate beta blockade thus improve clinical outcomes.

Chronic Heart Failure - Clinical

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Effect of heart failure reversal treatment as add-on therapy in patients with chronic heart failure:A randomized, open-label study

RM Sane[1]; R Mandole[2]; A Aklujkar[3]; A Patil[4]
[1]Madhavbaug Multidisciplinary Cardiac Care Clinics and Hospitals, Mumbai, India; *[2]Vaidya Sane Ayurved Labs Pvt Ltd, Thane, India*; *[3]Bhaktivedanta Hospital, Thane, India*; *[4]Shri Sai Baba Heart Institute, Nasik, India*

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Objectives: The present study was designed to evaluate effect of heart failure reversal therapy (HFRT) using herbal procedure (panchakarma) and allied therapies, as add-on to standard treatment (SCT) in chronic heart failure (CHF) patients.

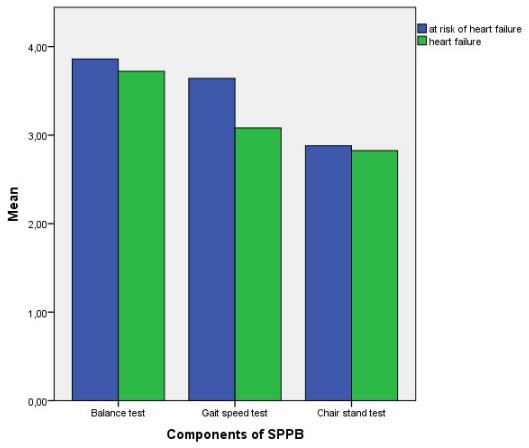
Methods: This open-label, randomized study conducted in CHF patients (aged: 25-65 years, ejection fraction: 30%-65%), had 3-phases: 1-week screening, 6-week treatment (randomized [1:1] to HFRT+SCT or SCT-alone) and follow-up (12-week). Twice weekly HFRT (60-75 minutes) consisting of snehana (external oleation), swedana (passive heat therapy),hrudaydhara (concoction dripping treatment) and basti (enema) was administered. Primary endpoints included evaluation of change in metabolic equivalents of task (MET) and peak oxygen uptake (VO2peak) from baseline, at end of 6-week treatment and follow-up at week-18 (non-parametric rank ANCOVA analysis). Safety and quality of life (QoL) was assessed.
Results: Seventy CHF patients (n = 35, each treatment-arm; mean [SD] age: 53.0 [8.6], 80% men) were enrolled in the study. All patients completed treatment phase. Add-on HFRT caused a significant increase in METs (least square mean difference [LSMD], 6-week: 1.536, p = 0.0002; 18-week: -1.254, p = 0.0089) and VO2peak (LSMD, 6-week: -5.52, p= 0.0002; 18-week: -4.517, p = 0.0089) as compared with SCT-alone. Results were suggestive of improved functional capacity in patients with HFRT (QoL; Mean [SD] HFRT+SCT vs. SCT-alone; 6-week: -0.44 [0.34] vs. -0.06 [0.25], p < 0.0001 and 18-week: -0.53 [0.35] vs. -0.29 [0.26], p = 0.0013). Seven treatment-emergent adverse events (mild severity) were reported in HFRT-arm.
Conclusion: Findings of this study highlight therapeutic efficacy of add-on HFRT vs. SCT-alone in CHF patients. The non-invasive HFRT showed no safety concerns.

P2196

The short physical performance battery and nutritional status assessment in patients with heart failure

E Eva Dora[1]; J Farkas-Lainscak[2]; D Omersa[3]; M Lainscak[2]
[1]Faculty of Medicine, University of Maribor, Maribor, Slovenia; *[2]General Hospital Murska Sobota, Murska Sobota, Slovenia*; *[3]General Hospital Jesenice, Jesenice, Slovenia*

Introduction: Sarcopenia is characterised by progressive and generalised loss of skeletal muscle mass and is an independent risk factor for mortality in patients with cardiovascular disease. The Short Physical Performance Battery (SPPB) is a simple and objective tool to assess sarcopenia with a cut-off at score = 8 that is indicating the presence of sarcopenia. Limited data is available about SPPB performance in populations at risk and with heart failure (HF).



Objectives: To investigate the prevalence of sarcopenia using SPPB and to compare individual SPPB components in patients with HF and those at risk of HF.
Methods: A cross sectional study assessing the prevalence of HF in general population aged 55 years or more has been conducted in city of Murska Sobota. Overall, 702 persons were screened with NT-proBNP and 290 had concentration = 125 pg/mL; they underwent detailed diagnostic visit with echocardiography, history and physical examination and electrocardiogram. HF diagnosis was based on 2016 European Society of Cardiology guidelines. SPPB, body mass index (BMI), handgrip strength and nutritional status (with Mini Nutritional Assessment (MNA) questionnaire with a cut-off at 23.5 points indicating risk of malnutrition) were used in all participants.
Results: We analysed 290 participants (71 ± 8 years, 35% male, BMI 28.6 ± 5.1 kg/m2); 86 were diagnosed with HF and 204 were at risk of HF. Higher proportion of patients with HF had SPPB score = 8 (26.7% vs 13.9%, p < 0.001), handgrip strength below 30 or 20 kg for men and women, respectively (53.9% vs 25%, p < 0,001), and MNA score < 23.5 (16.3 vs 4.0% p < 0.001). Patients with HF had lower SPPB score (9.63 ± 2.02 vs 10.32 ± 1.62, p = 0.002), handgrip strength (27.0 ± 8.9 vs 23.7 ± 10.5 kg, p = 0.006) and MNA score (25.8 ± 2.43 vs 27.11 ± 1,93, p < 0.001). In individual SPPB components (figure), patients with HF had lower gait speed (0.8 ± 0.2 vs 1.0 ± 0.2 m/s, p < 0.001) but comparable balance test and chair stand test score (p>0.1 for both) than persons at risk of HF. Gait speed test (r=-0.220, p < 0.001) but not SPPB score (r=-0.097, p = 0.082) or MNA score (r = 0.049, p = 0.396) was significantly correlated with NT-proBNP.
Conclusions: Prevalence of sarcopenia and risk of malnutrition is higher in patients with HF than in those at risk of HF. Gait speed test differs most between persons with HF and those at risk of HF.

P2197

Iron deficiency predicts skeletal muscle-derived hemojuvelin in men with heart failure with reduced ejection fraction

M Tkaczyszyn[1]; M Drozd[1]; K Wegrzynowska-Teodorczyk[2]; I Flinta[3]; M Kasztura[1]; M Dziegala[1]; K Kobak[1]; W Banasiak[4]; P Ponikowski[5]; EA Jankowska[1]
[1]Wroclaw Medical University, Laboratory for Applied Research on Cardiovascular System, Department of Heart Diseases, Wroclaw, Poland; *[2]University School of Physical Education of Wroclaw, Department of Physiotherapy, Wroclaw, Poland*; *[3]Wroclaw Medical University, Department of Physiology, Wroclaw, Poland*; *[4]Military Hospital, Cardiology Department, Centre for Heart Diseases, Wroclaw, Poland*; *[5]Wroclaw Medical University, Department of Heart Diseases, Wroclaw, Poland*

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Introduction: In patients with heart failure iron deficiency (ID) can negatively impact muscle performance. Protein hemojuvelin (HJV; produced mainly in the liver) regulates the expression of hepatic hepcidin (key modulator of iron metabolism). Interestingly, HJV is also noticeably expressed in cardiac and skeletal muscle, where its role for health and disease remains largely unknown.
Purpose: We investigated whether ID predicts muscle-derived HJV in men with heart failure with reduced ejection fraction (HFrEF).
Methods: Study population comprised of 50 men with stable HFrEF (left ventricular ejection fraction [LVEF]: 30 ± 7%; age: 64 ± 11 years; NYHA class I or II: 84%; ischaemic aetiology: 82%). Patients were asked to rhythmically handgrip the electronic dynamometer for 300 seconds at 50% of predetermined maximal voluntary contraction (150 squeezes). Before the exercise we catheterized (in a retrograde fashion) superficial vein in the antecubital fossa (which is connected to deep veins draining forearm muscles) to collect blood and measure HJV (ELISA) - before and immediately after exercise (muscle-derived HJV). HJV was also measured in standard peripheral blood. All other laboratory parameters were measured normally in peripheral blood. Iron deficiency (ID) was defined as serum ferritin < 100 μg/L or ferritin 100-299 μg/L with transferrin saturation (TSAT) < 20%.
Results: Concentration of HJV in peripheral venous blood (3.17 ± 0.39 ng/mL) was lower than muscle-derived HJV either before (3.62 ± 0.47 ng/mL) or after (3.55 ± 0.39 ng/mL) handgrip exercise (both p < 0.001), whereas muscle-derived HJV before and after exercise were similar (p = 0.4). In univariable linear regression analyses circulating (peripheral) HJV was not related to HFrEF symptoms, LVEF, laboratory parameters, iron status, and comorbidities (all p>0.05). Muscle-derived HJV before exercise was related to haemoglobin (Hb, ß = 0.34, p = 0.01) and estimated glomelural filtration rate (ß = 0.31, p = 0.03), and there was a trend (all p < 0.1) towards higher HJV in patients with serum ferritin = 100 vs. < 100 μg/L. Muscle-derived HJV after handgrip session was associated with serum ferritin (ß = 0.53, p < 0.001), hepcidin (ß = 0.34, p = 0.02), TSAT (ß = 0.35, p = 0.01), and the presence of ID (ß=-0.45, p = 0.001), and there was a trend (all p < 0.1) towards higher concentration of HJV in patients with higher Hb, lower tumor necrosis factor alpha, and in non-diabetics vs. diabetics. Interestingly, the more fatiguing was the exercise for the patient, the higher concentration of muscle-derived HJV after exercise was measured.
Conclusion: After fatiguing handgrip session men with HFrEF and ID have lower concentration of HJV in venous blood originating from exercising forearm muscles as compared with patients without ID. The interplay between muscle HJV and systemic iron status in HFrEF (in the context of symptomatology, muscle performance, and exercise capacity) needs further mechanistic studies.

P2198

The effect of treatment optimization on the prevalence of sleep disordered breathing and on its phenotype among patients hospitalized with acute decompensated heart failure

B Muk[1]; A Terray-Horvath[2]; P Bogyi[1]; D Vagany[1]; ZS Majoros[1]; B Szabo[3]; A Sztaniszlav[3]; D Pilecky[4]; M Szabo[1]; M Dekany[1]; Z Szakacs[2]; RG Kiss[1]; N Nyolczas[1]
[1]Medical Centre, Hungarian Defence Forces, Cardiology, Budapest, Hungary; *[2]Medical Centre, Hungarian Defence Forces, Neurology, Budapest, Hungary*; *[3]Orebro University Hospital, Cardiology Clinic, Orebro, Sweden*; *[4]Klinikum Passau, Internal Medicine and Cardiology, Passau, Germany*

Background: Sleep disordered breathing (SDB) is known as an underdiagnosed comorbidity associated with poor outcome in patients with heart failure. The recently published SERVE–HF study pointed out that adaptive servo-ventilation therapy, targeting central sleep apnea in HFrEF, might aggravate cardiovascular mortality in patients with stable HFrEF. Therefore, it is important to assess the existence of SDB in HF patients and determine its phenotype.
Aim: The aim of this study was to investigate the prevalence of SDB, the ratio of central and obstructive sleep apnea among patients hospitalized with acute decompensated heart failure (ADHF) during hospitalization and after treatment optimization (TO).
Methods: 122 consecutive HFrEF patients hospitalized due to ADHF (age:61.9 ± 17.0years, LVEF:28.7 ± 10.3%, NYHA:3.0 ± 0.6, ischemic etiology:39.3%, hypertension:56.5%, atrial fibrillation:26.2%, BMI:29.3 ± 6.5kg/m2, NTproBNP:8535 ± 3380pg/ml) were assessed for SDB with polysomnography (PSG) during hospital stay. Patients diagnosed with SDB underwent repeated PSG after TO of HFrEF in outpatient setting.
Results: During hospitalization 103 (84.4%) patients were found to have SDB with apnea-hypopnea
index (AHI) = 5/h and 60 patients (49.2% of the whole cohort) had SDB with AHI = 15/h. Forty (38.8%) of the patients diagnosed with SDB showed central–dominant pattern. No significant difference in the clinical, laboratory, or echocardiographic parameters was found between the SDB patients with different PSG patterns. LVEF (31.4 ± 10.0%) increased as well as NTproBNP (4736 ± 501pg/ml), AHI and central apnea index decreased significantly (29.0 ± 13.2/h vs. 21.7 ± 5.6/h, 14.6 ± 8.1/h vs. 3.6 ± 2.0/h, respectively) after TO (beta-blockers: 91.7%, ACEi/ARBs: 87.7%, MRAs: 73.7%) during the follow-up period. The number of patients with AHI = 15/h decreased from 60 to 48 (39.3% of the whole cohort) after TO, the ratio of central–dominant pattern was reduced to 19.4% (20 patients).
Conclusions: Compared to the results of the recently published heart failure registries, among our patients hospitalized with decompensated heart failure, SDB is highly prevalent comorbidity. In the effect of TO the ratio of patients having moderate or severe SDB decreases. A clear conversion from central to obstructive pattern in sleep apnea evaluated by PSG can be observed. Re-evaluation of SDB after TO, may help to identify those patients with HFrEF who can have benefit from positive airway pressure therapy.

P2199

Determinants of poor outcomes in patients with heart failure and iron deficiency

A Rakisheva[1]; S Berkinbayev[1]; A Klimenko[2]; A Mussagaliyeva[1]; G Junnusbekova[1]
[1]*Scientific Research Institute of Cardiology and Internal Diseases, Almaty, Kazakhstan*; [2]*RUDN University, Moscow, Russian Federation*

Background: Iron deficiency (ID) is very important and common comorbidity in patients with heart failure (HF). The presence of ID is associated with poor prognosis in HF patients. The aim of the study was to assess the determinants of long-term outcomes (6 months mortality rate and 6 months rate for HF rehospitalization) in HF patients with ID.
Methods: 40 patients with HF and ID (31 male, 59 ± 7 years (M ± SD), arterial hypertension (AH) 100%, ischemic heart disease (IHD) 75%, atrial fibrillation (AF) 38%, diabetes mellitus (DM) 30%, known CKD 38%, ejection fraction (EF) 37 ± 9.1) were included. ID was defined using 2016 ESC HF Guidelines (1) serum ferritin < 100 mg/L (absolute ID), 2) serum ferritin 100-299 mg/L and TSAT < 20% (functional ID)). Patients were divided into two groups depending on the presence/absence of ID treatment with i.v. iron (1000 mg once) in addition to standard HF therapy. The outcomes were assessed in 6 months. Mann-Whitney and multiple logistic regression analysis were performed. P < 0.05 was considered statistically significant.
Results: All 40 patients with HF had absolute ID (mean ferritin level 52.7 ± 46.7 mg/L). There were no differences in main patient's characteristics between groups (age 60 ± 6 vs 59 ± 8 years, p>0.05; smoke 25 vs 20%, p>0.05; IHD 85 vs 65%, p>0.05; AH 80 vs 70%, p>0.05; DM 40 vs 20% p>0.05), as well as in clinical presentation of HF symptoms and signs (dyspnoea 60 vs 70%, p>0.05; oedema 25 vs 40%, p>0.05; 6 min walking test 349 ± 110 vs 312 ± 90 m, p>0.05; NYHA II 70 vs 60%, p>0.05; NYHA III-IV 30 vs 40%, p>0.05; EF 39 ± 10 vs 36 ± 9 %, p>0.05, NT proBNP 1433 ± 525 vs 1708 ± 775, p>0.05) and ID criteria (ferritin 56 ± 66 vs 49 ± 27 mg/L, p>0.05 and TSAT 17 ± 10 vs 18 ± 11 %, p>0.05). There was lower rate of poor outcomes in group with i.v. iron (5 vs 26%, p < 0.05). The patients without i.v. iron therapy had higher 6 months mortality rate (5 vs 0%, p < 0.05) and higher 6 month rate for HF rehospitalizations (21 vs 5%, p < 0.05). DM (OR 2.6 95%CI 0.64-10.97), CKD (OR 1.33 95%CI 0.58-1.97) and absence of i.v. iron therapy (OR 2.3 95%CI 1.01-2.94) were determined to be significant and independent factors for poor outcomes in patients with HF and ID.
Conclusions: Diabetes mellitus, chronic kidney disease and absence of ID therapy are among main determinants of long-term outcomes in patients with HF and ID. The use of predictive factors might be useful for the clinician to suspect the patient population with higher risk of poor outcomes and to apply adequate preventive strategy.

P2200

Prevalence of depressive symptoms in patients hospitalized with heart failure in a Greek tertiary hospital amidst the financial crisis

G Michas[1]; K Grigoriou[1]; T Thomopoulos[1]; E Malaxianaki[1]; K Panourgia[1]; A Trikas[1]
[1]*Elpis General Hospital, Cardiology, Athens, Greece*

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Background/Introduction: Heart failure (HF) is a global pandemic affecting more than 26 million patients worldwide and its overall burden is expected to increase over time. Depression remains a major public health problem and by 2020 it will be the second leading cause of world disability. In Greece, since the beginning of the financial crisis there has been a steep increase in one-month prevalence of major depression (MDD) in the general population from 6.8% in 2009 to 12.3% in 2013. The average prevalence of MDD in HF patients is estimated at 33.6% when questionnaires are used.
Purpose: The purpose of the study was to estimate the prevalence of depression in HF patients using the Patient Health Questionnaire-9 (PHQ-9), which is proposed by the American Heart Association as a screening tool of depression in HF, and to explore potential associations of depressive symptoms with socio-demographic and clinical characteristics of HF patients.
Methods: The study sample consisted of 104 HF patients who were hospitalized in the Cardiology Department of a tertiary hospital in Athens, Greece within a period of ten months. Inclusion criteria were diagnosis of HF, age = 18 years, and sufficient understanding of the Greek language. Patients were excluded if they were diagnosed with another life-threatening disease (e.g. cancer) or a chronic severe psychiatric condition (e.g. psychosis), had a history of alcohol abuse or dependence in the past six months, and were receiving antidepressant medication. Data collection was performed using a questionnaire consisting of three parts: The socio-demographic and clinical characteristics, the results of laboratory and diagnostic work-up, and the PHQ-9 scale.
Results: Of the 104 HF patients, 66 (63.5%) were males and 38 (36.5%) females with an average age of 71.4 ± 13.6 years. Proportion of patients with NYHA classes I, II, III, and IV were 7.8%, 45.1%, 40.2%, and 6.9%, respectively. When the ejection fraction (EF) was considered, the proportion of patients with reduced, preserved, and mid-range EF were 56.7%, 26%, and 17.3%, respectively. A staggering 75% reported depressive symptoms (PHQ-9 score = 5), whereas the prevalence of MDD was 47.1% (PHQ-9 score = 10). Among the factors examined, worse self-reported heath status (p = 0.001), NYHA class (p = 0.014), and lower folate levels (p = 0.03) were associated with the presence of MDD.
Conclusion(s): The medical community must take measures to identify, evaluate and manage depression in HF patients, the prevalence of which is particularly high in this population. Furthermore, HF patients with certain characteristics seem to be more prone to MDD. A recent study conducted in Greece showed that 24.2% of HF patients suffered from MDD; our study findings suggest that this prevalence has almost doubled within the last four years. The financial crisis might have exerted a negative effect on the prevalence of depression amongst HF patients.

P2201

The association of iron deficiency in patients with different types of heart failure

O Ozcan Orscelik[1]; EE Sahin[1]; H Uyar[1]; IT Ozcan[1]; A Celik[1]
[1]*Mersin University, Cardiology, Mersin, Turkey*

Introduction: Iron deficiency (ID) is common in patients with chronic heart failure and it is associated with poor functional status and quality of life. Although there are many studies showing that the incidence of ID is high in heart failure patients with reduced-preserved ejection fraction, insufficient studies are in the literature related to ID linked other types of heart failure. This study aimed to show the iron deficiency in patients with different types of heart failure.
Methods: This is a single center observational study included the consecutive 138 patients with HF. Iron deficiency was defined as follows: serum ferritin <100 mg/L, or transferrin saturation <20% in case of serum ferritin level is 100-299 mg/L. We divided the patients into three groups as according to HF types (HFrEF, HFmrEF and HFpEF).
Results: 78 of 138 patients had HFrEF, 28 patients had HFmrEF and 32 patients had HFpEF. There was no significant difference in age, gender, hemoglobin, MCV, Na, K, Cre, AST levels, pro-BNP and diastolic blood pressure between groups of heart failure. ID was seen in 68% patients in HFrEF group, 82.1% patients in HFmrEF groups and 68.8% patients in HFpEF group and there was no statistical significant difference between the three groups (Table 1, Figure 1A). When all heart failure patients were examined for ID, it was seen that ID was not affected by sex, diabetes

and hypertension. However, higher iron deficiency ratios were seen in patients with ischemic HF than non-ischemic heart failure. (Figure 1B).
Conclusion: Iron deficiency is a common comorbidity in all types of heart failure. The patients with ischemic HF might be more related to iron deficiency.

Table 1

	HFrEF (n = 78)	HFmrEF (n = 28)	HFpEF (n = 32)	p
Age, year	62.4 ± 13.3	66.5 ± 13.8	68 ± 12.7	0.09
Diabetes mellitus, n/%	34/%43.6	12/%42.9	16/%50	0.80
Hypertension, n/%	42/%53.8	12/%42.9	24/%75	0.033
Ischemic etiology, n/%	39/%50	16/%57.1	12/%35.7	0.29
Hemoglobin, g/dL	12.6 ± 2.2	12.1 ± 1.8	11.8 ± 1.8	0.16
MCV, fl	86 ± 6.6	87.5 ± 5.7	83.6 ± 8.1	0.08
EF, %	28.1 ± 8.2	43.2 ± 6.8	57.7 ± 10.3	<0.001
Ferritin, ng/mL	75.8 (13-1411)	52 (4.7-559)	63.1 (5-872)	0.38
TSat, %	25.7 (6.2-392)	21.6 (7-771)	20.3 (5.7-228)	0.78
Iron deficiency, n/%	53/%68	23/%82.1	22/%68.8	0.34
Pro-BNP, pg/mL	2165 (10-35000)	995 (3-25177)	1346 (12.4-14066)	0.08

Baseline features of heart failure groups.

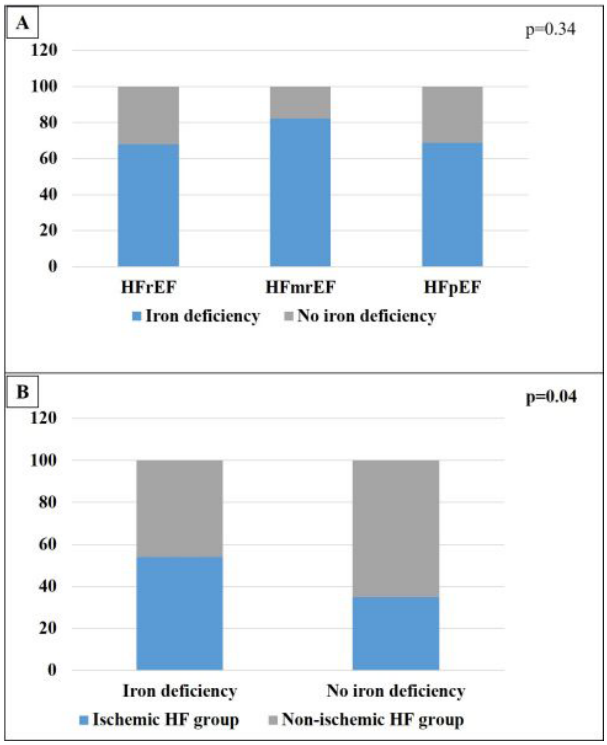


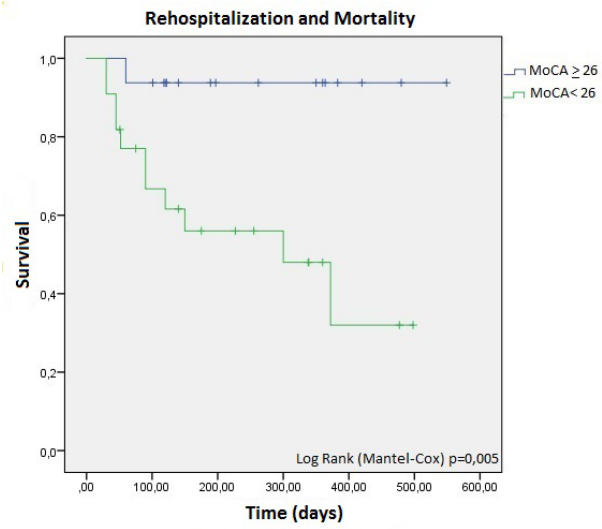
Figure 1

P2202
Cognition and heart failure

J Rigueira[1]; J Ribeiro Agostinho[1]; I Aguiar-Ricardo[1]; R Santos[1]; N Andre[1]; A Nunes-Ferreira[1]; ISS Goncalves[1]; N Cunha[1]; R Pires[2]; F Veiga[1]; M Pedro[1]; FJ Pinto[1]; D Brito[1]
[1]Santa Maria Hospital, CHLN, CCUL, Lisbon University, Cardiology Department, Lisbon, Portugal; *[2]Faculty of Psychology and Educational Sciences, CINEICC, University of Coimbra, Coimbra, Portugal*

On behalf of: RICA-HFTeam

Introduction: Cognitive impairment (CI) is common in patients with heart failure (HF), and may be associated with deterioration of quality of life and a negative prognosis.
Aim: To evaluate the prevalence of CI in a population of patients with HF and to identify the most affected cognitive domains and their prognostic impact.
Methods: Single center prospective study of patients admitted for acute or chronic decompensate HF (index-admission), who gave written informed consent to be included in a post-discharge HF-program (by protocol).
Cognitive function was assessed at hospital discharge and at 12+3 months during follow-up, using the validated Portuguese version of the Montreal Cognitive Assessment (MoCA), which defines CI by a score < 26. Correlations between CI and HF therapy prior to admission, blood tests results, chronic anxiety/ depression (Hospital Anxiety and Depression Scale, validated Portuguese version), and rehospitalization and/or mortality during follow-up, were looked for. Statistics: Cox regression, Kaplan-Meier survival analysis, Spearman, Mann-Whitney and Wilcoxon correlation analysis, were used.
Results: 43 patients included, mean age 67+11.3 years, 68.9% men; 48.9% had CI, focused mainly on the following cognitive domains: visuospatial, language and delayed recall. Men appeared to perform better at MoCA (p = 0,026), as well as patients on ACE inhibitors/ARB therapy prior to index-hospitalization (p = 0,009).
CI was associated with HbA1c (p = 0,021, r= 0,395), albumin (p = 0,07, r= -0,76) and bilirubin (p = 0,04, r= -0,48). Anxiety and depression were not associated with CI.
Patients with a better MoCA performance showed greater ability to deal with their disease status (assessed by the Kansas City Cardiomyopathy Questionnaire) (p = 0,38).
During follow-up there was no significant difference in the CI score, but a decline in the naming ability was observed (p = 0,031). The rates for rehospitalization and mortality were 31% and 2.3%, respectively. The presence of CI predicted the occurrence of rehospitalization/mortality (p = 0,026).
Conclusion: CI was frequent in HF patients, may be related in part to the nutritional profile, and was associated with a reduced capacity to deal with their HF condition, being a predictor of rehospitalization and/or mortality in this population.



P2203
Importance of an intradialysis changes of cardiac troponin-t measured by sensitive assay in anuric hemodialysis patients

S K R Vamsi Varahabhatla[1]; INGRID Prkacin[2]; A Savuk[2]; TOMO Svagusa[3]; PETER Fekete[4]; PAVAO Findri[4]
[1]Zaporizhzhya State Medical University, General medicine , Zaporizhzhya, Ukraine; *[2]Clinical hospital Merkur , Internal medicine , Zagreb, Croatia*; *[3]University Hospital Dubrava, Internal medicine , Zagreb, Croatia*; *[4]University of Zagreb School of Medicine, Internal medicine , Zagreb, Croatia*

Background: Compared with the general population cardiac morbidity and mortality is much higher in hemodialysis patients (HD pt). Improved survival after acute myocardial infarction(AMI) with structural cardial abnormalities have led to an increased incidence of heart failure (HF): 1-3% in general population, 10% of elderly and approximately 40% of HD pt. In 25-87% HD pt regional left ventricular dysfunction developed early during HD and is associated with worse outcome and progressive HF. Levels of cardiac troponins in plasma are often elevated in hemodialysis (HD) patients without evidence of AMI. We hypothesized that

systemic inflammation could be explanation of elevated troponins in HDpt because of negative effects on endothelial function of the myocardial microcirculation.
Aim: We investigated the effect of hemodialysis (HD) on elimination of cardiac troponin T (TnT-hs) in anuric patients.
Patients and Methods A total of 45 adult (= 18 years) anuric patients without cardiac symptoms of 2 Dialysis Center in Croatia were on maintenance HD for more than 3 months and gave informed consent were eligible for this prospective study.
The median age was 66 (IQR 56.5-75.5) years and 17 (35%) of patients were female. Patients were on bicarbonate dialysis for a median of 2.5 years. 91% patients had hypertension.Patients with recent acute myocardial infarction or with heart failure NYHA class 3-4 were excluded. The concentration of high sensitive troponin T (hsTnT) was determined by the immunochemical method with electrochemiluminiscent detection on a Roche cobas® e411 analyzer using Roche Diagnostics Troponin T high sensitive (TnT-hs) assay. Blood samples for TnT-hs and hematocrit were collected before (preHD) and at the end (postHD) of the first dialysis session of the week. Samples were centrifuged within 30 min of collection at 3,500 rpm for 10 min. Plasma levels of cTnT were corrected for hemo-concentration.
Mann-Whitney U test and Student T test analyses were used for the comparison of parametric and non-parametric variables to identify factors that were associated with intradialysis changes in concentration of TnT-hs.
Results: Cardiac TnT-hs was elevated in all patients before HD (100 %). The difference between median concentration of TnT-hs pre (82.99 ± 47.44 ng/L) and postHD (82.39 ± 44.91 ng/L) was not statistically significant (Z -0.38228, p = 0.70394). The difference between the mean value of the total measured TnT-hs concentration pre and postHD was 113.275ng (CI 84.34-142.21ng. Difference in total quantity of TnT-hs in pre and postHD was statistically significant (t = 7.8906 uz p < 0.001).
Conclusions: The mechanism why cTnT levels are elevated in HDpt is not clear but it may be related to the HD procedure and end stage kidney disease. Future studies should address whether HD-related factors are associated with changes in troponins and possible impact on earlier prevention of silent HF .

P2204
Association of atrial fibrillation and chronic heart failure, FAR NHL registry - FARmacology and NeuroHumoraL activation

R Labrova[1]; J Spinar[1]; J Parenica[1]; L Spinarova[2]; F Malek[3]; O Ludka[1]; K Labr[2]; M Spinarova[2]; J Jarkovsky[4]
[1]Masaryk University, Faculty Hospital Brno, Department of Internal Cardiology Medicine, Brno, Czech Republic; *[2]St. Anne's University Hospital, Brno, Czech Republic*; *[3]Na Homolce Hospital, Prague, Czech Republic*; *[4]Institute of Biostatistics and Analyses of Masaryk University, Brno, Czech Republic*

Background: Atrial fibrillation is a very common accompanying disease of heart failure and affects one another negatively. Each of these diseases can be the cause and consequence of the other. Increasing age in the population and better treatment of cardiovascular disease leads to more and more frequent occurrences in the population in both of these diseases. Patients hospitalized with heart failure have three times more often atrial fibrillation than patients without heart failure. It is not entirely clear whether atrial fibrillation is an independent risk factor for death in patients with heart failure.
Methodology and Results: Three 1050 patients with chronic systolic heart failure with moderate or severe left ventricular dysfunction - with EF less than 50% - were enrolled in three university hospitals within the FARmacology and NeuroHumoraL activation registry (FAR NHL) over 12 months. Patients had to be stable for at least one month for established medication. Men were 848 (80.8%), mean age 63.9 (SD + -12.0), BMI 29.1 (SD + -4.9), average heart rate 73.6 / min (SD + -12.8). The main etiological factor for chronic heart failure was 49.4% ischemic heart disease, 42.3% dilated cardiomyopathy, a small part was a combination of both in 0.8%, hypertrophic cardiomyopathy was 0.5%. Diabetes mellitus was present at 38.3%. 13% patients were in New York Heart Association (NYHA) functional class I, 61.3% NYHA II and 25.7% NYHA III and IV. Based on echocardiography, mean left ventricular ejection fraction was 30.6% (SD + -8.8). Atrial fibrillation was present in the enrollement day and / or in a medical history in one third of patients - 362 (34.5%). In patients with chronic heart failure, when compared atrial fibrillation was not and was present, there was a significant difference in heart rate of 71 vs 80 (p < 0.001), betablocker use did not differ significantly in both groups 94.1 vs 92.2% (p = 0.354). There was difference in digoxin treatment 29.0 versus 61.0% (p < 0.001), as well as a combination of beta-blocker and digoxin 27.0 versus 58.9 (p < 0.001). Compared to group of patients without atrial fibrillation present and present atrial fibrillation, hypertension is present in 64.2 vs 73.8%, CMP 9.5 vs 12.1%, COPD 12.8 vs 17.0%, previous hospitalization for heart failure in last year 24.2 vs. 29.8%. This corresponds to the average levels of NTproBNP 1247 vs 2218 pg / ml. Conclusion: According to FAR NHL, patients with chronic heart failure have up to one third of atrial fibrillation. Patients with atrial fibrillation have more comorbidity, their strict treatment is necessary to prevent myocardial remodeling and thus to maintain arrhythmia. In addition, to reduce the risk of CMP, hospitalization for heart failure and reduce mortality. The results of the FAR NHL and the one-year follow-up will be presented at the Congress of Heart Failure 2018 in Vienna.

P2205
The external respiration function in pulmonary hypertension at patients with dilated cardiomyopathy

YR Akhmatov[1]; TA Abdullaev[1]; I A Igor Tsoy[1]; RSH Bekbulatova[1]
[1]Specialized Cardiology Center of the Republic of Uzbekistan, heart failure , Tashkent, Uzbekistan

The aim: Comparative evaluation of the function of external respiration in pts with dilated cardiomyopathy (DCM), depending on the presence or absence of pulmonary hypertension (PH).
Material and methods: 91 pts with idiopathic DCM (34/57 as w/m, mean age = 46.4 ± 13.7 years old) were included in the study, of which 25 (27.4%) had right ventricular DCM (RVDCM). The 6-minute walking test (6MWT), ECG, EchoCG and ERF were evaluated. I gr - 48 pts with mean pulmonary artery pressure (MPAP)- 48.1 ± 10.7 mmHg. II gr - f 43 pts with MPAP of 25.7 ± 8.3 mmHg. There were 11 (23%) in 1gr. And 14 (32.5%) in 2 gr. with RVDCM
Results: According to EchoCG, it was found that the systolic pressure in the pulmonary artery was 48.1 ± 10.7 mm Hg in I gr. - 71% of cases had PAH of 1 degree and 29% of pts had PAH of II degree. In the 2d. The mean degree in II gr. was 25.7 ± 8.3 mmHg. According to the results of spirometry in pts of I gr there was a significant decrease in every indicators of ERF. Performing the correlation analysis, an inverse relationship was found between MPAP and the Tiffno index (p <0.05), as well as a direct relationship between FVC (53.17 ± 9.21%) and the length of the distance traveled by 6MWT (206.7 ± 80.3 m, p = 0.017). There were significantly higher results in the 2 gr. There were abnormalities of EFR in pts with DCM, characterized as restrictive, i.e. caused by stagnation of blood in the pulmonary system (decrease in FVC, FEV1, ratio of FEV1/FVC). At the same time, There were no signs of bronchial obstruction (FEV1 / FVC was above 75%) in all cases.
Conclusion: Our study shows a high prevalence of secondary pulmonary hypertension (52.7%) in pts with DCM with biventricular heart failure and primary right ventricular lesion. There is a direct statistically significant correlation between the systolic pressure in the pulmonary artery and the Tiffno index as well as in 6MWT.

P2206
Long-term effect of patiromer for hyperkalaemia treatment in patients with HFmrEF and diabetic nephropathy on RAAS inhibitors

B Pitt[1]; M Mayo[2]; D Garza[2]; S Arthur[2]; M Lainscak[3]
[1]University of Michigan, Ann Arbor, United States of America; *[2]Relypsa, Inc., a Vifor Pharma Group Company, Redwood City, United States of America*; *[3]General Hospital Murska Sobota, Murska Sobota, Slovenia*

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Background: Heart failure (HF) patients (pts) with mid-range ejection fraction (HFmrEF, 40-49%) are an important subgroup requiring further study. Renin-angiotensin-aldosterone system inhibitors (RAASi) have not been shown to reduce mortality in these pts but are often used to manage coexisting conditions, such as hypertension (HTN), diabetes (DM), and CKD, or to provide symptom relief. Chronic hyperkalaemia (HK) and CKD may complicate use of RAASi. Patiromer, a sodium-free nonabsorbed potassium (K+)-binder that uses calcium as the counter-exchange ion, is approved for the treatment of HK, including in the US, the EU, and Australia.

Table

Mean serum K+ over 52 weeks in the subgroup of HFmrEF patients

Timepoint (n)	Mean serum K+, mmol/L (SE)	LSM Δ from baseline in serum K+, mmol/L (SE)
Baseline (n = 44)*	5.21 (0.06)	
Day 3 (n = 42)	4.91 (0.06)	-0.31 (0.06)
Week 4 (n = 40)	4.51 (0.06)	-0.64 (0.09)
Week 24 (n = 37)	4.60 (0.06)	-0.66 (0.08)
Week 52 (n = 31)	4.66 (0.07)	-0.62 (0.10)

From an ANCOVA model with HK stratum at baseline as a fixed effect and baseline serum K+ as a covariate. LSM, least squares mean. Values in parentheses are standard error. *Two patients were excluded from the analysis as they had no central laboratory serum K+ values at baseline.

Purpose: The long-term effects of patiromer on serum K+ in HFmrEF pts on RAASi were examined in a post-hoc analysis of AMETHYST-DN.
Methods: Pts with CKD, type 2 DM and HK (baseline K+ >5.0– < 6.0 mmol/L) were randomized to patiromer starting doses 8.4-33.6 g/d, divided twice daily. Pts with HTN were eligible if uncontrolled at screening (SBP: >130 to = 180mmHg; DBP >80 to = 110mmHg). Pts remained on RAASi during study treatment. Changes in mean K+ (central lab) from baseline through 52 wks were evaluated in the HFmrEF subgroup.
Results: 46/306 randomized pts had HFmrEF (100% Caucasian, 74% male, 72% = 65 yr; mean [SD] EF = 44 [3] % and eGFR = 42 [14] mL/min/1.73m^2). All had HTN (baseline mean BP 154/84 mmHg). K+ was reduced to < 5.0 mmol/L at the 1st post-baseline visit (day 3) and through 52 wks (Table). Thirty-three (72%) pts reported = 1 adverse event (AE); influenza and worsening of CKD were the 2 most common AEs (5 pts each; none severe). Two pts had K+ < 3.5 mmol/L; 1 pt had serum Mg < 0.49 mmol/L. Mean (SE) change from baseline to 52 wks was: eGFR, +5 (4) mL/min/1.73m^2; SBP/DBP, -21 (4)/-10 (2) mmHg.
Conclusions: These post-hoc results suggest that patiromer allows control of HK in HFmrEF pts on RAASi and require prospective evaluation.

P2207
Awareness of heart failure is insufficient in Poland-results from awareness survey

MI Marta Izabela Kaluzna-Oleksy[1]; J Migaj[1]; M Dudek[1]; A Gwizdala[1]; A Pietrucha[2]; P Leszek[3]; EA Jankowska[4]; I Uchmanowicz[4]; S Stoerk[5]; E Straburzynska-Migaj[1]
[1]Poznan University of Medical Sciences, Ist Department of Cardiology , Poznan, Poland; *[2]John Paul II Hospital, Krakow, Poland*; *[3]Institute of Cardiology in Anin, Warsaw, Poland*; *[4]Wroclaw Medical University, Wroclaw, Poland*; *[5]University Hospital of Wurzburg, Wurzburg, Germany*

Introduction: Heart failure (HF) is a clinical condition with a diverse background. The most prevalent cause of HF in Europe is coronary artery disease (CAD). Depending on etiology of HF, its natural history may vary; nevertheless, it is always associated with significant morbidity and mortality. The burden of HF is rising globally, which makes general awareness of HF the more significant. Previous studies show that patients' knowledge of heart failure, its incidence, risk and symptoms, seems poor. This study aimed to analyze the HF awareness in general population in Poland and possibly to show the need for improvement of information sources.
Methods: This study analyzed information from surveys conducted during International Heart Failure Awareness Day in Poland (in 2016 and 2017). The questions concerned demographics, knowledge of HF, its symptoms, natural history, and treatment possibilities. Points were awarded for each question concerning the heart failure awareness (awareness score), and the mean results were compared between various demographic groups as well as between the years 2016 and 2017.
Results: 454 and 273 responders completed the HF awareness survey in 2016 and 2017 respectively. The participants were mostly women (65%), young people <65 years (82%) and non-medical profession (77%). Most of the participants declared awareness of the heart failure symptoms (68%). The awareness score showed no differences between both sexes and a better HF awareness in older (= 65 years) and in more educated people in 2016 (both p <0,001), but this relationship was not observed in 2017 (p = 0,42). The mean awareness score was worse in 2017 compared to 2016 (p <0,001).
Conclusions: The knowledge on HF in Poland is relatively poor. Lack of public awareness of symptoms, prognosis, and management of HF may lead to worse self-care and late reaction to exacerbation of the disease. In spite of numerous campaigns to increase the awareness of HF, it has not improved during the last year. Perhaps a multi-level individualized education depending on age should be provided.

Chronic Heart Failure - Other

P2208
Health care assistance in heart failure: the mexican perspectives

EJJ Eduardo Julian Jose Chuquiure[1]; C Silva-Ruz[1]; M Chuquiure-Gil[2]; M Gabriela Mendez[3]; R Hernandez-Isidro[1]; E Morales-Hinojosa[1]; K Jacobo-Garcia[1]; O Fiscal-Lopez[1]
[1]Instituto Nacional de Cardiologia "Ignacio chavez", Mexico City, Mexico; *[2]Instituto Tecnologico de Estudios Superiores de Monterrey, Escuela de Medicina, Monterrey, Mexico*; *[3]Universidad del estado de México, Medicina, ciudad neza, Mexico*

Purpose: In Latin America, there are few data of Heart Failure (HF). The purpose of the present investigation was to obtain information from prominent cardiologists on the prospects of heart failure care in Mexico.
Material and Method: On July 2017, 43 semi-structured surveys were carried out by cardiologists with more than 10 years of experience from different states of the republic. The survey consists of 18 closed (8) and open (10) questions, in five relevant topics: Objectives, Therapeutics, Follow up (Hospital Re-admission and mortality), Guidelines Adherence and Medical Team (guidelines) and Team conformation for the treatment of HF in Mexico.
Results: In this HF Mexican expert consensus, we conclude: 56% of respondents attend 312 to 520 patients-year per center. Quality of life is the most important objective in HF Treatment (44.2%). Main objectives for prevention in general population are: Massive information campaigns and strengthen preventive medicine. On the other hand, Economic factor is the principal negative aspect, due to the high costs of medicines. 81.4% of specialists consider that their adherence to clinical guidelines is good or excellent, to improve clinical practice and unify criteria. We describe that ACE-I / ARB's plus Beta-blockers are the most commonly used drugs (81.4%). Principal objectives: Decrease mortality and hospitalizations, improve the quality of life, and optimize management. The main strategies to avoid hospital readmissions and mortality are: HF specialized Centers Conformation, at all attention's levels, to monitor and manage clinical follow-up. We recommend that communication with the multidisciplinary team is essential, and the creation of a model of care adapted for our Mexican population.
Conclusions: We recognize an inherent need in Mexico, so we propose to organize health services in a planned manner to prevent, intervene, organize and provide optimal treatment for the adverse effects of heart failure

P2209
Needs and burden of informal heart failure caregivers: the HF2Care study

A Durante[1]; R Juarez-Vela[2]; J Boyne[3]; E Vellone[1]
[1]University of Rome Tor Vergata, Biomedicine and Prevention, Rome, Italy; *[2]University of San Jorge, Zaragoza, Spain*; *[3]Maastricht University Medical Centre (MUMC), Maastricht, Netherlands*

On behalf of: HF2Care Team
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Background: People affected by HF require a high level of care and must perform good self-care to prevent the worsening of the disease and to maintain their psychological well-being. Given this issue, informal caregivers (CG) may offer an important contribution to patients' care. However, knowledge on caregivers' needs-physical, psychological, social, economic and environmental needs-is still poor. Recent literature shows that being a CG imposes a substantial burden that increases over the trajectory of the illness and affects CG quality of life. Despite the importance of CG in HF care, few studies have explored the needs and burdens of HF CG in relation to the CG and patient characteristics.
Purpose: The aim of this study is to describe HF caregivers' needs and burdens, and to associate HF caregivers need and burden to specific caregivers' (e.g., amount of caregiving hours) and HF patients' characteristics (e.g., NYHA class) in three European countries.
Methods: This is an exploratory sequential mixed-method study that is going to be conducted in two phases. The first phase is qualitative and data have been already collected on Spanish and Italian HF caregivers with face-to-face interviews. The interviews, with 21 open-ended questions, have been conducted in each country in the native language, have been digitally recorded and transcribed verbatim. Content analysis will be used to analyse them. The second phase, that is quantitative and is still ongoing, will consist of two data collections at 6 and 12 months from enrolment. Quantitative data will be analysed with descriptive and inferential statistics. Qualitative and quantitative data will finally be merged to understand the complex nature of HF caregiving, matching caregivers'need and burden with patients and CG characteristics.
Results: Spain has already concluded the first phase of the study, while Italy and Netherlands are still enrolling the caregivers. To date, 92 caregiver and patient dyads have been enrolled in Spain. These caregivers were 59.7 (±14.4) years old, mostly females (77.2%), patients' spouses (31.6%) or adult children (60%). HF patients were 82.2 (±8.3) years old and equally distributed among females (50.5%) and males. The caregivers provided their patients with an average of 11.6 (±9) hour of caregiving per week, and most of them declare to live with the patients (52.2%). The 23.9% of caregivers were unemployed because of caregiving and just the 17.4% of caregivers reported enough income which allowed them to live well. Content analysis on the interviews is in progress, results will be available for the Congress.
Conclusion: Results of this study will allow a better characterization of HF caregiver needs and burden. Since literature shows that caregivers'need and burden influence HF patients' outcomes, we expect the results of this study have the potential knowledge to develop interventions for caregiver well-being and indirectly for patients' outcomes.

Acute Heart Failure - Pathophysiology and Mechanisms

P2210
Relationship between early drop 16% in systolic blood pressure and worsening renal function in patients with acute heart failure

T Takehiko Kido[1]; T Okabe[1]; Y Asukai[1]; S Simazu[1]; T Kimura[1]; J Saito[1]; Y Oyama[1]; W Igawa[1]; M Ono[1]; S Ebara[1]; K Yamasita[1]; M Yamamoto[1]; T Yakusizi[1]; N Isomura[1]; M Ochiai[1]
[1]Showa University Northern Yokohama Hospital, Division of Cardiology and Cardiac Catheterization Laboratories, Yokohama, Japan

Background: Worsening renal function (WRF) is associated with poor prognosis in patients with heart failure (HF). We hypothesized that early drop in systolic blood pressure (SBP) is associated with WRF.
Purpose: Our purpose was to identify the association between early drop in SBP and WRF.
Methods: We retrospectively investigated predictors of WRF in patients hospitalized for acute HF between April 2010 and July 2016. WRF was defined as a relative increase in serum creatinine of at least 25% or an absolute increase in serum creatinine ?0.3 mg/dL from the baseline. SBP was measured on admission and each 4 hours. The early drop was defined as drop in SBP within first 24 hours.
Results: A total of 411 patients with acute HF were enrolled. The mean age was 73.0 ± 15.0 years and 60.7% were male. WRF occurred in 139 patients (34%). Mean SBP on admission was significantly higher in patients with WRF than in patients without WRF. However, mean SBP after 24 hour from admission was significantly lower in patients with WRF than in patients without WRF. The receiver operating characteristic curve analysis identified that the optimal cut-off value for WRF was 16% drop in SBP. Multivariate Cox regression analysis showed that early drop in SBP ?16% (OR, 6.565; 95% CI 3.242-14.221; < 0.001), inotropic agents, and tolvaptan were associated with WRF.
Conclusion: Early drop in SBP ?16% was a strong predictor of WRF in patients with HF.

P2211
Dynamic changes in serum chloride concentrations during worsening of heart failure and its recovery following conventional diuretic therapy

H Hajime Kataoka[1]
[1]Nishida Hospital, Oita, Japan

Background: I recently demonstrated that changes in vascular volumes are independently associated with the changes in serum chloride concentration during worsening of heart failure (HF) and its resolution by diuretic therapy (AHA2015/ESC2016). Few data are available, however, regarding the dynamic changes in the serum chloride concentrations in HF pathophysiology.
Purpose: The aim of the present study was to investigate changes in the serum chloride concentration, including its relation to the serum sodium concentration, under worsening HF and its recovery following conventional diuretic therapy.
Methods: Blood test data, including measurements of serum albumin/solutes and b-type natriuretic peptide, at both worsening and recovery of HF status were obtained from 47 HF patients.
Results: Under clinically stable to worsening HF, the serum sodium concentration increased from 139 ± 4.1mEq/L to 141 ± 5.07mEq/L (P < 0.05) and the serum chloride concentration increased from 101 ± 5.36mEq/L to 104 ± 5.44mEq/L (P < 0.01) among all patients. After resolution of worsening HF by treatment with conventional diuretics, both the serum sodium concentration and serum chloride concentration decreased significantly to 138 ± 5.12mEq/L and 99.5 ± 5.33mEq/L, respectively (P < 0.0001 for each). The absolute changes in the serum chloride concentration from clinically stable HF to worsening HF tended to be greater than those in the serum sodium concentration (2.72 ± 6.02mEq/L vs. 1.70 ± 4.34mEq/L, P = 0.079), and absolute changes in the serum chloride concentration from worsening HF to its recovery following treatment with conventional diuretics were greater than those in the serum sodium concentration (-4.45 ± 5.23mEq/L vs. -2.87 ± 4.38mEq/L, P = 0.0068).
Conclusions: Differential changes exist between serum sodium and chloride concentrations under worsening of HF and its resolution by conventional diuretic therapy. The greater changes in the serum chloride concentration than in the serum sodium concentration under HF state transitions suggests that chloride contributes more to serum tonicity and to HF pathophysiology than sodium.

Acute Heart Failure - Epidemiology, Prognosis, Outcome

P2212
Is there an obstructive sleep apnea paradox in cardiovascular disease? effect of obstructive sleep apnea on outcomes of acute heart failure exacerbations

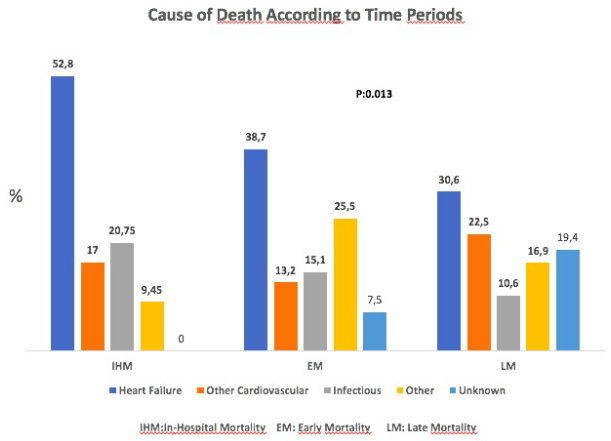
M Mario Rodriguez[1]; W Rzechorzek[1]; C Krittanawong[1]; X Wei[1]; A Manguba[1]; B Sabharwal[1]; C Godoy Rivas[2]; J Puma[3]; E Herzog[1]
[1]Icahn School Of Medicine at Mount Sinai/ Mount Sinai St. Lukes-West Hospital, Department of Medicine, Division of Cardiology , New York, United States of America; *[2]Cleveland Clinic Foundation, Cleveland, United States of America*; *[3]Columbia University Medical Center, New York, United States of America*

Background: Obstructive Sleep Apnea (OSA) is known to increase morbidity and mortality in patients with chronic heart failure, but impact on outcomes during acute heart failure exacerbations is unknown.
Purpose: describe the impact that obstructive sleep apnea has on the outcomes of acute heart failure exacerbations and evaluate the possibility of an OSA paradox in cardiovascular disease.
Methods: A retrospective analysis using the 2014 United States Nationwide Inpatient Sample was performed. Patients above 18 years with primary diagnosis of acute heart failure (AHF), systolic heart failure (SHF) and diastolic heart failure (DHF) and secondary diagnosis of OSA were included. End stage renal disease patients were excluded. Primary outcome was in-hospital mortality. Secondary outcomes included length of stay, cost of stay, shock, utilization of mechanical ventilation, acute kidney injury requiring dialysis (AKID), use of non-invasive ventilation (NIV), cardiac arrest, and short term mechanical circulatory support. Diagnoses were identified using ICD-9- CM codes .Multivariate logistic regression analysis adjusting for obesity, age, race, gender and hospital location was done using STATA 15.
Results: 135,008 patients with AHF were identified. In the overall AHF cohort 101,070 patients had a
history of OSA, corresponding to 43% of patients with SHF and 57% of patients with DHF. 41% of OSA
with AHF patients were female. Mean age was 66 years. Multivariate regression analysis showed decreased odds of death in the AHF(OR 0.68 p < 0.001), SHF (OR 0.65 p < 0.001) and DHF (OR 0.67 p = 0.001) groups, along with decreased odds of mechanical ventilation utilization in the AHF(OR 0.85 p = 0.01) cohort. There was also a trend towards decreased cardiac arrest in the AHF (OR 0.73 p = 0.005) and SHF (OR 0.64 p = 0.01) groups , as well as decreased odds of AKID (OR 0.75 p = 0.02) and short term mechanical circulatory support (OR 0.70 p = 0.02) in the AHF group. NIV utilization odds was increased among the AHF (OR 2.44 p < 0.001) , SHF (OR 2.5 p < 0.001) and DHF (OR 2.2 p < 0.001) groups. There was a non statiscally significant increased in length of stay along with decreased total charge.
Conclusions: Patients with diagnosis of obstructive sleep apnea had decreased mortality and increased
non invasive ventilation utilization during acute heart failure exacerbation. It is unclear if this represents a true paradox after adjusting for obesity or if it represents the effect of non invasive ventilation utilization. Further studies adressing this issue are needed.

P2213
Heart failure mortality: a multi-causative event

E Enrique Fairman[1]; F Delfino[1]; V Mauro[1]; A Charask[1]; Y Castillo Costa[1]; A Raffaeli[1]; F Bottini[1]; A Barsotti[1]; C Barrero[1]
[1]Clinica Bazterrica Clinica Santa Isabel, buenos aires, Argentina

Acute decompensated heart failure is frequently observed in advanced age and portends an ominous evolution, particularly in the first year after the acute event. Nevertheless, in many cases mortality is not attributed to heart failure. The objective of this analysis is to determine the different causes of mortality and their relative prevalence throughout the first year of evolution in patients admitted with acute decompensated heart failure.
Methods: Between February 2010 and December 2016, 865 consecutive patients admitted with heart failure at 2 coronary care units entered this analysis. Vital status within one year, cause of death and time interval where events occurred were recorded. Cause of death comprised: heart failure (HF), other cardiovascular (namely infarction, sudden death, stroke), infectious, miscellaneous and unknown causes. Mortality was analyzed according to time intervals after admission as follows: in hospital (IH), early post discharge (E) (< 90 days after discharge) and late (L) (between 3 months and one year after discharge). Follow-up was performed by a visit or a phone contact at 90 days and at 1 year after admission.



Cause of Death According to Time Periods

Results: Out of 865p, 71(8.2%) were lost to follow- up (with similar baseline characteristics to those who completed follow-up). Finally, 794 p were analyzed with a median age of 81 years (IQR 72-87), 47.1% females, 49.7% with preserved ejection fraction, 25.8% diabetic, 79% hypertensive, 32.9% with atrial fibrillation, 23.4% with chronic renal disease. Annual mortality was 40.15%; 37% of the deaths corresponded to heart failure. Hospital mortality was 6.12% (52.8% of the deaths were due to heart failure), E mortality was 13.64% (38.7% due to heart failure) and L mortality was 25.2% (30.6% due to heart failure). Heart failure was the main cause of death but its relative impact decreased throughout the year ($p < 0.0135$).
Conclusion: In patients with acute decompensated heart failure one year mortality after admission remains high. Although heart failure is the main cause of death, its relative importance decreases throughout the year. Advanced age and comorbidities turn acute decompensated heart failure patients into a vulnerable population where heart failure progression acts not only as a cause of mortality but also as a facilitator of death due to non- cardiac causes. Thus, a comprehensive approach for the management of these patients is mandatory.

P2214

Clinical characteristics and post-discharge outcomes according to diabetes status in patients hospitalized with acute decompensation for systolic heart failure

ISLAM Alsoudi[1]; SVEN Piepenburg[1]; OLIVER Vollrath[1]; STEFAN Stoerk[1]; GEORG Ertl[1]; C E Angermann[1]
[1]Comprehensive Heart Failure Center, Dept. of Medicine I, University Hospital and University of Würzburg, würzburg, Germany

Introduction: & Aim: Diabetes mellitus (DM) is associated with higher rates of incident heart failure (HF), higher prevalence in symptomatic HF, and adverse outcomes. Better understanding of the interrelations of DM and HF is important since some antidiabetic drugs show beneficial, others harmful effects on cardiovascular (CV) and renal outcomes, with respective mechanisms of action remaining largely unclear. To better clarify the pathophysiology driving HF progression and prognosis in patients with DM we compared clinical characteristics and outcomes at 180 days in consecutive patients hospitalized for decompensated HF according to diabetes status.
Methods: & **Results:** All 1022 participants of the Interdisciplinary Network Heart Failure (INH) program (67.9 ± 12.5 years, 28.2% female, left ventricular ejection fraction before discharge = 40%) were included in this post-hoc analysis. Patients were diagnosed with DM when having a history of DM, being on antidiabetic drugs or having HbA1c-values = 6.5%. Univariable Cox regression analysis was used to estimate hazard ratios (HR) and 95% confidence intervals (CI). DM was present in 408 patients (39.5%). Compared with non-DM patients, DM patients were older (70.4 ± 10.2 vs 66.2 ± 13.7 years, $p < 0.001$) and had more often New York Heart Association class III-IV (53.2 vs 37.3%, $p < 0.001$) and ischemic HF etiology (56.6 vs 45.8%, $P < 0.001$), higher mean blood pressure (89.4 ± 12.7 vs 87.4 ± 11.9mmHg, $p = 0.008$) and heart rate (73.6 ± 11.5 vs 71.8 ± 11.2 b/min, $p = 0.009$), more peripheral edema (44.0 vs 28.2%, $p < 0.001$) and pulmonary rales (26.4 vs 15.9%, $p = 0.001$), obesity (= 30 kg/m^2, 32.0 vs 18.2%, $p < 0.001$), renal dysfunction (eGFR < 60ml/min/173m2, 52.2 vs 34.9%, $p < 0.001$), anemia (WHO, 39.2 vs 26.2%, $p < 0.001$), atrial fibrillation (33.7 vs 26.4%, $p = 0.012$), peripheral artery disease/stroke (30.1 vs 18.6%, $p < 0.001$), systemic inflammation (hsCRP: 12.8 (4.2-28.8) vs 7.7 (2.4-20.6) mg/L, $p < 0.001$; interleukin-6: 6.1 (2.4-12.5) vs 4.2 (2.0-9.7) pg/ml, < 0.001), worse quality of life (Kansas City Cardiomyopathy Overall Summary Score 52.9 (35.9-67.3) vs 59.4 (41.3-77.7), $p < 0.001$), and more depression (mean 9-item Patient Health Questionnaire sum-score 8.3 ± 5.7 vs 7.3 ± 5.4, $P = 0.006$). At 180 days, all-cause death had occurred in 57 DM and 47 non-DM patients (13.9 vs 7.7%, HR 1.88, 95% CI 1.28-2.77, $p = 0.001$), and CV death in 35 DM and 31 non-DM patients (8.6 vs 5.1%, HR 1.75 (1.07-2.84), $p = 0.023$), respectively. The composite of all-cause death or hospitalization had occurred in 191 DM and 226 non-DM patients (46.8 vs 36.8%, HR 1.34 (1.11-1.63), $p= 0.002$.
Conclusion: The HF phenotype differs between patients with and without DM discharged from hospital after systolic cardiac decompensation. Higher age, more obesity, and higher prevalence rates of multiple comorbidities with known adverse prognostic impact, systemic inflammation and residual congestion may play a key role to explain the worse 180-day outcomes of DM patients in our cohort.

P2215

Differences in outcomes of acute heart failure with reduced and preserved ejection fraction in patients with non end stage chronic kidney disease: a nationwide analysis

M Mario Rodriguez[1]; W Rzechorzek[1]; A Manguba[1]; S Sabharwal[1]; C Krittanawong[1]; X Wei[1]; C Godoy Rivas[2]; J Puma[3]; E Herzog[1]
[1]Icahn School Of Medicine at Mount Sinai/ Mount Sinai St. Lukes-West Hospital, Department of Medicine, Division of Cardiology , New York, United States of America; *[2]Cleveland Clinic Foundation, Cleveland, United States of America*; *[3]Columbia University Medical Center, New York, United States of America*

Background : There are 915 000 new heart failure cases annually in United States. As the most common diagnosis for hospitalization, acute heart failure and the impact comorbidities have on in hospital outcomes is of tremendous importance. Patients with end stage renal disease have increased mortality during acute exacerbations of heart failure, but data on Non end stage chronic kidney disease patients is limited.
Purpose: Investigate the effect of non end stage chronic kidney disease on the in hospital outcomes of acute heart failure exacerbations
Methods: A retrospective analysis using the 2014 United States Nationwide Inpatient Sample was performed. Patients above the age of 18 with a primary diagnosis of acute heart failure (AHF) were included and further subcategorized into systolic heart failure (SHF) and diastolic heart failure (DHF). Secondary diagnosis of chronic kidney disease (CKD) stage III and IV was done. Stage I and II was not taken into consideration in this study. End stage renal disease were excluded. Primary outcome was in-hospital mortality. Secondary outcomes included length of stay, cost of stay, cardiogenic shock, utilization of mechanical ventilation, dialysis , use of non-invasive ventilation, cardiac arrest and short term mechanical circulatory support. Multivariate logistic regression analysis was done using STATA IC 15.
Results: A total of 271,905 patients with AHF and CKD stage III and IV were identified of which 48% corresponded to SHF and 52% to DHF, 46% were female and mean age was 75 years. Mortality was statiscally significantly lower in the AHF (OR 0.87 $p = 0.002$) and in the DHF group (OR 0.74 $p < 0.001$) but not in the SHF population (OR 0.94 $p = 0.375$). There was a non statistically significant trend towards less invasive mechanical ventilation utilization across the 3 subgroups. Also, increased dialysis requirements across the AHF (OR 1 .69 $p < 0.001$), SHF(OR 1.71 $p = 0.005$) and DHF(OR 1.65 $p = 0.01$) groups was observed, along with a decreased non invasive ventilation utilization in the AHF (OR 0.83 $p < 0.001$), SHF(OR 0.79 $p < 0.001$) and DHF (OR 0.86 $p = 0.001$) group. Length of hospital stay and total charge of hospitalization was also lower among the CKD and heart failure subgroups.
Conclusions: patients with non end stage CKD (stage III and IV) that develop an acute heart failure exacerbation are prone to undergo more dialytic interventions with less non invasive ventilation utilization and a trend towards decreased mortality. length of stay and total charge are lower as well.

P2216

Outcomes of acute heart failure exacerbations in patients with alcoholic and non-alcoholic cirrhosis: a 5 year nationwide analysis

M Mario Rodriguez[1]; W Rzechorzek[1]; B Sabharwal[1]; C Krittanawong[1]; A Manguba[1]; X Wei[1]; C Godoy Rivas[2]; E Herzog[1]; J Puma[3]
[1]Icahn School Of Medicine at Mount Sinai/ Mount Sinai St. Lukes-West Hospital, Department of Medicine, Division of Cardiology , New York, United States of America; *[2]Cleveland Clinic Foundation, Cleveland, United States of America*; *[3]Columbia University Medical Center, New York, United States of America*

Background: Although pathophysiological heart and liver interactions have been described, data on outcomes of acute heart failure patients with secondary diagnosis of cirrhosis is limited
Purpose: evaluate the difference in outcomes of alcoholic and non alcoholic cirrhosis patients presenting with acute heart failure exacerbation
Methods: A retrospective analysis using the 2010-2014 United States Nationwide Inpatient Sample was done. Patients above age 18 with primary diagnosis of acute heart failure (AHF), systolic heart failure (SHF) and diastolic heart failure (DHF) were included. Secondary diagnosis of cirrhosis was generated with further sub division

in alcoholic and non alcoholic cirrhosis. End stage renal disease patients were excluded. Primary outcome was in-hospital mortality. Secondary outcomes included length of stay, cost of stay, shock, utilization of mechanical ventilation, acute kidney injury requiring dialysis (AKID), use of non-invasive ventilation (NIV), cardiac arrest, and short term mechanical circulatory support. Diagnoses were identified using ICD-9- CM codes . Multivariate logistic regression analysis adjusting for age, race, hospital location and gender was done using STATA 15.
Results: 2,778,114 patients with AHF were identified. 45,980 had a history of cirrhosis in general,
corresponding to 71% patients with SHF and 29% patients with DHF. 36% of general cirrhosis with AHF were female. Mean Age was 65 years. Increased mortality was shown in general cirrhosis with AHF (OR 1.6 $p < 0.001$), SHF (OR 1.5 $p < 0.001$) and DHF (OR 1.77 $p < 0.001$). In non alcoholic cirrhosis, odds of mortality was increased in the SHF(OR 1.48 $p < 0.001$) and DHF group(OR 1.5 $p < 0.001$) along with increased odds of AKID in the general AHF(OR 1.43 p=.004) and SHF(OR 1.48 $p = 0.04$) but not statiscally significant in the DHF group(OR 1.31 $p = 0.18$). There was a trend towards decreased non invasive ventilation utilization across the AHF(OR 0.63 $p < 0.001$), SHF(OR 0.68 $p < 0.001$) and DHF groups(OR 0.61 $p < 0.001$). Increase in total charge and length of stay across all heart failure subgroups was shown. Results for shock(SHF OR 1.2 $p = 0.21$), mechanical ventilation (SHF OR 1.02 $p = 0.61$), short term mechanical circulatory support(SHF OR 1.04 $p = 0.85$) and cardiac arrest (SHF OR 1.24 $p = 0.22$) were not statiscally significant. In alcoholic cirrhosis cohort, increased odds of mortality was seen in the AHF(OR 2.03 $p < 0.001$), SHF(OR 1.70 $p = 0.001$) and DHF(OR 2.6 $p < 0.001$) groups. Increased odds of mechanical ventilation in the AHF(OR 1.37 $p = 0.006$) and DHF(OR 1.6 $p = 0.02$) but not in the SHF group(OR 1.33 $p = 0.06$) was seen as well. In the AHF group of alcoholic cirrhotic patients, decreased odds of non invasive mechanical ventilation(OR 0.80 $p = 0.01$) with increased odds of cardiac arrest(OR 1.68 $p = 0.007$) was seen.
Conclusions: acute heart failure exacerbation in patients with alcoholic and nonalcoholic cirrhosis is associated with an increased mortality, length of stay and total cost.

P2217

Killip class on admission in acute coronary syndrome - is there any influence of previous regular use of heart failure medication?

K Kevin Domingues[1]; MJ Vieira[1]; D Durao[1]; M Leal[1]
[1]*Hospital of Santarem, Cardiology, Santarem, Portugal*

On behalf of: Investigators of the National Registry of Acute Coronary Syndrome of the Portuguese Society of Cardiology

Introduction: The prevalence of acute coronary syndromes (ACS) is higher in patients with hypertension, chronic kidney disease and other previous cardiovascular events. These patients are frequently on drugs which are also used in the treatment of heart failure (HF). However, it is unknown whether their previous regular intake influences Killip Class on admission in patients with ACS.
Aim: To assess the influence of previous regular use of drugs which are commonly used in heart failure in the Killip Class on admission in patients with ACS.
Methods: A retrospective study of patients inserted the National Registry of ACS of the Portuguese Society of Cardiology was performed. The sample was divided in two groups: patients with Killip class = 1 (KK = 1) and patients with Killip class > 1 (KK>1). Clinical variables and drug history were analysed.
Results: A total of 16172 patients were included, predominantly men (73.1%), with a mean age of 66 ± 13 years. There was a known history of hypertension in 69.3%, chronic kidney disease in 5.8%, HF in 4.3% and previous ACS in 19.6%. Most patients (84.7%) presented in KK = 1 (II 9.6%; III 3.8%; IV 1.9%).
In total, 24.4% were previously on regular diuretics, 23.7% on beta-blockers (BB), 26.7% on angiotensin-converting enzyme inhibitors (ACEi), 22.5% on angiotensin II receptor blockers (ARB), 12.2% on nitrates, 3.8% on digoxin, 2.6% on mineralocorticoid receptor antagonists (MRA) and 1.9% on ivabradine.
All of these drugs were associated with a higher prevalence of KK>1: BB 30.4% vs 22.5% ($p < 0.001$), ACEi 35.2% vs 25.2% ($p < 0.001$), ARB 25.5% vs 22.0%, ($p < 0.001$), nitrates 18.2% vs 11.1%, ($p < 0.001$), ivabradine 3.4% vs 1.6% ($p < 0.001$), MRA 5.4% vs 2.0% ($p < 0.001$), diuretics 41.3% vs 21.4% ($p < 0.001$) and digoxin 3.8% vs 1.0% ($p < 0.001$).
In the multivariate analysis, with age, sex, comorbidities (including HF) and time from the beginning of symptoms to the first medical contact, only previous regular intake of diuretic drugs ($p = 0.009$, OR = 1.23, CI95 = 1.05-1.40) and digoxin ($p = 0.018$, OR = 1.62, CI95 = 1.09-2.41) were independent predictors of KK>1 on admission.
Conclusion: In this study of ACS patients, previous regular intake of drugs which are commonly used in heart failure was not associated with a lower incidence of KK>1. On the contrary, previous regular intake of diuretics and digoxin were both independent predictors of KK>1 on admission.

P2218

Liver dysfunction assessed by model for end-stage liver disease predicts adverse outcome in patients with acute decompensated heart failure

J Y Jae Yeong Cho[1]; K H Kim[1]; H Park[1]; H J Yoon[1]; K H Lee[1]; D S Sim[1]; N S Yoon[1]; Y J Hong[1]; H W Park[1]; J H Kim[1]; Y Ahn[1]; M H Jeong[1]; J G Cho[1]; J C Park[1]
[1]*Chonnam National University Hospital, Cardiology, Gwangju, Korea Republic of*

Background: Left ventricular functional recovery (LVFR) is not uncommon in patients with dilated cardiomyopathy (DCM). SHIFT trial showed that ivabradine has a favorable impact on LV reverse remodeling. However, there is lack of data regarding the effect of ivabradine on LVFR in real clinical practice.
Purpose: Therefore, the aim of this study was to investigate the impacts of added ivabradine on LVFR in patients with DCM.
Methods: A total of 395 patients consecutively visited a tertiary hospital between May 2011 and March 2013. Hepatic and renal function test including total bilirubin, prothrombin time-international normalized ratio (PT-INR), and serum creatinine were checked in those patients. The MELD score was calculated for all eligible patient and they were divided into two groups by MELD score: high MELD group (n = 66, 70.6 ± 13.8 years, males) vs. low MELD group (n = 163, 68.4 ± 14.1 years, 82 males). Baseline characteristics, echocardiographic findings, and laboratory findings were compared between two groups. In addition, the diagnostic utility of the MELD score was examined through the use of the receiver-operating characteristics (ROC) curves (Figure). Primary end-point was all-cause mortality at 1-year follow-up.
Results: MELD score was quite different between patients with long-term survivor vs. non-survivor (7.0 ± 3.9 vs. 10.7 ± 4.7, $p < 0.0001$). Age and gender were not different between the two groups. Left ventricular (LV) ejection fraction and LV dimension were not different between the two groups. However, left atrial diameter was larger in the high MELD group (49.1 ± 9.2 vs. 45.5 ± 9.2 mm, $p = 0.010$). Hemoglobin level was lower (11.4 ± 2.5 vs. 12.5 ± 2.1 g/dL, $p < 0.0001$) and white blood cell count was higher (10425.4 ± 4906.3 vs. 9078.5 ± 3845.5 /uL, $p = 0.047$) in the high MELD score group. Serum cholesterol level was not different between the two groups. Other liver function testing like ALP level was higher in the high MELD score group (103.3 ± 65.1 vs. 80.7 ± 30.3, $p = 0.046$). Long-term all-cause mortality was higher in patients with high MELD score (42.4% vs. 11.7%, $p < 0.00001$) (Figure). In multivariate analysis using COX proportional hazard model, high MELD score was an independent predictor of long-term all-cause mortality in Korean ADHF patients (HR 3.66, 95% CI 1.90-7.03, $p < 0.0001$).

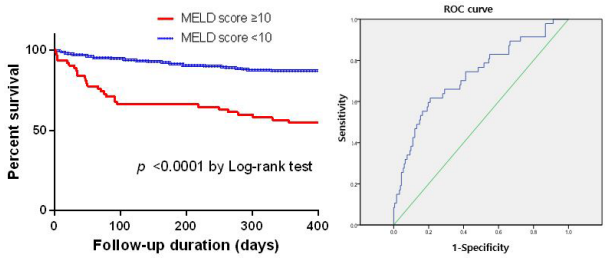


Figure. ROC curve analysis to identify optimal cut-off value of MELD score for predicting long-term mortality in patients with ADHF (Area under the curve=0.727; p <0.0001; Sensitivity 63.8%, specificity 72.0%).

Figure

Conclusion: High MELD score turned out to be an independent predictor of long-term mortality in ADHF patients. Assessment of liver dysfunction using the MELD scoring system has additional value in risk stratification of ADHF patients. Reflection of this result above in establishing novel Korean risk scoring system is warranted.

P2219

Differences in acute heart failure all-cause re-admissions and mortality, between heart failure phenotypes, within northern kuala lumpur

REF Bin Raja Shariff[1]; MK Borhan[1]; MR Yusoff[1]; C Lee[1]
[1]*Hospital Sungai Buloh, General Medicine, Sungai Buloh, Malaysia*

Background: Current phenotypes of heart failure (HF) include heart failure with reduced EF (HFrEF), mid-range (HFmEF) and preserved EF (HFpEF). However, little is known on how the prognosis of all three entities compare within an Asian population.

Purpose: To identify differences in readmissions and mortality, between HF phenotypes in Malaysians.
Methods: A retrospective study was performed on 327 patients with baseline echocardiography, admitted for acute HF to Hospital Sungai Buloh between 1st Jan 2012 to 31st December 2013. Information on demographics, readmission and mortality were compared between HFrEF (n = 186; 56.9%), HFmEF (n = 52, 15.9%) and HFpEF (n = 89, 27.2%) patients.

Precipitants, Readmission and Mortality

Variables	Heart Failure Phenotypes	p-values		
HFrEF (n (%))	HFmEF (n (%))	HFpEF (n (%))		
Precipitants	Non-Compliance	82 (44.1)	28 (53.8)	39 (43.8) 0.425
Acute Coronary Syndrome	58 (31.2)	10 (19.2)	29 (32.6)	0.194
Readmissions	30-days	33 (17.7)	5 (9.6)	14 (15.7) 0.366
90-days	37 (19.9)	9 (17.3)	24 (27.0)	0.300
6-months	37 (19.9)	9 (17.3)	26 (29.2)	0.146
12-months	45 (24.2)	11 (21.2)	24 (27.0)	0.734
Mortality	30-days	20 (10.8)	9 (17.3)	14 (15.7) 0.326
90-days	3 (1.6)	2 (3.8)	2 (2.2)	0.614
12-months	12 (6.5)	3 (5.8)	5 (5.6)	0.958
24-months	7 (3.8)	2 (3.8)	4 (4.5)	0.957
36-months	6 (3.2)	4 (7.7)	6 (6.7)	0.267

Results: The mean age of HFrEF, HFmEF and HFpEF patients were 62.1 (S.D. = 12.4), 63.5 (S.D. = 10.6) and 63.0 (S.D. = 17.7) years respectively (p = 0.387). 108 (58.1%), 29 (55.8%) and 40 (44.9%) patients were male (p = 0.120) respectively as well. Common precipitants in acute HF were non-compliance to fluid restriction and medications, and acute coronary syndrome in all cohorts (Table). There were no significant differences in all-cause readmission at 30-days, 90-days, 6-months and 12-months, between the cohorts and there was also no significant difference in all-cause mortality within 30-days, 90-days, 12-months, 24-months and 36-months as well (Table).
Conclusion: Our study demonstrates similarly poor prognosis (in the context of re-admissions and mortality rates) when comparing acute decompensation in all 3 phenotypes of HF, indicating a need for equal level of awareness and efforts to reduce risk of progression, independent of ejection fraction.

P2220

One-year outcomes in elderly patients with mid-range ejection fraction hospitalized for acute heart failure: data from the ATHENA registry.

F Fedeli[1]; A Pratesi[1]; F Orso[1]; A Herbst[1]; G Biagioni[1]; AC Baroncini[1]; S Parlapiano[1]; C Ghiara[1]; A Lo Forte[1]; A Berni[2]; C Tozzetti[2]; M Di Bari[1]; N Marchionni[3]; A Ungar[1]; S Baldasseroni[1]
[1]Careggi University Hospital (AOUC), Department of medicine and geriatrics, Florence, Italy; *[2]Careggi University Hospital (AOUC), Department of emergency and internal medicine, Florence, Italy*; *[3]Careggi University Hospital (AOUC), Cardiothoracovascular Department, Florence, Italy*

On behalf of: ATHENA Study group

Background: Recently, the European Society of Cardiology (ESC) has recognized the presence of a "gray area" of patients with ejection fraction (EF) between 40 and 49% defined "mid-range" (HFmrEF) and has redefined the specific cut off values for HF with preserved EF (= 50%, HFpEF) and HF with Reduced EF (< 40%, HFrEF). Differences in clinical profile and outcomes in this new sub-group of HF pastients are still under investigation.
Purpose: to describe this new population of HF patients by comparing clinical charateristics and long-term outcomes with the other two traditional groups of HF: HF with preserved ejection fraction (HFpEF) and HF with reduced ejection fraction (HFrEF).
Methods: The analysis was based on the retrospective observational ATHENA registry (AcuTe Heart failurE in advaNced Age), which enrolled 401 elderly patients (= 65 years old) with a diagnosis of acute HF during hospitalization. Only the 291 patients with an echocardiographic measurement of left ventricular ejection fraction during hospitalization were considered for this study. One year follow-upwas conducted by phone interviews to evaluate patients' clinical conditions.
Results: During the hospitalization 58 patients (19.9%) had HFmrEF, 95 patients (32.6%) had HFrEF and 138 (47.4%) had HFpEF. The clinical profile of the HFmrEF population was intermediate between the HFpEF and the HFrEF ones. Patient charateristics - such as age, gender and comorbidity rate – were similar to patients of the HFpEF group. An ischemic etiology was as frequent in the HFmrEF group as in the HFrEF population. The mortality rate during follow-up was not significantly different among the three categories, while significant was the difference in disability (p= 0.001), defined as the loss of one or more BADLs. The disability rate was: 85.7% for HFpEF, 76.2% for HFmrEF and 54.3% for HFrEF. In the univariate analysis, age, female gender, history of cognitive impairment, delirium during hospitalization, glycemia on Emergency Department (ED) admission, hemoglobin (Hb) on admission to the ward, Charlson comorbidity index and total number of drugs were associated with disability. In the multivariate analysis, age (OR1.07, 95%CI 0.99-1.15, p = 0.071); glycemia on ED admission (OR 1.01, 95%CI 1.00-1.03, p = 0.031); Hb on admission to the ward (OR 0.77, 95%CI 0.59-0.99, p = 0.021) and 2016 ESC HF classification subgroup (OR 2.37, 95%CI 1.42-3.93, p = 0.001) were independent predictors of disability.
Conclusions: HFmrEF patients have defined clinical characteristics compared to HFpEF and HFrEF patients. One-year mortality rates are very similar in the three groups, while there is a significant difference in the developement disability rate during follow-up with HFpEF group having the highest disability rate.

P2221

Acute heart failure complicating an acute coronary syndrome in elderly patients: prevalence, predictors and prognostic significance

PM Pedro Azevedo[1]; T Mota[1]; J Bispo[1]; J Guedes[1]; D Carvalho[1]; D Bento[1]; S Pereira[1]; W Santos[1]; J Mimoso[1]; I Jesus[1]
[1]Faro Hospital, Cardiology, Faro, Portugal

Introduction: The prevalence of elderly patients with an acute coronary syndrome (ACS) is rising progressively and is a major cause for mortality and morbidity. Acute heart failure (AHF) complicating an ACS has been associated with a worse prognosis. Early identification of patients at higher risk for AHF is of paramount importance to ensure adequate monitoring and prompt therapy.
Purpose: Evaluate the prevalence, predictors and prognostic impact of AHF in elderly patients with an ACS.
Methods: Retrospective, descriptive and correlational study with all patients aged 80 years or older admitted to a Cardiology department with the diagnosis of ACS between the 1st of October 2010 and 31st September 2017. Patients with a Killip class (KK) = 2 at admission or with development of AHF during hospitalization were classified as having AHF and were compared with those without AHF. Univariate and multivariate statistical analysis in SPSS were used to identify predictors and the prognostic impact of AHF in ACS.
Results: 673 patients were included, 360 (53.5%) were male, 239 (35.5%) had ST-segment elevation myocardial infarction (STEMI), 366 (54.4%) had non-STEMI, 12 (1.8%) had unstable angina and 56 (8.3%) had MI of unknown location. 203 (30.2%) patients had AHF, 143 (21.2%) had a KK = 2 on admission and 60 (8.9%) only developed HF later during hospitalization.
Patients with AHF were more frequently female and were more likely to have diabetes, STEMI, a history of ACS, valvular heart disease, HF and chronic kidney disease. They had lower left ventricular ejection fraction (LVEF) (mean 45.3%vs57%, p < 0.001), higher creatinine levels (p = 0.04), lower haemoglobin (p = 0.01) and higher glycemia on admission (p < 0.001).
Patients with AHF were less likely to have coronary angiography and percutaneous coronary intervention (PCI) (23.2%vs41.1%, p < 0.001), and had more frequently atrial fibrillation (AF) (17.7%vs7.4%, p < 0,001), major haemorrhage and need for both non-invasive and invasive ventilation. Overall in-hospital mortality rate was 9.5% (65 patients) and AHF was associated with higher mortality (22.7%vs3.8%, p < 0.001) in univariate and multivariate analysis (OR 2.77, 95%CI 1.15-6.7, p = 0.02)
On multivariate analysis, female sex (OR 1.82, 95%CI 1.12-2.9, p = 0.02), no PCI (OR 2.03, 95%CI 1.15-3.58, p = 0.01), AF (OR 2.82, 95%CI 1.5-5.3, p = 0.001), lower LVEF (p < 0.001) and higher glycemia (p = 0.009) were independent predictors of AHF. In patients admitted in KK 1, STEMI (OR 2.99, 95%CI 1.32-6.8), lower FEVE (p < 0.001) and AF (OR 4.3, 95%CI 1.8-10.3, p = 0.01) were independently associated with HF developing during hospitalization.
Conclusion: AHF is a common complication in octogenarians with ACS and increases in-hospital mortality by almost 3-fold. Female sex, no PCI, AF, lower LVEF and higher glycemia were independently associated with AHF. In patients initially admitted in KK 1, lower LVEF, AF and STEMI predicted the development of AHF during hospitalization.

Acute Heart Failure - Diagnostic Methods

P2222

Indicators of left ventricular remodeling in patients with acute heart failure

K Akmal Koyirov[1]; S R Kenjaev[1]; U SH Ganiev[1]; S SH Khaitov[1]; Z A Kambarova[2]; M S Mirmaksudov[3]
[1]Republican Research Center of Emergency Medicine, Tashkent, Uzbekistan; *[2]Tashkent Pediatric Medical Institute, Tashkent, Uzbekistan*; *[3]Tashkent Medical Academy, Tashkent, Uzbekistan*

Aim: The aim is to evaluate echocardiographic parameters in patients with ST-segment elevation myocardial infarction (STEMI), depending on the class of acute heart failure (AHF).
Material and Methods: 79 patients (50 men and 29 women) with STEMI were examined. The average age is 63.8 ± 1.69 years. Depending on the presence of signs of AHF patients are divided into two groups: 1 group - I class by Killip - 47 patients; 2nd group - II-IV class by Killip - 32 patients. The analysis was carried out based on the results of echocardiography (ECHO) after one day from the development of myocardial infarction.
Results: A number of significant differences identified between these groups by comparison of the echocardiographic data. According to results of the analysis, the avarege values of EDV, ESV, ESD, EF in the Killip I group were significantly different from the Killip II-IV group. Thus, the values of EDV in groups Killip I and II-IV were 148.6-163.9 and 165.5-207.1 ml, respectively. ESV were 70.4-83.3 and 90.2-131.2 ml; ESD 3,8-4,2 and 4,4-5,2 cm; EF - 49,1-53,3% and 36,9-45,9%, respectively. Thus, high values of EDV, ESV, and ESD were observed in group II-IV of AHF classes, and ejection fraction of left ventricle was vice versa, was higher in group I of class AHF. There were no significant differences between the groups in the values of EDD, IVS, PWLV, although patients with II-IV classes of AHF showed higher values of these parameters. Comparing the variances of the Killip I and Killip II-IV groups, statistically significant differences in the EDD (p = 0.010), EDV (p = 0.003), ESV (p = 0.0003), IVS (p = 0.005), LVPW (p = 0.04), E/A ratio (p = 0.0001). According to our data, on the basis of EDV and ESV, differences were found, both in the mean values and in the variances.
Conclusion: Thus, left ventricular myocardial remodeling in the early post-infarction period is caused by a complex of structural and functional changes, the main of which are dilatation of the left ventricular cavity, worsening of the contractile function of the myocardium.

P2223

Biomarkers in acute cardiorenal syndrome

M Dankova[1]; M Luknar[1]; P Lesny[1]; Z Minarikova[2]; B Zitny[3]; P Pontuch[2]; E Goncalvesova[1]
[1]The National Institute of Cardiovascular Diseases, Department of Heart Failure and Heart Transplant, Bratislava, Slovak Republic; *[2]University Hospital, 4th Department of Internal Medicine, Bratislava, Slovak Republic*; *[3]STUVital, Bratislava, Slovak Republic*

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Aim: The aim was to identify independent predictors of acute kidney injury (AKI) in patients admitted due to acute heart failure (AHF).
Methods: We evaluated clinical, echocardiographic parameters and selected biomarkers in 74 patients admitted to ICU due to AHF. In 41 patients (55,4 %) it was newly diagnosed AHF, in 33 patients (44,5 %) - decompensation of chronic heart failure. The average age was 69 ± 10,3 years with gender distribution 48/26 (men/women). HFrEF/HFmrEF/HFpEF was in 34/24/16 patients. Acute kidney injury was defined according to the KDIGO recommendations based on the dynamics of serum creatinine and daily diuresis. Patients were divided into groups without (AKI-, n = 54) and with (AKI+, n = 20) acute kidney injury. Parameters as: age, BMI, systolic blood pressure, u-NGAL, u-TIMP2, u-IGFBP7, s-NTproBNP, s-hemoglobin and LVEF were included into the multivariate regression analysis.
Results: In 27% of patients we observed development of AKI within 72 hours after admission. Patients with AKI + were older [76 vs. 64 years (median), p = 0,007], with lower BMI [27 vs. 29 kg/m2 (median), p = 0,02], more often in the HFrEF group (45,8 %, p = 0,002). Median of urinary NGAL at admission was significantly higher in the AKI+ group compared to patients in the AKI- (154 vs. 19,5 ng/ml; p = 0,0001). Median of u-TIMP2 was 194,1 in the AKI + group versus 42,5 ng/ml in the AKI- group of patients (p = 0,0001). Median of u-IGFBP7 was 379 in the AKI+ verzus 92,4 pg/ml in the AKI- patients (p = 0,001). Except of BMI, parameters as age, systolic blood pressure, u-NGAL, u-TIMP2, u-IGFBP, s-NTproBNP, s-hemoglobin and LVEF significantly identified AKI [AUC ROC]: u-NGAL = 0,89 (p = 0,0001); u-TIMP2 = 0,87 (p = 0,001), u-IGFBP7 = 0,92 (p = 0,0001), EFLK= 0,79 (p = 0,001); s-NTproBNP = 0,73 (p = 0,01); s-hemoglobín = 0,71 (p = 0,01); s-TK = 0,71 (p = 0,02).
Conclusion: Predictors of acute kidney injury in acute heart failure patients were: age, systolic blood pressure, elevated heart failure markers (s-NTproBNP) and renal injury markers (u-NGAL, u-TIMP2, u-IGFBP7) together with LVEF determination and levels of s-hemoglobin at admission.

P2224

Is there a variation of CA-125 levels with changes in glomerular filtration rate in patients with heart failure?

D Carrillo[1]; R Lopez[1]; I Sanchez-Lazaro[1]; C Aguado[2]; B Laiz[2]; L Almenar[1]
[1]Hospital Universitario y Politécnico La Fe, Heart Failure and Transplant Unit, Valencia, Spain; *[2]Hospital Universitario y Politécnico La Fe, Clinical analysis service, Valencia, Spain*

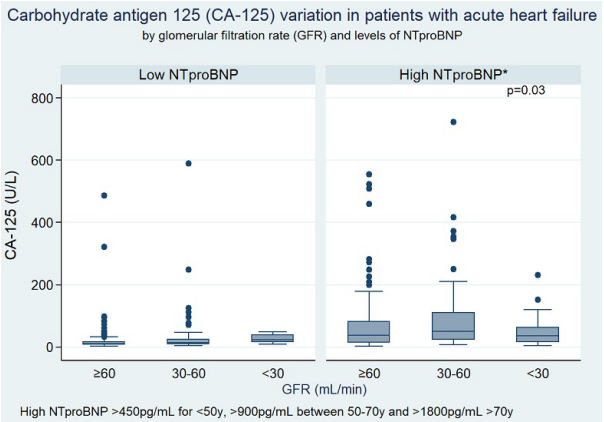
Background/introduction: Carbohydrate antigen 125 (CA-125), known as a tumor marker, is used as congestion marker in heart failure (HF). However, few report exist on CA-125 measurement in patients with HF and impaired renal function.

Multivariate linear regression model.

CA-125	Coeficient	95% Conf Interval	p	
GFR (mL/min)				
≥60mL/min	1			
30-60mL/min	15.16	-2.58	32.92	0.09
<30mL/min	-25.39	-55.52	4.72	0.09
NTproBNP				
Low	1			
High*	55.21	38.34	72.07	0.00

*High NTproBNP >450pg/mL for <50y, >900pg/mL between 50-70y and >1800pg >70y
CA-125 Carbohydrate antigen 125, GFR Glomerular filtration rate.

Purpose: To determine the relationship between CA-125 and glomerular filtration rate (GFR) in patients with HF, considering the levels of NTproBNP.
Methods: Cross-sectional study of patients with acute HF who have the biomarkers NTproBNP, CA-125, GFR in the same blood sample between 01 august to 30 nov 2017. A multivariable linear regression to examine covariates associated with CA-125 results was used. A boxplot of distribution of CA-125 according to the categories of renal function and levels of NTproBNP was done.
Results: 173 patients were included. The median of age was 71 years (interquartile range [IQR] 61-79), 64.74% were male. Median of CA125 was 42.1 U/L (IQR 16.2 to 88) and 54.9% have CA-125 higher than 35 U/L. The median of GFR was 59mL/min (IQR 41-78), NTproBNP 2310 pg/mL (IQR 918-4665). There were differences of the CA-125 levels by GFR categories, in patients with high NT-proBNP (Figure). However, in the multivariable regression model, the GFR categories weren't related to the change of CA-125. Elevated levels of NTproBNP were related to the elevation of CA-125 (Table).



CA-125 in patients with heart failure

Conclusions: CA-125 is a surrogate marker in HF, apparently not affected by GFR. However, further studies including clinical variables are required.

P2225

Monocyte subsets distribution predicts mortality in patients with acute heart failure

KA Konstantin A Krychtiuk[1]; M Lenz[1]; SP Kastl[1]; K Huber[2]; J Wojta[1]; G Heinz[1]; WS Speidl[1]
[1]Medical University of Vienna, Department of Internal Medicine II, Division of Cardiology, Vienna, Austria; *[2]Wilhelminen Hospital, 3rd Department of Internal Medicine, Cardiology and Emergency Medicine, Vienna, Austria*

Background: The pathogenesis of acute heart failure (AHF) includes a strong activation of the innate immune system. Monocytes are a heterogenous cell population and act as key regulators of innate immunity. According to their surface expression pattern of CD14, CD16 and CCR-2 they can be distinguished into at least three cell populations, namely classical monocytes (CD14++CD16-; CM), intermediate monocytes (CD14++CD16+CCR2+; IM) and non-classical monocytes (CD14+CD16++CCR2-; NCM).
Purpose: The aim of this prospective, observational study was to analyze whether monocyte subset distribution is associated with 30-day survival in patients with AHF.
Methods: We included 81 patients with acute heart failure admitted to a cardiac ICU. Blood was taken at admission and after 72 hours and monocyte subset distribution was analyzed by flow cytometry.
Results: Median age was 64 IQR 50-74 years and 77.8 % of patients were male. Median NT-proBNP was 4896 IQR 1370-14008 pg/mL and 30-day mortality was 33.3%. Monocyte subset distribution at day 0 was not associated with mortality. In contrast, compared to 30-day survivors, patients that did not survive showed a significantly higher percentage of IM (4.2 IQR 2.1-7.7 % vs 7.7 3.9-12.4 %; $p < 0.05$) and a lower percentage of CM (90.7 IQR 85.4-92.1 % vs. 87.2 IQR 79.2-89.0 %). Patients in the lowest tertile of CM showed a 8.9-fold increased mortality risk as compared to patients in the third tertile independent of age, sex, creatinine and NT-proBNP levels.
Conclusion: Monocyte subset distribution is associated with 30-day mortality in AHF patients requiring ICU admission. Thus, activation of the innate immune system may play a major role in the pathophysiology and outcome of this disease.

P2226

The examination about the relation between polyunsaturated fatty acid condition in blood on admission and prolongation of hospitalization in congestive heart failure cases.

Y Kato[1]; K Hayashi[1]; M Hasegawa[1]; N Matsuo[1]; T Fujiwara[1]; M Tanimoto[1]; K Kagwa[1]; Y Nakano[1]; N Onishi[1]; A Atsushi Takaishi[1]; M Ueeda[1]; S Hirohata[2]
[1]Mitoyo General Hospital, Kanonji, Japan; *[2]Okayama University, Graduate School of Health Sciences, Okayama, Japan*

Background: We introduced original clinical pathway(CP) for congestive heart failure(CHF) cases required admission and achieved wide shortening of hospitalization period by reduction of useless medical care. But many cases(43%) still stay over two weeks in our hospital. Although there may be various reasons for prolongation of hospitalization, we can find several reports about relation between the condition of polyunsaturated fatty acid(PUFA) and clinical course of CHF like that of ischemic heart failure.
Purpose: In this study we examined the data of PUFA in CHF cases introduced CP and considered about the characteristics of PUFA data in cases who required long stay in our hospital.
Method: We enrolled 197 patients who admitted with CHF in our hospital and introduced CP at the first time from August 2015 to July 2017 (mean age 81+/-11 years old, male/female 112/85). And we divided them into two groups, S-group(hospitalization was within 14days: 112cases, mean age 82+/-10 years old) and L-group(hospitalization was over 14days: 85cases, mean age 80+/-11 years old). We examined their activity before admission, the prevalence of dementia and cardiac function on admission. And we examined blood test data about lipid and PUFA on adomission. We investigated about the difference of these data between two groups.
Results: In L-group the rate of the cases without activity limitation out of doors was lower(39 vs 60%; $p < 0.05$) and the prevalence of dementia was higher(48 vs 26%; $p < 0.01$) than in S-group. Between L-group and S-group there was no difference about the value of Brain Natrium Peptide in blood(873+/-803 vs 752+/-552 pg/mL) or ejection fraction of left ventricle by echocardiography(52+/-20 vs 51+/-20%). About lipid in blood, the value of triglyceride, low dense lipoprotein(LDL) and oxidized LDL(Malondialdehyde Modified LDL) ware not different between two groups , only the value of high dense lipoprotein(HDL) was lower in L-group(44+/-16 vs 50+/-14 mg/dl; $p < 0.05$). About the value of PUFA arachidonic acid(AA) and docosahexaenoic acid(DHA) ware not different between two groups, but the value of eicosapentaenoic acid(EPA) was significantly lower in L-group(51+/-28 vs 67+/-44mg/dl; $p < 0.01$). The ratio of EPA and AA(EPA/AA) was also lower in L-group(0.34+/-0.19 vs 0.44+/-0.34; $p < 0.01$).
Conclusions: We found the relation between prolongation of hospitalization and high age, low activity before admission or presence of dementia in CHF cases. And we found that the value of EPA or EPA/AA on admission was clearly low in the cases required long hospitalization. It is not still unclear whether the simple supplement of EPA is useful for improvement of acute or chronic prognosis in CHF cases. But we should not only pay attention to general known factor relating to prognosis of CHF. It seemed to be also useful for management of CHF to check PUFA data on admission.

P2227

The value of 24-hour ambulatory blood pressure monitoring in patients admitted with acute heart failure and systolic dysfunction

A Frigy[1]; I Varga[2]; Z Fogarasi[2]; I Kocsis[2]
[1]University of Medicine of Targu Mures, Internal Medicine IV, Targu Mures, Romania; *[2]Clinical County Hospital Mures, Cardiology, Targu Mures, Romania*

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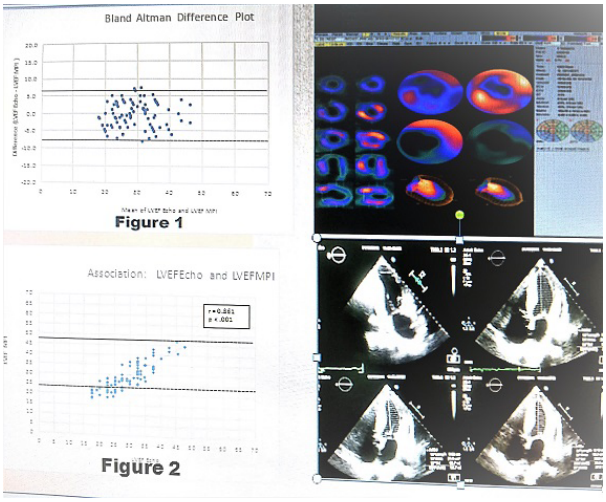
In acute heart failure (AHF), blood pressure (BP) is a major hemodynamic parameter with therapeutic and prognostic implications, however the value of 24-hour BP data has been less studied before.
Methods: In 35 patients (28 men, 7 women, mean age 61.28 years), hospitalized with AHF, 24-hour ambulatory BP monitoring (ABPM, EC-3H/ABP Cardiospy, Labtech) was performed on the day before hospital discharge, when the patients reached a stable hemodynamic status. All the patients had systolic heart failure (mean left ventricular EF 34%) and were free of hypertension. Besides classical ABPM parameters (max, min, mean values), the diurnal index and the standard deviation (a measure of BP variability) were obtained.
Results: The most important ABPM parameters had the following mean values (24-hour, day and night): systolic BP - 113.85 mmHg, 115.08 mmHg, 110.51 mmHg; diastolic BP - 66.58 mmHg, 67.7 mmHg, 63.51 mmHg; pulse pressure - 46.85 mmHg, 46.82 mmHg, 46.63 mmHg. The systolic and diastolic diurnal index was over 10% only in 8 and 11 patients, respectively. 24-hour, day and night standard deviations of systolic and diastolic BP values were smaller with 1 mmHg in average than the reference values found in the PAMELA study.
Conclusions: Patients hospitalized with systolic AHF, prior to discharge, clinically stabilized, are characterized generally by low BP values and a blunted circadian and global BP variability - phenomena related to the decreased cardiac output and neurohumoral activation. Predischarge ABPM could provide useful informations regarding the therapeutical reserve (risk of hypotension) and prognosis (low BP variability).

P2228

Is assessment of left ventricular ejection fraction a reality on an ultra low dose gated rest redistribution myocardial perfusion scintigraphy with ultra fast solid state detector gamma camera

ATUL Verma[1]; S Pandey[1]
[1]Fortis Escorts Heart Institute, New Delhi, India

Aims & objectives: The present study is aimed to assess the efficacy of cardiac dedicated solid state detector SPECT in the estimation of Left Ventricular Ejection Fraction on a gated rest redistribution thallium 201 myocardial perfusion scintigraphy (G-RRT-MPS) used for myocardial viability assessment in patients with gross Left ventricular dysfunction.
Materials and Methods: A group of consecutive patients: (N = 106) irrespective of age & sex with left ventricular failure (LVF) from ICUs/emergency department were subjected to G-RRT-MPS for myocardial viability. All the patients were imaged after iv injection of ultra-low dose Tl201 (1-1.5mCi) immediately & 4 hrs post injection under solid state detector SPECT gamma camera (GE-Discovery NM 530C) with the imaging time of 5 min each. 10 subjects with normal LVEF were subjected to Gated Tc99MIBI SPECT & 2DE for comparing the LVEF by echo & gated MPS to use it as the standard. The images were processed using 3D iterative reconstruction & LVEF were calculated by two nuclear physicians separately using commercially available QGS/QPS software. Similarly, All patients were subjected to 2DE where LVEF was calculated by two echocardiography experts in a double blinded manner using modified Simpsons' rule. The mean results of G-RRT-MPS & 2DE were compared for LVEF.
Results: The results showed mean LVEF of 28.9% ± 07% & 29.3% ± 6.8% for 2DE & G-RRT-MPS respectively which showed almost comparable results($p = 0.293$).



All LVEF measurements by both the modalities showed good correlation (r = 0.861, P= <.001) (fig 1). The concurrence was good as analysed by Bland-Altman method (fig 2). The mean discrepancy between the modalities was -0.4 with a 95% confidence range of -1.2 to 0.4. Discussion: Very few studies have compared 2DE & RRT for LVEF estimation because of low gated image quality on standard SPECT gamma camera. The physical characteristics of solid state detector technology which includes direct conversion of energy into counts & negligible dead time thus resulting into high energy & spatial resolution & hence good quality gated study enables to look at myocardial contractility, thickness as well as centripetal excursion & thus proper estimation of LVEF which shows excellent correlation with that of 2DE.
Conclusion: From the above results the LVEF can be estimated quite accurately & can be used in addition to Myocardial viability.

P2229
Worsening renal function in acute decompensated heart failure patients with regard to its reversibility

E Amosova[1]; I Gorda[2]; A Bezrodnyi[1]; A Sablin[2]
[1]O. O. Bogomolets National Medical University, Kiev, Ukraine; *[2]Kiev Alexander Clinical Hospital, Kiev, Ukraine*

Background: Our purpose was to determine the influence of worsening of the renal function (WRF) on clinical course of the hospital period in "wet and warm" patients with acute decompensated heart failure (ADHF).
Methods: In to the prospective study were included 141 patients with ADHF at the age from 38 to 85 years (mean age 66,4 ± 2,2). Transient WRF was defined as increase of creatinine = 26.5 mmol/L after 48 hours with subsequent decrease to baseline at discharge. Patients with persistent WRF didn't have decrease of creatinine to baseline at discharge. Endpoints were CVP at day 4 (D4), ortho-oedema congestion index Lala, E/E' and NT-proBNP at discharge (Dsc).
Results: WRF occurred in 38 (27%) patients, including 30 pts with transient WRF and 8 pts with persistent WRF. The patients with persistent WRF comparing to patients transient WRF and with no WRF had significantly more increased values of ortho-oedema index Lala, E/E', NT-proBNP, CVP and worse results of decongestion treatment. In the same time the patients with transient WRF didn't have significant differences in main parameters and endpoints (see in table).

P2229	No WRF	WRF transient	P1-3	P2-3	
Ortho-oedema index Lala D1	3,32 ± 0,10	3,47 ± 0,10	3,91 ± 0,12	p <0,01	p <0,01
Ortho-oedema index Lala Dsc	2,3 ± 0,05***	2,12 ± 0,05***	2,72 ± 0,08**	p <0,01	p <0,01
CVP D1	174 ± 10,4	179 ± 10,74	199 ± 11,94	p <0,05	p <0,05
CVP D 4	83 ± 4,98**	91 ± 5,46**	112 ± 6,72**	p <0,05	p <0,05
E/E' D1	18,1 ± 1,09	18,4 ± 1,10	21,1 ± 1,27	p <0,01	p <0,01
E/E' Dsc	12,9 ± 0,77 **	14,3 ± 0,86**	17,2 ± 1,03**	p <0,01	p <0,01
NT-proBNP D1	1147 ± 68	1211± 72,66	1362 ± 81,72	p <0,01	p <0,05
NT-proBNP Dsc	751 ± 45***	783 ± 46,98***	944 ± 56,64**	p <0,05	p <0,05

* - p < 0,05, ** - p < 0,01, *** - p < 0,001 compared to D1;

Conclusion: In the "wet and warm" patients with ADHF only presence of persistent WRF is associated with significantly worse clinical course and outcome comparing to patients with transient WRF and with no WRF

Acute Heart Failure - Treatment

P2230
Spironolactone treatment does not cause significant hyperkalemia at patients hospitalized because of chronic or acute heart failure - a meta-analysis

J Wagner[1]; B Wobbe[1]; I Rostas[1]; N Farkas[1]; P Hegyi[1]; L Czopf[1]
[1]University of Pecs, Division of Cardiology and Angiology and Centre for Translational Medicine, Pecs, Hungary

Background: Chronic heart failure (CHF) patients are shown to benefit from spironolactone treatment, especially if their left ventricular systolic function is significantly decreased (HFrEF). Recent randomized clinical trials at acute decompensated heart failure (ADHF) patients questioned the clinical importance of hyperkalemia as a significant adverse event.
Purpose: We conducted a systematic meta-analysis of the available studies, whether the side effect hyperkalemia is clinically significant at the different dosages of spironolactone in ADHF and CHF?
Methods: We searched EMBASE, the Cochrane Registry and PUBMED to identify randomized controlled studies comparing 25 to 100 mg spironolactone with placebo on top of the usual care therapy at patients hospitalized for ADHF and CHF. Search terms "acute heart failure", "chronic heart failure", "spironolactone" and "randomized controlled trials" were used, and studies until March 2017 were analyzed. 12 randomized controlled trials were identified enrolling 7948 participants. 46.88% (529 with ADHF and 3197 with CHF) were randomized to spironolactone and 53.12% (465 with ADHF and 3757 with CHF) to placebo.
Results: Overall, there was no significant difference between groups concerning the incidences of hyperkalemia (RD: 0.016; 95% CI: -0.017 - 0.049, p = 0.336). Our subgroup analysis showed no increased risk for hyperkalemia for the setting of ADHF (RD: -0.002; 95% CI: -0.036 - 0.032; p = 0.906). However, the subgroup analysis showed an increased risk for hyperkalemia in CHF patients treated with spironolactone (RD: 0.032; 95% CI: 0.003 - 0.060; p = 0.028). As an adverse event a significant risk of hypokalemia was found (RD: -0.029, 95% CI: -0.048 - -0.009; p = 0.004). CHF patients showed a higher incidence of hypokalemia than ADHF patients (RD: -0.046, 95% CI: -0.075 - -0.017; p = 0.002 versus RD: -0.006; 95% CI: -0.043 - 0.031; p = 0.745). At least our subgroups showed a benefit in risk of mortality but there was no significant difference between high dose (50-100 mg/d), medium dose (25-50 mg/d) and low dose (12.5-25 mg/d) spironolactone treatment (RD: -0.021; 95% CI: -0.049 - 0.006; p = 0.134). Meta-regression showed no correlation between mortality and hypokalemia, but between mortality and hyperkalemia on follow up.
Conclusion: Limitation of our study was that we did not differentiate between systolic and diastolic heart failure. Further limitation was the lack of reduction in mortality at the spironolactone group compared to placebo, even if we evaluated only the subgroup of the chronic heart failure patients. Compared to the placebo group spironolactone treatment represented no significant risk of hyperkalemia but was paradoxically rather associated with hypokalemia. The available evidence suggests that the risk of hyperkalemia at spironolactone treatment is clinically not important in ADHF and CHF patients on the usual medium dose but it is influenced by the follow up time.

P2231

Acute heart failure un the elderly: which is the treatment of choice at discharge? Real world data from the ATHENA registry

A Lo Forte[1]; F Orso[1]; A Pratesi[1]; A Herbst[1]; S Parlapiano[1]; G Biagioni[1]; F Fedeli[1]; C Ghiara[1]; AC Baroncini[1]; F Bacci[2]; G Ciuti[2]; M Di Bari[1]; N Marchionni[3]; A Ungar[1]; S Baldasseroni[1]

[1]Careggi University Hospital (AOUC), Department of medicine and geriatrics, Florence, Italy; *[2]Careggi University Hospital (AOUC), Department of emergency and internal medicine, Florence, Italy*; *[3]Careggi University Hospital (AOUC), Cardiothoracovascular Department, Florence, Italy*

On behalf of: ATHENA Study group

Background: the prognosis of patients with heart failure (HF) with reduced ejection fraction (HFrEF) has improved in recent years thanks to the availability of evidence based treatments. Currently, equally effective treatments are not available for patients with HFpEF (HF with preserved EF) and for those with HFmrEF (HF with mid-range EF), the new category of patients with HF, recently introduced by the European Society of Cardiology.
Purpose: to evaluate treatments at discharge in a real world setting of elderly patients after an episode of acute HF in the three different groups of HF: HFpEF, HFrEF and HFmrEF.
Methods: data derived from the ATHENA retrospective observational study which included elderly patients (= 65 years) admitted with diagnosis of AHF to a tertiary University teaching-hospital in the period 01.12.2014-01.12.2015.
Results: The final study population was composed by 291 patients: 19.9% of them with HFmrEF, 32.6% with HFrEF and 47.4% with HFpEF. Mean age of three group of patients was respectively 84.2, 84.3 and 80.3 years, $p < 0.001$. Pharmacological treatments at discharge in the three HF groups are shown in the attached table. BBs and MRAs were the only two classes of drugs that had a statistically different prescription rate across the three HF groups: patients with HFmrEF received BBs in similar percentage to patients with HFrEF. Instead MRAs prescription rate in HFmrEF was more similar to the one of patients with HFpEF.
Conclusion: at present, in the absence of specifical evidences from randomised clinical trials, patients with HFmrEF are treated similarly to those with HFrEF. Also, a high percentage of patients with HFpEF, receive treatments that only have been to improve prognosis in HFrEF patients. Randomised clinical trials evidences are needed to appropriately treat HFmrEF patients

Drug	Tot n = 291	HFrEF n = 95	HFmrEF n = 58	HFpEF n = 138	P Value
ACEI (%)	37.5	34.4	41.5	34.1	0.612
ARB (%)	19.5	22.2	17	18.6	0.703
BB (%)	68.4	82.2	73.6	56.6	0.001
MRA (%)	39.3	53.3	35.9	31	0.003
IVABR. (%)	4.4	6.7	5.7	2.3	0.271
FURO. (%)	89.7	93.3	88.7	87.6	0.375
DIGOX (%)	12.1	13.3	11.1	11.6	0.912

P2232

Pulmonary congestion, VA-ECMO output and outcome after cardiac surgery

W S Walter Stefan Speidl[1]; D Wiedemann[1]; K Lampichler[1]; D Toth[1]; B Steinlechner[1]; G Heinz[1]; G Laufer[1]; K Distelmaier[1]; G Goliasch[1]

[1]Medical University of Vienna, Vienna, Austria

Introduction: Venoarterial-extracorporeal membrane oxygenation (VA-ECMO) is a life-saving method for patients with low-output failure after cardiac surgery. However, VA-ECMO therapy may increase left ventricular afterload due to retrograde blood flow in the aorta, which may lead to progression of pulmonary congestion. The aim of this study was to examine the role of pulmonary congestion in patients that need VA-ECMO support after cardiovascular surgery.
Methods: We included 299 adult patients undergoing VA-ECMO support following cardiovascular surgery. Primary endpoint was 30-day survival. Pulmonary edema was assessed on bedside chest X rays at day 0, 3, 5 after VA-ECMO implantation.
Results: Median age was 65 (57-72) years, 69% of patients were male and 30-day survival was 63%. The median SAPS-3 score and the median EuroSCORE of the study population were 43 (37-52) and 10 (8-13), respectively. At ICU-admission 20% of patients had mild, 54% had moderate and 26% showed severe pulmonary congestion. Pulmonary congestion at day 0 was not associated with outcome (adjusted HR 1.31; 95%-CI 0.89-1.93;P = 0.18), whereas pulmonary congestion at day 3 (adj. HR 2.81; 95%-CI 1.76-4.46;P < 0.001) and day 5 (adj. HR 3.01;95%-CI 1.84-4.93;P < 0.001) was significantly associated with survival independent from SAPS-3 score, ECMO rotation, fluid balance, ECMO cannulation site, use of intra-aortic balloon pump (IABP) and type of cardiovascular surgery. Linear regression revealed that out of left ventricular function, cardiac output, central venous saturation, maximum dobutamine and norepinephrine dose as well as fluid balance solely ECMO rotation was associated with the evolution of pulmonary congestion (P = 0.007).
Conclusion: Pulmonary edema three and five days after ECMO implantation are associated with survival. Interestingly, a high VA-ECMO output was the most important determinant of worsening pulmonary congestion within the first five days.

P2233

Refractory cardiogenic shock: emergency mechanical circulatory support as a bridge to recovery

N S Piatrovich[1]; L G Shestakova[1]; Y P Ostrovsky[1]

[1]Republican Scientific and Practical Centre of Cardiology, Department of extracorporeal blood circulation, Minsk, Belarus

Background: Cardiogenic shock as an extreme degree of LV failure is one of the main causes of death. Out-hospital survival rate is 8-10%. The probability of achieving return of spontaneous circulation decreases after 10 minutes of conventional cardiopulmonary resuscitation(CPR).Extracorporeal membrane oxygenation (ECMO) plays role of a rescue and maintains adequate organ perfusion in catastrophic conditions of deterioration despite inotropes or vasopressors.
Purpose: To evaluate the effectiveness of MCS in patients with refractory cardiogenic shock.
Methods: Comprehensive single-centered retrospective review of 10 patients at the age of 55,7 ± 15,15 years(3 women and 7 men) after peripheral veno-arterial ECMO assisted CPR during the period 2015-2017years. For improvement of residual LV pump function we also used: percutaneous balloon atrioseptostomy (n = 1), intraaortic balloon pumping (n = 2), active drainage of LV (n = 1), combination of methods(n = 1). In 4 cases (40%) patients required renal replacement therapy. Selective antegrade perfusion was performed in 5 cases (50%)to prevent ischemia of lower limbs.
Results: During the period 2015-2017years 52 ECMO were applied.19,23%(n = 10) were used as a resuscitation. Initial characteristic of patients:LVEF 30,2 ± 10,2%, lactate 13,8 ± 5 mmol/l, BE -16,9 ± 4,4 mmol/l, pH 7,11 ± ,13, AP 61 ± 6,4/41 ± 8,8 mmHg. Doses of inotropic agents: dobutamine 5,86 ± 1,5 mcg/kg/min, noradrenaline 0,28 ± 0,22 mcg/kg/min,adrenaline 0,26 ± 0,12 mcg/kg/min. Mean support time was 7,3 ± 5,1 days(7 hours-13,6 days). Stay in ICU was13,9 ± 8,1 days. Stay in hospital- 34,3 ± 7,5 days. We had 2 fatal outcomes because of sepsis, irreversible multiorgan dysfuntion and neurological complications. Hospital survival was 80%.
Conclusions: MCS can be used as an effective rescue tool for stabilization of patients with refractory cardiogenic shock, during cardiopulmonary resuscitation before the return of spontaneous circulation. It gives an extra time for thorough diagnosis and treatment and enhances survival.

P2234

Comparison of the effectiveness of transcatheter aortic valve implantation in patients with pure aortic valve regurgitation versus aortic stenosis

E Munoz-Garcia[1]; M Munoz-Garcia[1]; A J Antonio Jesus Munoz Garcia[1]; JM Pinilla-Garcia[1]; F Carrasco-Chinchilla[1]; AJ Dominguez-Franco[1]; JH Alonso-Briales[1]; JM Hernandez-Garcia[1]; MF Jimenez-Navarro[1]; E De Teresa Galvan[1]

[1]University Hospital Virgen de la Victoria, Department of Cardiology, Malaga, Spain

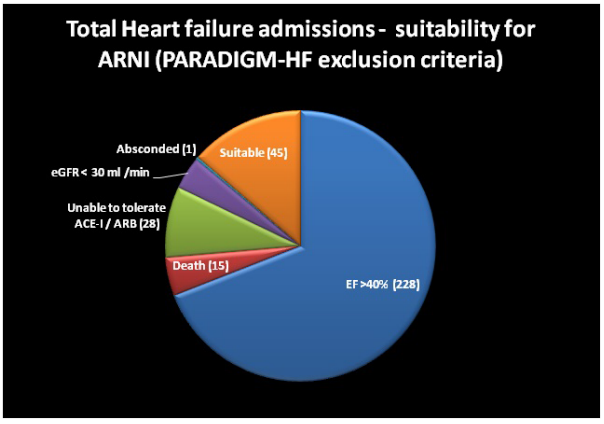
Limited data exist about safety and efficacy of transcatheter aortic valve replacement (TAVR) in patients with pure native aortic regurgitation (AR).
The aim this study was to evaluate the clinical outcomes of patients with pure native aortic valve regurgitation undergoing with Transcatheter Aortic Valve Replacement and comparing them with patients with aortic stenosis.
Methods: Between April 2008 and December 2017, 20 consecutive patients with severe pure aortic regurgitation (AR) underwent TAVR with the self-expandable aortic valve prosthesis (CoreValve) and 596 patients with severe aortic stenosis (AS).
Results: The mean age and logistic EuroSCORE were (AR vs. AS) 73.8 ± 16 vs. 79.6 ± 6.2 years, p = 0.001 and 16.9 ± 9% vs. 17.4 ± 12, p= 0.878 respectively.
There were significant differences in measurement of annulus and ascending aortic size (23.7 ± 2 vs. 22 ± 1.8 mm, p < 0.001 and 35 ± 6 vs. 31.1 ± 4 mm, p = 0.001, respectively). Implantation of prosthesis was performed successfully in 95% patients with AR. The degree of aortic regurgitation after procedure in patients with compared with AS were: none (40% vs. 41.5%) mild (35% vs. 33.6%) moderate (15% vs. 23.4%) and severe (10% vs. 1.5%), p= 0.430
The NYHA functional class improved from 3.2 ± 0.61 (baseline) to 1.37 ± 0.51 (one month) and remained stable at follow-up (1.4 ± 0.54). The mortality at 30 days was 10 % in patients with AR compared to 3.4% in patients with AS, p = 0.157 and there

was non-significant differences with late mortality (27.8% vs. 35.4%, p = 0.348) after a mean follow-up of 41.4 ± 27 months.
The patients with AR had similar complications after procedure than patients with AS: Occurrence new-onset left bundle branch block 27.8% vs. 44.3%, p= 0.05, stroke 5% vs. 3.9% p = 0.533, vascular complications 5% vs. 3.2% p = 0.468, acute myocardial infarction 5% vs. 1.7% p = 0.306, respectively.
Conclusions: Patients with pure native aortic regurgitation and at high surgical risk might benefit from transcatheter-based therapy. The long-term outcome is favourable compared with patients with aortic stenosis underwent with TAVR.

P2235
It is difficult to be first in class - Suitability of heart failure admission patients for ARNI

D Daniel O'hare[1]; S Quinn[2]; C O'connor[1]; R Murphy[1]; C Daly[1]
[1]St James Hospital, Dublin, Ireland; [2]Galway University Hospital, Galway, Ireland

Introduction:
The first in class angiotensin receptor neprilysin inhibitor (ARNI) Sacubitril / valsartan was included in the 2016 European Society of Cardiology heart failure guidelines following the results of PARADIGM-HF. This demonstrated superiority over Enalapril in reducing the risks of death and heart failure admissions in heart failure with reduced ejection fraction (HFrEF).
It has a class 1B indication for the treatment of patients with a reduced ejection fraction (< 40%), who remain symptomatic (NYHA II-IV) despite optimal treatment with an ACE-I, beta-blocker and MRA.
The aim of our study was to assess the indication and suitability of Sacubitril / valsartan in patients presenting with acute decompensated heart failure.
Methods: We performed a retrospective review of all patients admitted to a tertiary referral hospital during a one year period from 1st January to 31st December 2015, prior to the ESC recommendation of an ARNI, with a principal diagnosis of congestive cardiac failure. A total of 330 patients were included. The sub-group of patients with reduced ejection fraction were further analysed to assess suitability for Sacubitril / valsartan.
Results: Heart failure with reduced Ejection fraction (= 40%) accounted for 102/330 (31%) of patients. 15/102 (14.7%) did not survive until discharge and one patient absconded from the hospital. Of the remaining 86 patients, 13 had an estimated glomerular filtration rate (eGFR) less than 30 ml/min/1.73m2.
At the time of discharge of the remaining 73 patients, 62% were on an ACE-I or ARB, 70% were on a beta-blocker, and 34% were on a mineralocorticoid receptor antagonist.
18 out of 73 (25%) were prescribed each of an ACE-I(or ARB), a beta-blocker, and mineralocorticoid receptor antagonist.
Conclusion: The angiotensin receptor neprilysin inhibitor sacubitril/valsartan represents a new option in the pharmacological treatment of HFrEF. When the inclusion / exclusion criteria of PARADIGM-HF are applied to real world heart failure admissions, the majority of patients will be excluded. Only 45/330 or 13.6% of patients in this cohort would have been suitable for commencement on sacubitril/valsartan.
The majority of patients (<70%) in PARADIGM-HF were NYHA class I or II, therefore we must attempt to identify these patients in an outpatient setting prior to their presentation to hospital with an episode of decompensation.



Suitability for Sacubitril / Valsartan

Acute Heart Failure - Clinical

P2236
Differences in quality of life between acute heart failure patients with and without comorbidities

J C Van Den Berge[1]; LC Van Vark[1]; E Boersma[1]; HL Hillege[2]; I Lesman-Leegte[2]; KM Akkerhuis[1]
[1]Erasmus Medical Center, Department of Cardiology, Rotterdam, Netherlands; [2]University Medical Center Groningen, Department of Epidemiology, Groningen, Netherlands

Background: Heart failure (HF) patients with comorbidities have higher morbidity and mortality than those without comorbidities but little is known about differences in quality of life (QoL) between HF patients with and without comorbidities.
Purpose: We compared the QoL and the determinants of Qol of patients with HF with and without comorbidities.
Methods: This multicentre, clinical cohort study included patients with acute HF in the Netherlands. At discharge, patients were asked to complete the Kansas City Cardiomyopathy Questionnaire (KCCQ) and Hospital Anxiety and Depression Scale (HADS). History of cerebrovascular accident, diabetes mellitus, chronic kidney disease and chronic obstructive pulmonary disease (COPD) were considered as the most significant comorbidities.
Results: We included 327 patients (72 years old, 65% male) who completed at least one questionnaire at discharge. Of these, 198 patients (61%) had at least one comorbidity. Patients without comorbidities had lower New York Heart Association (NYHA) class, more depression and higher KCCQ scores, corresponding with better QoL (Table). Male sex, higher NYHA classification, previous HF, ischaemic aetiology, COPD, higher BMI, lower systolic blood pressure and higher NT-proBNP were associated with a worse QoL in the total population. These factors were also determinants of QoL in patients with comorbidities but not in those without comorbidities.
Conclusions: Acute HF patients with comorbidities had higher NYHA class at discharge, worse QoL and more depressive symptoms than patients without comorbidities. Furthermore, the determinants of QoL differed between patients with and those without comorbidities.

Table. NYHA classification and QoL score

		Comorbidity -	Comorbidity +	p value
NYHA class	I/II	71 (66)	88 (54)	0.049
	III/IV	36 (34)	74 (46)	
KCCQ	Physical limitation score	42 (21-71)	33 (13-63)	0.03
Clinical summary score		35 (25-61)	31 (16-54)	0.01
Overall summary score		35 (21-56)	30 (18-51)	0.13
HADS	Anxiety	46 (36)	63 (32)	0.43
Depression		38 (30)	83 (42)	0.03

Data reported in N (%) or median (IQR).EQ-5D, EuroQol 5 Dimensions; HADS, Hospital Anxiety and Depression Scale; KCCQ, Kansas City Cardiomyopathy Questionnaire ; NYHA, New York Heart Association; VAS, Visual Analogue Scale

P2237
Evaluation of worsening renal function in patients with acute decompensated heart failure, depending on ngal changes

I Igor Gorda[1]; E Amosova[2]; A Bezrodnyi[2]
[1]Kiev Alexander Clinical Hospital, Kiev, Ukraine; [2]O. O. Bogomolets National Medical University, Kiev, Ukraine

Background: Our purpose was to determine the value of worsening renal function (WRF) depending on the NGAL and in so-called "wet and warm" patients with acute decompensated heart failure (ADHF).
Methods: In 141 patients with ADHF at the age of 38 to 85 years old (mean age 66,4 ± 2,2) were involved in the prospective study. Worsening renal function (WRF) for creatinine occurred in 38 (27%) patients (WRF+), including 23 pts with increasing NGAL on D3 more than 15% relative to D1 (WRF+NGAL+) and 15 pts without (WRF+NGAL-)

P2237

	No WRF	WRF+ NGAL -	WRF+ NGAL+	P1-2	P1-3	P2-3
Dyspnea Borg D1	7,8 ± 0,47	8,1 ± 0,49	8,9 ± 0,53		p <0,05	
Dyspnea Borg Dsc	2,5 ± 0,15***	2,9 ± 0,17***	4,0 ± 0,24***		p <0,01	p <0,05
CVP,D1	174 ± 10,4	177 ± 10,6	196 ± 11,7		p <0,05	p <0,05
CVP D 4-6	83 ± 4,98***	89 ± 5,34***	110 ± 6,60***		p <0,01	p <0,05
E/E' D1	18,1 ± 1,09	18,6 ± 1,12	20,9 ± 1,25***		p <0,05	p <0,05
E/E' Dsc	12,9 ± 0,77 ***	14,1 ± 0,85**	16,8 ± 1,12**		p <0,05	p <0,05
Hospital period	11,8 ± 0,7	14,3 ± 1,0	16,7 ± 1,1	p <0,01	p <0,01	p <0,01

* - p < 0,05, ** - p < 0,01, *** - p < 0,001 compared to D1

Endpoints were CVP at days 4-6 (D 4-6), dyspnoe by Borg scale, E/E' at discharge (Dsc) and duration of hospital period.
Results: The WRF group with elevated NGAL differed from patients with WRF without elevated NGAL in dyspnoe, E/E' and CVP. In the same time the WRF group without elevated NGAL was comparable with no WRF group. The hospital period was the largest in WRF+NGAL+ group (see in table).
Conclusion: In the so-called "wet and warm" patients with ADHF WRF associated with an increase in signs of congestion only in patients with an increase in NGAL after 48 hours.

P2238
Hyperhydration by bioimpedance vector analysis at discharge is common and is associated with severe baseline congestion in patients with decompensated heart failure

M Bayarsaikhan[1]; A Soloveva[1]; V Aleshin[1]; A Metelkin[1]; S Villevalde[1]; Z Kobalava[1]
[1]Peoples' Friendship University of Russia (RUDN University), Department of Internal Diseases, Moscow, Russian Federation

Objective: Relieve of congestion is one of the main targets in treatment of patients with decompensated heart failure (DHF). The aim of the study was to assess the incidence and associations of residual congestion in patients with DHF using bioimpedance vector analysis (BIVA).
Methods: In 148 patients with DHF (99 male, 71 ± 11 years (M ± SD), arterial hypertension 95%, myocardial infarction 42.5%, atrial fibrillation 65%, diabetes mellitus 42.5%, chronic kidney disease 26%, ejection fraction (EF) 41 ± 14%, EF < 40% 44.6%, baseline NT-proBNP 4148 (1635;5567 pg/ml) hydration status was assessed by BIVA on admission and discharge, using resistance (R) and reactance (Xc) standardized by height (h). Less values of R/h and Xc/h mean more severe hydration. Deviation from the 50th, 75th and 95th vector percentile of the healthy reference population was considered as mild, moderate and severe hyperhydration. Hyperhydration by BIVA at discharge was defined as residual congestion. Mann-Whitney and Pearson chi-squire tests were performed. P < 0.05 was considered significant.
Results: 64.2% of patients had residual congestion by BIVA (mild, moderate and severe in 25.7, 31.1 and 7.4% of cases). Patients with vs without residual congestion had higher rate of baseline severe hyperhydration by BIVA (61 vs 26%, p < 0.001), lower baseline R/h (226 ± 49 vs 245 ± 40 Om/m, p = 0.008) and Xc/h (17 ± 5 vs 20 ± 5 Om/m, p = 0.002), achieved R/h (260 ± 48 vs 315 ± 49 Om/m, p < 0.001) and Xc/h (21 ± 4 vs 30 ± 5.5 Om/m, p < 0.001), absolute ?R/h (32 (10;56) vs 63 (43;89) Om/m, p < 0.001) and ?Xc/h (3.6 (1.1;7.1) vs 9.5 (6.3;13.7) Om/m, p < 0.001), relative ?R/h (14 (4;29) vs 26 (19;37) %, p < 0.001) and ?Xc/h (24 (5;53) vs 49 (28;83) %, p < 0.001). Patients with vs without residual congestion more often had oedema on admission (98 vs 89%, p = 0.017) and at discharge (48.4 vs 11.3%, p < 0.001), inferior vena cava (IVC) dilation (62 vs 43%, p = 0.028), hydropericardium (29 vs 13%, p = 0.026), absence of IVC collapsibility (65 vs 43%, p = 0.009), higher IVC diameter (24 (22;27) vs (23 (20;24) mm, p = 0.007) and pulmonary artery pressure (51 (40;68) vs 46 (33;58) mmHg, p = 0.028), received longer and higher dose of iv furosemide therapy (7 (5;9) vs 6 (4;8) days, p = 0.037, total dose (640 (420;940) vs 360 (240;780) mg, p = 0.012) and maximum daily dose (100 (80;160) vs 80 (60;120) mg, p = 0.032), had lower rate of switching to per os furosemide therapy (80 vs 94%, p = 0.019) and thiazide therapy (9.5 vs 24.5%, p = 0.042).
Conclusions: 64.2% of patients with residual congestion had more pronounced baseline BIVA hyperhydration, IVC dilation and diameter, hydropericardium. Despite more intensive loop diuretic therapy patients with vs without residual congestion had higher rate of oedema at discharge and lower R/h and Xc/h dynamics. BIVA can be a useful tool in monitoring congestive status in DHF.

Coronary Artery Disease - Pathophysiology and Mechanisms

P2239
Chronobiology in acute coronary syndromes, is global warming changing our incidence?

JP Gameiro[1]; L Teles[1]; MJ Vieira[2]; JP Sousa[1]; L Puga[1]; J Ribeiro[1]; J Silva[1]; L Goncalves[1]
[1]University Hospitals of Coimbra, Cardiology B, Coimbra, Portugal; *[2]Hospital of Santarem, Santarem, Portugal*

Introduction: The chronobiology of many cardiovascular syndromes is very well described in the literature, with seasonal variations on the incidence of heart failure acute episodes and hypertensive emergencies. However, the data concerning acute coronary syndromes are controversial and dependent on the climate variation of which region.
Purpose: Evaluate the existence of significant differences in the seasonal distribution of acute coronary syndromes at the centre region of Portugal.
Methods: A retrospective study, including all the patients admitted with acute coronary syndrome on the emergency room at one medical centre, between January 2009 and December 2013. We proceeded to the evaluation of the seasonal distribution (spring, summer, autumn and winter) of those syndromes in general and then divided by the 3 types (STEMI, NSTEMI and unstable angina). The statistical analysis was made using SPSS version 23. Significance chi-squared (X2) tests were applied.
Results: In this study, 1281 patients were included with the diagnosis of acute coronary syndrome (mean age of 68 ± 13.2 years) with predominance of the masculine gender (69.5%). Of those episodes, 37% were classified as STEMI, 42% classified as NSTEMI and 17% classified as unstable angina. The autumn season was the one with the most acute coronary syndrome episodes (27.5%). The general distribution of the acute coronary syndromes correlated significantly with the different seasons (X2 = 11.768, p-value= 0,008). The distribution of the 3 types of syndromes, did not presented significant statistical differences during the four seasons (X2 pearson = 11,301, p-value= 0.26).
Conclusions: The different seasons of the year have an impact on the incidence of the acute coronary syndromes. The autumn was the season with most cases, a fact that was not observed on other european countries. The type of acute coronary syndrome (STEMI, NSTEMI and unstable angina) was not influenced by the different seasons.

P2240
Evaluation of the role of ischemia reversal programme in ischemic heart disease using stress myocardial perfusion imaging: A pilot study.

RM Sane[1]; R Rahul Mandole[1]
[1]Madhavbaug Multidisciplinary Cardiac Care Clinics and Hospitals, Mumbai, India

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Background: Ischemic heart disease (IHD) incidence has increased in India at a rapid speed and shows regional variations, early onset, greater mortality and poor management. Stress thallium test is useful in diagnosing IHD early in patients who may be at risk for a heart attack.T he aim of the present study was to assess the cardiac muscle activity in IHD patients before and after ischemic reversal programme (IRP).
Methods: The present open label study involved fourteen IHD patients who underwent IRP (21 IRP sittings) at multiple centres. The inclusion criteria were patients with known IHD, age group between 40-70yrs, BMI >20kg/m2, and stress test positive for inducible ischemia. However, patients with recent myocardial infarction/ known hypo- or hyper- thyroidism/ chronic kidney disorder were excluded. Stress thallium test was performed after - enrolment, 21 IRP sittings and 25-30 IRP sittings. VO2max

and time of ischemia after stress test were also recorded in all the patients. Further, Seattle Angina Questionnaire (SAQ) was taken via telephonic conversation by research coordinators.
Results: Observations from Stress thallium test showed significant difference in Summed Stress Score [SSS] (13.5 ± 10.3, baseline vs. 10.7 ± 10.1, post 21 IRP sittings; p = 0.01) as well as Summed Difference Score [SDS](8.9 ± 6.2, baseline vs. 6.2 ± 6.3 , post 21 IRP sittings; p = 0.03) in IHD patients. Similarly we observed increase in VO2max levels (12.8 ± 5.7, baseline vs. 19.4 ± 7.8, post 21 IRP sittings and 23.6 ± 6.0, post 25-30 IRP sittings) and time of ischemia in seconds (370.7 ± 201.1, baseline vs. 597.8 ± 201.9, post 21 IRP sittings and 702.0 ± 138.0, post 25-30 IRP sittings).Further assessment of SAQ scores showed significant improvement post IRP (30.2 ± 3.6, baseline vs. 32.7 ± 3.5, post 21 IRP sittings) whereas, ejection fraction score was not found to be significantly changed post IRP as compared with baseline.
Conclusion: Results of the present study suggest an improvement in cardiac muscle activity after IRP in IHD patients and depicts positive role of IRP in IHD management.

Coronary Artery Disease - Treatment

P2241
Veno-arterial extracorporeal membrane oxygenation in patients with massive pulmonary embolism: single center experience

J Jorge Garcia Carreno[1]; I Sousa Casasnovas[1]; M Juarez Fernandez[1]; C Devesa Cordero[1]; V Bruna Fernandez[1]; F Diez Delhoyo[1]; R Sanz Ruiz[1]; F Fernandez Aviles[1]; M Martinez Selles[1]
[1]*University Hospital Gregorio Maranon, Madrid, Spain*

Introduction: Massive pulmonary embolism (PE) is a critical condition with a wide mortality range from 25% to 65%, especially in patients with hemodynamic instability or cardiac arrest. Pulmonary reperfusion therapies are indicated in this kind of patients in order to reduce right ventricle afterload and correct ventilation/perfusion mismatch. Systemic thrombolysis is the most validated therapy but its potential benefit is often offset because of its bleeding effects. There is limited data about the use veno-arterial extracorporeal membrane oxygenation (VA-ECMO) in the setting of massive PE.
Purpose: It is difficult to routinely implant VA-ECMO in patients with massive PE and cardiogenic shock because it requires the availability of an interventional cardiologist or a cardiac surgeon, who will cannulate and decannulate the ECMO system, and facultatives with expertise in extracorporeal life support, who will manage the mechanical support in the acute critical care unit. We present our experience in the use of VA-ECMO in patients with high risk PE.
Methods: We conducted a retrospective analysis of data prospectively collected in a tertiary hospital. Massive PE was defined as low systolic blood pressure (< 90 mm Hg) requiring vasoactive drugs. The ECMO system was cannulated percutaneously, by the interventional cardiologist at the hemodynamic lab, using the Seldinger technique under fluoroscopy guidance. The usual approach consisted in advancing a 15-17 French (F) cannula to the descending aorta and placing a 21-23F cannula at the level of superior vena cava, through femoral access. A small anterograde cannula (5-6F) was placed in the superficial femoral artery. Anticoagulation with unfractionated heparin was provided both for the ECMO circuit and as treatment of PE.
Results: From November 2015 to January 2018, VA-ECMO was initiated in nine cases with massive PE, six were male and mean age was 58.2 ± 7.8 years. Every patient had severe right ventricle disfunction at admission. Mean serum lactate before VA-ECMO implant was 11.8 ± 3.2 mmol/L and five patients had cardiac arrest (55.6%). Pulmonary reperfusion either with thrombolytic drugs or mechanical thrombectomy was performed in five patients (55.6%). The mean time with VA-ECMO support was 3.3 days (SD 1.7) and the overall survival at hospitalization discharge was 44.4%. Interestingly, the survival among patients without pulmonary reperfusion, who only received anticoagulation and VA-ECMO support, was 100%.
Conclusion: In our experience, the use of VA-ECMO support in patients with massive PE is feasible, although it implicates high mortality rate. We believe that a "no reperfusion" approach with only VA-ECMO support and anticoagulation is superior to pulmonary reperfusion plus VA-ECMO, due to lesser coagulopathy and hemorrhagic events, resulting in better survival rate at discharge. Nevertheless, further studies with a larger cohort of patients are required in order to confirm these results.

P2242
Effect of different generations of drug-eluting stents on the prognosis of patients with stenting unprotected left main coronary artery.

Z KH Shugushev[1]; D A Daniil Maximkin[1]; AG Chepurnoy[1]; OO Safonova[1]
[1]*Peoples Friendship University of Russia (RPFU), Moscow, Russian Federation*

Aims: to evaluate long-term results of patients who underwent unprotected left main coronary artery (ULMCA) interventions with different generations of drug-eluting stents (DES).
Methods: there is long-term comparative clinical outcome data of percutaneous coronary intervention (PCI) in unprotected left main coronary artery (LMCA) disease treated with the single (provisional-T) stent technique in the drug-eluting stent (DES). The primary outcome was the occurrence of major adverse cardiac events (MACE) defined as total death, non-fatal myocardial infarction (MI), target lesion revascularization (TLR). Data from a single center registry, which included 189 patients, who ULMCA PCI with different generations DES. All interventions were conducted by final 'kissing-balloon' dilatation with high pressure balloons and under IVUS/OCT guidence. Long-term results were assessed by following criteria: frequency of MACE (death, myocardial infarction, re-intervention), IVUS//OCT data (residual area of vessel lumen in the proximal segment of LM, zone of bifurcation, the ostia of LAD and LCx).
Results: there were 72 patients receiving everolimus-eluting stent (EES) second generation ('Xience V'), 68 patients receiving biolimus-eluting stent (BES) third generation ('Nobori'), and 49 patients receiving everolimus-eluting stent (EES) IVth generation ('Synergy'). During 12-months follow-up, the PS adjusted Cox-proportional hazard ratio (HR) was not significantly different between the three groups for total death, cardiac death, TLR and MI. The narrowing of LCX ostial area at follow-up was more pronounced in BES compared with EES (13.2% vs. 2.5%, respectively, p <0.001). Linear regression analysis showed a high correlation between the number of stent struts in LCX ostium and ostial area narrowing (r = 0.771, p <0.001). Re-intervention was required in the LCX ostial area only in 3,1% of cases in group second generation EES and in 5,6% of third generation BES. During 3-years follow-up, there was no statistical difference in major adverse cardiovascular events, cardiac death, myocardial infarction and stent thrombosis between the groups different generations stents (HR: 0.63, 95% Confidence interval (CI): 0.33-1.17; P = 0.149).
Conclusions: The endovascular treatment of patients with unprotected left main bifurcation lesions with different generations of drug-eluting stents is associated with good long-term clinical outcomes. Clinical outcome seems to be independent of lesion complexity and the number of stent struts in LCX ostium. There are no differences in clinical events among patients receiving different generation drug-eluting stents for ULMCA disease.

P2243
The impact of soluable st2 to predict mortality and morbidity in patients with impaired left ventricular function undergoing coronary artery graft bypass surgery

A Ahmet Dolapoglu[1]; E Avci[2]; T Yildirim[3]; H Kadi[2]; A Celik[4]
[1]*Balikesir Ataturk State Hospital, Cardiovascular Surgery, Balikesir, Turkey*; [2]*Balikesir University, Cardiology, Balikesir, Turkey*; [3]*Balikesir State Hospital, Cardiology, Balikesir, Turkey*; [4]*Mersin University, Cardiology, Mersin, Turkey*

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Background: This study was aimed to investigate the prognostic value of soluble ST2 (sST2) for perioperative early mortality and morbidity in patients with impaired left ventricular ejection fraction (LVEF) and stable coronary artery disease (SCAD) undergoing coronary artery graft bypass (CABG) surgery.
Methods: 80 consecutive patients with SCAD and impaired left ventricular function (ejection fraction = 45%) underwent on-pump coronary artery bypass graft surgery were included into the study. We measured baseline ST2 preoperatively. The association between baseline sST2 levels and early perioperative mortality, postoperative adverse outcomes and length of stay were assessed.
Results: Patients were divided two group according to sST2 level of 35 ng/ml. Patients with sST2 >35 ng/ml (n = 14 patients) had an increased perioperative early mortality (p = 0.029), need of postoperative inotropic agents (p < 0.0001) and need of intraaortic balloon pump (p = 0.002). While LVEF was significantly lower (p = 0.019), left ventricular end-diastolic diameter (LVEDD), New York Heart Association (NYHA) class, Syntax score and NT-pro BNP levels were significantly higher in this group (p = 0.043, p = 0.0009, p < 0.0001 and p < 0.0001 respectively). And also postoperative complications such as arrhythmia and respiratory failure were more common and postoperative length of stay was significantly longer in patients with elevated ST2 level. In univariate regression analysis, sST2 was associated with increased postoperative mortality risk (p = 0.0068).
Conclusion: Higher sST2 levels were associated with adverse outcomes after CABG in patients with impaired LVEF and SCAD. Preoperative sST2 levels may predict postoperative outcomes after surgery in these patients with other traditional surgical risk scores.

P2244

Influence of age on quality of life after operative myocardial revascularization

K Katharina Huenges[1]; A Lorey[1]; B Panholzer[1]; J Jussli-Melchers[1]; P Kolat[1]; T Puehler[1]; J Cremer[1]; A Haneya[1]
[1]*University Medical Center of Schleswig-Holstein, Cardiovascular Surgery, Kiel, Germany*

Background: Relevant coronary artery disease still has a high prevalence in the western world, especially in younger patients surgical strategies might be beneficial for survival and outcome. But the impact of surgery on postoperative quality of life remains vague.
The possible influence of age on quality of life after operative myocardial revascularization (CABG) was evaluated in this study.
Methods: After informed consent and approval of our local ethic committee, patients with operative myocardial revascularization between 2005 and 2012 were analyzed in this retrospective study. Preoperative baseline characteristics, perioperative data and outcome were collected. Postoperative quality of life was assessed with the SF-36 questionnaire. Patients were divided into two groups, group young (age <50 years) and group elderly (>80 years).
Results: A total of 790 patients with operative myocardial revascularization were identified. Patients with combined procedures were excluded. In the young group were n = 305 patients and in the elderly group n = 485 patients. Elective surgery was more often in the elderly group (49.8% vs. 66.2%, p = 0.02). Severe reduced left ventricular function was more common in the young group (8.9% vs. 3.7%).
Perioperative data was comparable within both groups. After discharge and rehabilitation the patients were followed-up for assessment of quality of life.
The SF-36 questionnaire was conducted in 287 patients (young group: n = 175, elderly group: n = 112). It revealed no significant difference comparing the subscales social role functioning (83.7 vs. 79.5, p = n.s.), mental health (72.5 vs. 70.0, p = n.s.) and physical functioning (61.7 vs. 59.2, p = n.s.) between the young and elderly group. But subscale scores were higher in the younger group regarding bodily pain (81.0 vs. 25.1, p <0.01) general health perceptions (76.0 vs. 52.5 p <0.01), physical role functioning (55.2 vs. 20.2, p <0.01, vitality (70.1 vs. 47.4, p <0.01), emotional role functioning (78.2 vs. 68.4, p <0.03)
Conclusion: Even though in the younger patients more often preoperative cardiopulmonary reanimation and emergent surgery were required, young patients seem to benefit from operative myocardial revascularization with higher physical quality of life subscales. However, mental health did not differ between the two groups and also in the octogenarians elderly group satisfying results can be generated with regard to quality of life after operative myocardial revascularization.

Valvular Heart Disease - Epidemiology, Prognosis, Outcome

P2245

The five-year prospective observation of patients with rheumatic heart disease

V Petrov[1]; S Iakushin[1]; E Evgeny Philippov[1]
[1]*Ryazan State Academician I.P. Pavlov Medical University, Ryazan, Russian Federation*

The presence of valvular disease, especially stenosis, leading to pressure overload is an indication for surgical correction of the defect. Questions of medical therapy before a surgical correction of the recommendations discussed little.
Objective: investigate heart failure, quality of life and the possible causes of death in patients with rheumatic heart diseases.
Methods: The study involved 123 persons with rheumatic heart disease (RHD), including 16 patients who died. The average age of patients 57,56 ± 0,98 years; 31 (25.2%) men and 92 (74.8%) women.
Results: Patients at CHF FC as follows: I FC - 25.7%; FC II - 45.7%; FC III - 20,0%, IV FC - 5.7% and the dynamics for 5 years was not observed. Comparison of the results of the test 6 min walk showed no change in functional class CHF. There was only a significant increase in the linear dimensions of the left atrium (LA), from 4,5 to 4,8 ± 0,09 cm.
According to the SF 36 there was no significant difference in the physical health component (from 31,59 ± 1,02 to 32,47 ± 1,18) and the mental component of health (from 38,85 ± 1,67 to 35,85 ± 1,04).
Only 32 (29.9%) patients were operated: from 6 commissurotomy performed, in 26 prostheses. On average, after surgery before the study took 7.5 ± 1.4 years. The age of patients (58,14 ± 1,49 - operated and 56,26 ± 1,3 - non-operated), the size of heart chambers, the test results 6 min walk (359,92 ± 14,3 m - operated and 355 5 ± 18,25 m - non-operated) did not differ significantly.
The frequency of prescribing for HF was next): ACE inhibitors - 73.3%, ßAB - 60.0%, digoxin - 62.7%, spironolactone - 73.3%, loop diuretics - 32%, aspirin - 63 %, amiodarone - 7.4%, verapamil - 4.6%. From ßAB often used metoprolol tartrate - 66,7%, bisoprolol - 16.7%, carvedilol - 5.6% and 5.6% of nebivolol. Because ACE inhibitor enalapril more often used - 52.2% and perindopril - 23.9%, less lisinopril - 17.4% and fosinopril - 4.3%.
In the analysis of 16 patients who died within 5 years following the data obtained in the rheumatology department: the average age of the deceased was 60,6 ± 2,1 years; 12 patients (75.0%) as a cause of death, heart failure decompensation set against the backdrop of the mitral or aortic stenosis. Among frequent concomitant diseases to be noted permanent atrial fibrillation - 75%, and diabetes - 50%. In patients who died echocardiography data differed significantly from that of the whole group: the linear dimensions of the LA (5,24 ± 0,18 cm vs 4,8 ± 0,12 cm) and the area of the mitral orifice (1,19 ± 0,16 cm2 vs 1,73 ± 0,09 cm2)
Conclusions: In patients with chronic rheumatic heart disease for 5 year follow-up there is no progression of chronic heart failure and a significant deterioration in the quality of life, despite the negative trend indicators echocardiography. The combination of atrial fibrillation, type II diabetes, severe mitral stenosis and left atrial dilation increases the risk of death in patients with chronic rheumatic heart disease.

P2246

The impact of the infective endocarditis restrictive prophylaxis in the complication rates

AC Ana Catarina Gomes[1]; I Cruz[1]; AI Marques[1]; S Alegria[1]; R Pereira[1]; D Sebaiti[1]; I Rangel[1]; I Joao[1]; H Pereira[1]
[1]*Hospital Garcia de Orta, Cardiology, Almada, Portugal*

Background: Despite improvements in management and treatment of infective endocarditis (IE), it is still associated with high morbidity and mortality. There is an increasing number of patients at risk of IE, particularly because of aging, long-term survival in congenital population and both valvular post-operative and post-device implantation. The 2015 ESC guidelines restricted IE prophylaxis to the population at high-risk to develop IE.
Methods: We studied the endocarditis population in our hospital in the last 10 years. The clinical and imaging data were collected as well as the complication rates.
Purpose: To study the difference between IE severity and complications until and after 2015, to assess the effects of less restrictive criteria for IE prophylaxis.
Results: 148 patients, 75% males, 61.5 ± 15.9 years. 51.4% with hypertension (HTN), 18.9% with diabetes mellitus (DM). Etiology of valvular heart disease: 2 patients with previous IE (infective endocarditis), 9 with degenerative disease, 1 with congenital heart disease, 1 with rheumatic heart disease. Comorbidities: heart failure (HF) in 27% (6.8% with HF device), pulmonary disease (PD) in 14%, chronic renal disease (CRD) in 14.9% (3.4% on haemodialysis (HD)), chronic hepatic disease (CHD) in 22.3%, HIV seropositive in 13.5%, cancer in 9.5%, 98.6% on immunosuppression (medical cause or drug-related).
76.4% with single valve endocarditis, 14.9% with double valve endocarditis. 56.8% with aortic valve disease, 39.2% with mitral valve disease and 13.5% with right valve heart disease. Native valve disease in 72.3%.
Echocardiographic presentation: vegetation in 80.4%, abcess in 13.5%, pseudoaneurism in 4.7%, valve obstruction in 6.1%, aneurysm in 3.4%, fistula in 4.1%. Regurgitation was observed in 54.1%.
Endocarditis complications: septic shock in 20.9%, embolic complications in 38.5%, local complications in 41.2%, death in 45.3%. Mortality causes: septic shock 12.2%, HF in 7.4%, septic embolization in 8.1%, tamponade in 0.7%.
The populations were similar in terms of gender (p = 0.56), HTN (p = 0.61), PD (p = 0.47), previously known valvular heart disease (p = 0.60), valvular aetiology (p = 0.29), native valve disease (p = 0.534), CHD (p = 0.36), cancer (p = 0.65), HIV infection (p = 0.58), IV drug use (p = 0.70). After 2015, pts had more DM (p = 0.04) and CRD (p = 0.02).
There was no difference in the total embolization rate (p= 0.03), cerebral embolization (p = 0.64), cardiac abcess (p = 0.72), pseudoaneurism (p = 0.21), fistula (0.56), obstruction (p = 0.32), septic shock (p = 0.12) and global mortality (p = 0.29). Although, there was more HF (p < 0.001) and large vegetations (p < 0.001) from 2015 on.
Conclusion: Patients with endocarditis until and after 2015 were similar in terms of risk factors for endocarditis. Although there were no differences in hard endpoints such as mortality and the majority of complications, we observed more HF and large vegetations in recent years.

Valvular Heart Disease - Treatment

P2247

Mitral valve repair and myocardial revascularization in patients with terminal heart failure assigned to status UNOS 2 as a "bridge" to orthotopic heart transplantation.

O Olesya Shatova[1]; T Troyanova-Shchutskaia[1]; A Kurlianskaya[1]; U Ostrovsky[1]; V Shumovets[1]; L Rachok[1]; T Denisevich[1]
[1]*Republican Scientific and Practical Centre of Cardiology, heart failure, Minsk, Belarus*

P2247

Parameters	Ischemic cardiomyopathy	P	Dilated cardiomyopathy	P		
Before	6 months after surgery	Befor	6 months after surgery			
Ejection fraction (B-mode), %	29 (26;31)	33 (27;36)	0.112	27 (24;30)	29 (26;33)	0.441
End diastolic dimension, mm	71 (67;77)	66 (60;69)	0.049	74 (69;84)	70 (62;74)	0.201
End systolic dimension, mm	62 (56;67)	52 (45;58)	0.067	63 (59;74)	58 (50;65)	0.529
End diastolic volume(B-mode), ml	255 (206;278)	216 (191;227)	0.142	266 (234;335)	235 (189;301)	0.859
End systolic volume (B-mode), ml	182 (148;208)	150 (120;168)	0.207	198 (170;240)	163 (126;223)	0.953
Left Atrium, mm	50 (47;54)	51 (47;52)	0.256	53 (48;56)	51 (46;55)	0.094
Left Atrium 1 (4-chamber view), mm	52 (48;56)	46 (45;49)	0.004	54 (50;59)	49 (48;54)	0.091
Left Atrium 2 (4-chamber view), mm	66 (61;70)	61 (58;63)	0.004	69 (62;73)	61 (60;65)	0.091
Pulmonary artery pressure, mmHg	56 (45;62)	36 (28;54)	0.012	47 (38;50)	37 (34;42)	0.124
Mitral regurgitation	3 (3;4)	1 (0;2)	0.001	3 (3;4)	2 (2;1)	0.012
Tricuspid regurgitation	3 (2;3)	0 (0;1)	0.001	2 (2;3)	1 (0;1)	0.151

Background: Orthotopic heart transplantation is a radical method of treatment of patients with terminal heart failure. Due to this surgical interventions are of particular interest and relevance as a "bridge" to heart tranplantation.
Purpose: to estimate the efficiency of surgical treatment of patients with terminal heart failure (HF).
Methods: The study included 60 patients in the status of UNOS 2. 35 patients with ischemic cardiomyopathy underwent coronary artery bypass grafting and atrioventricular valve repair (group 1). 25 patients with non-ischemic cardiomyopathy underwent surgery mitral valve repair (group 2). All patients underwent echocardiography and 6-minute walktest at baseline and in 6 months after surgery. In addition the quality of life was assessed in both groups of patients with the Minnesota Living with heart failure Questionnaire.
Results: Table 1 demonstrates parameters of intracardiac hemodynamics in both groups. An improvement in the quality of life was noted in 6 months after the surgery. It was confirmed by a decrease in the score on the Minnesota Living with heart failure Questionnaire (at baseline 64 points, in 6 months - 39 points, $p < 0.038$) The results of a 6-minute walk test significant increased (at baseline - 227 (185;290)m, in 6 months - 328 (196;310)m, $p < 0.041$).
Conclusion: Mitral valve repair in combination with myocardial revascularization in patients assigned to status UNOS 2 can be considered as a "bridge" to orthotopic heart transplantation.

Table 1. Characteristic of patients

Characteristics of patients (n = 672)	Values
Age, years*	64.3 ± 11.6
Atrial fibrillation, n (%)	311 (46)
Body mass index, kg/m^2*	26.9 ± 11.8
Chronic kidney disease (GFR < 60 ml/min/1,73 m^2), n (%)	201 (29.9)
Chronic obstructive airways disease, n (%)	69 (10.2)
Coronary artery disease, n (%)	189 (28.1)
Insulin dependent diabetes mellitus, n (%)	21 (3.1)
LV ejection fraction (%)*	56 ± 13
NYHA (classes)*	2.5 ± 0.5
Hemoglobin, g/dL*	13.6 ± 1.1
RDW (%)*	13.85 ± 2.1
Red blood cell count, mln/uL*	4.3 ± 0.6
EuroSCORE II*	3.92 ± 2.51
Postoperative Hs-TnT, ng/L*	417 ± 143
Aortic stenosis, n (%)	243 (36.1)
Aortic regurgitation, n (%)	208 (30.9)
Mitral stenosis, n (%)	112 (16.6)
Mitral regurgitation, n (%)	109 (16.2)

Abbreviations: ESII = EuroSCORE II, Hs-TnT = High sensitivity Troponin T, LV = Left Ventricular, RBC = Red Blood Cell Count, RDW = Red Cell Distribution Width.

P2248

High-sensitivity troponin T is a prognostic marker of postoperative hemodynamic instability in patients undergoing valve surgery

P Duchnowski[1]; T Hryniewiecki[1]; M Kozma[1]; M Kusmierczyk[2]; P Szymanski[1]
[1]Institute of Cardiology in Anin, Department of Acquired Cardiac Defects, Warsaw, Poland; *[2]Institute of Cardiology in Anin, Department of Cardiosurgery and Transplantology, Warsaw, Poland*

On behalf of: Institute of Cardiology, Warsaw, Poland
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Introduction: Several studies have reported that elevated hs-TnT is associated with poor outcomes in patients with myocardial infarction or heart failure. The usefulness of hs-TnT as a predictor of perioperative hemodynamic instability in patients undergoing valve surgery is currently unknown.
Methods: A prospective study was conducted on a group of 672 consecutive patients with significant valvular heart disease who underwent valvular surgery. The primary end-point at the 30-day follow-up was perioperative hemodynamic instability defined as the need for a supply of catecholamines more than 48 hours after completing the cardiopulmonary bypass surgery.
Results: The perioperative hemodynamic instability occurred in 230 patients. At multivariate analysis: hs-TnT (P = 0.01) and RDW (P = 0.0006) remained independent predictors of the primary end-point.
Conclusions: Elevated postoperative hs-TnT was associated with a poorer outcome in patients following heart valve surgery in a 30-day follow-up.

P2249

TAVI on cardiopulmonary bypass; our experience in patients with a very low ejection fraction .

C Corrado Cavozza[1]; AA Audo[1]; AC Campanella[1]; CM Coscia[1]; BP Bianchi[1]; AC Cardinale[1]; PG Parodi[1]; EM Martuscelli[1]; CZ Zazza[1]; GM Mai[1]
[1]Ospedale SS. Antonio e Biagio e Cesare Arrigo, cardiothoracic and vascular department, Alessandria, Italy

Objective: Severe left ventricular dysfunction negatively impacts short and long-term survival after conventional aortic valve replacement . A subgroup of these patients with very low ejection fraction (EF= 20%) shows the highest operative risk. Transacatheter aortic valve implantation on cardiopulmonary bypass might be beneficial, either allowing better tolerance of rapid pacing and a precise prosthetic valve deployment, either improving the outcome.
Methods: Ten high-risk patients discussed in an interdisciplinary heart team, after informed consent, underwent TAVI using balloon expandable device. According to our institutional TAVI evaluation protocol, in every patient, a preoperative coronary angiogram, a transesophageal echocardiogram and an angio-CT scan were performed.
Results: Transacatheter aortic valve implantation was performed in a hybrid operative theatre by an interdisciplinary team of cardiac surgeons, cardiologists and cardiac anesthesists.
Cardiopulmonary bypass was instituted via femoro-femoral in all patients. The transcatheter valves were implanted using femoral, transapical approach. All patients

survived to the procedure and were discharged from the hospital uneventfully. Left ventricular ejection fraction increased
Conclusions: According to our experience, TAVI on cardiopulmonary bypass allows a safer treatment of high risk patients with a very low ejection fraction, in whom should be contraindicated both conventional AVR and TAVI.

Myocardial Disease - Clinical

P2250
The value of cardiovascular magnetic resonance in myocarditis with different clinical presentation

E M Elena Gupalo[1]; NA Mironova[1]; OV Stukalova[1]; PV Chumachenko[1]
[1]Russian Cardiology Research Center, Moscow, Russian Federation

Clinical manifestations of myocarditis vary from subclinical status to severe heart failure and cardiac arrhythmias also it can mimicking acute coronary syndrome. The diagnosis is based on the endomyocardial biopsy (EMB) which is strongly limited by possibility of complications. The only noninvasive alternative is cardiovascular magnetic resonance (CMR), but its diagnostic value may be different.
Purpose: to determine the value of CMR in patients (pts) with different clinical forms of myocarditis and to compare CMR with EMB data.
Methods: and Materials: 11 pts (group I, mean age 32.8 ± 11.1 years, 8 male) with infarct-like clinical presentation (troponin positive chest pain, changes on ECG, preserved contractility, normal coronary angiography); 48 pts (group II, mean age 43.1 ± 12.7, 31 male) with heart failure and sighs of non-coronary dilated cardiomyopathy (end diastolic diameter 7.0 ± 0.84 sm, left ventricular ejection fraction (LV EF) 30.1 ± 7.6%,) and 20 pts (group III, mean age 39.5 ± 14, 12 male) with sustained or non-sustained ventricular tachycardia, decreased LV EF (42.8 ± 8.8%) and excluded coronary artery disease underwent CMR with assessment of myocardial edema (ME), early (EGE) and late gadolinium enhancement (LGE). In 38 pts EMB was performed.
Results: CMR had maximal diagnostic value in group I pts : subepicardial or midwall, inferolateral or septal LGE lesions indicated inflammation in 9 (81.8%) pts. In 8 (72.7%pts) LGE was accompanied with ME, in 4 (36.3%) pts EGE was detected. In group II various LGE lesions (the most common were subepicardial or midwall, sometimes in combination with subendocardial or transmural) were found in 27 (56.3%), EGE - in 7 (14.6%) and ME in 10 (20.8%) pts. In group III 17 (85%) pts were LGE, 4 (20%) were EGE positive and in 7 (35%) pts ME was detected. LGE lesions were various and reminded the LGE lesions in group II. According to CMR data we denoted active inflammation in the presence of = 2 positive MRI criteria (n = 21), in pts with isolated LGE - resolved inflammation (n = 33), in pts with = 1 phenomenon (EGE or ME only) - minimal structural changes (n = 25). EMB confirmed active inflammation in 13 (34.2%) of pts (Fig 1A). In 11 (28.9%) pts EMB revealed resolved myocarditis with huge areas of fibrosis (Fig. 1B). In 14 cases (36.8%) the sighs of active inflammation were not detected and the morphological changes were minimal (Fig. 1C). According to above mentioned classification for both EMB and CMR data the total sensitivity of cardiac MRI was 76.9% with 66.7% specificity.
Conclusion: CMR gives key diagnostic information in pts with infarct-like clinical presentation of myocarditis. In pts presented with heart failure of ventricular tachycardia the introduced classification (active or resolved inflammation, minimal structural changes) increases the value of CMR and may be used in the definition of further diagnostic steps (f.e. EMB or ICD implantation

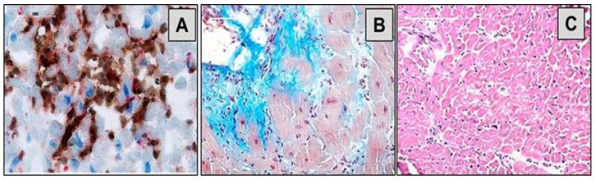


Fig. 1. The EMB samples. A – EMB samples of pts with **active myocarditis** manifesting with focal inflammatory cells infiltration (immunohistochemistry double staining for CD3+ (pink) and CD68+ (brown) cells); B – EMB samples of pts with **resolved myocarditis** (no inflammatory cells infiltration) and huge areas of focal fibrosis. Masson's trichrome staining (collage fibers are stained blue); C – EMB sample of patient with **minimal morphological changes.** Hematoxylin and eosin staining.

P2251
Immunosuppressive therapy of biopsy proved immune-mediated lymphocytic myocarditis in the virus-negative and virus-positive patients

O V Olga Blagova[1]; AV Nedostup[1]; EA Kogan[1]; AE Donnikov[2]; VV Kadochnikova[2]; VA Zaidenov[3]; AG Kupriyanova[4]
[1]I.M.Sechenov I Moscow State Medical University, Moscow, Russian Federation; *[2]DNA technology, Moscow, Russian Federation*; *[3]Institute of Transplantology and Artificial Organs, Moscow, Russian Federation*; *[4]Moscow Institute for Paediatry and Pediatric Surgery, Moscow, Russian Federation*

Purpose: to study the effect of immunosupressive therapy (IST) in the virus-negative and virus-positive patients with biopsy proved immune-mediated subacute / chronic lymphocytic myocarditis.
Methods: in 60 patients (45 male, 46.7 ± 11.8 years, mean left ventricle, LV, end-diastolic diameter, EDD, 6.7 ± 0.7 cm, LV ejection fraction, EF, 26.2 ± 9.1%) active/borderline myocarditis was verified by endomyocardial biopsy (n = 38), intraoperative biopsy (n = 10), examination of explanted heart (n = 3) and autopsy (n = 9). Anti-heart antibodies measurement as well as virus detection were performed. Indications for IST determined individually based on histological, immune, viral activity. The mean follow-up was 19.0 [7.25; 40.25] months.
Results: The viral genome in the myocardium was detected in 32 patients (V+ group), incl. parvovirus B19 in 23. The degree of histological activity did not differ depending on the presence of the viral genome in the myocardium. At baseline V+ patients had greater LV EDD compared with V- patients (6.8 ± 0.7 v 6.4 ± 0.7 cm) and lower EF (24.2 ± 9.1 v 29.5 ± 8.3%), p <0.05. The anti-heart antibody level was equally high in the V+ and V- patients. Antiviral therapy was administered in 24 patients. IST (in 22 V+ and 24 V- patients) include steroids (n = 40, 30 [20; 40] mg/day), hydroxychloroquine (n = 20, 200 mg/day), azathioprine (n = 21, 150 [75; 150] mg/day). The significant decrease of NYHA class (3 [3;3] to 2 [1;2], ? <0.001), LV EDD (6.7 ± 0.7 to 6.4 ± 0.8), systolic pulmonary artery pressure (48.9 ± 15.5 to 39.4 ± 11.5 mm Hg, ? <0,01), increase of LV EF (26.5 ± 0.9 to 36.0 ± 10.8), and significantly lower mortality (23.9% and 64.3%, p <0.01; RR 0.37, 95% CI 0.19-0.71) were found only in IST group. The best result is received in group V- patients with IST (EF increased from 28.2 ± 9.2% to 40.7 ± 9.8%, p <0.001). Significant improvement due to IST were achieved not only in V-, but also in V+ patients (EF increased from 24.7 ± 9.0% ?? 31.0 ± 9.8%, p <0.01). Only in V+ patients without IST no positive dynamics were observed, there was a trend to a decrease in EF. The mortality and the need for surgical treatment were highest in the V+ patients not receiving ICT. V+ patients had significantly higher mortality in comparison with V- patients (42.3 v 16.0%, p <0.01, RR 2.64, 95% CI 1.44-4.86). But mortality was lower in V+ patients receiving IST in comparison with V+ patients without IST (36.4% v 70.0%, p = 0.082)
Conclusions: IST in patients with immune-mediated lymphocytic myocarditis is effective and is associated with lower mortality both in virus-negative and virus-positive patients. The presence of the viral genome in the myocardium (especially herpes virus, but not parvovirus B19) followed by more severe dysfunction, less pronounced effect IST and higher mortality. The virus-positive patients in the absence of IST had no clinical improvement. The increasing in ejection fraction in the first 2 months of more than 10% associated with a good prognosis.

P2252
heart failure connected death in hypertrophic cardiomyopathy: clinical phenotype and mutation range

S Svetlana Komissarova[1]; N Chakova[2]; S Niyazova[2]; E Zakharava[1]
[1]Republican Scientific and Practical Centre of Cardiology, Minsk, Belarus; *[2]Institute of Genetics and Cytology of NAS, Minsk, Belarus*

Purpose: to assess clinical phenotype and mutation range in genes encoding sarcomere proteins of cardiomyocytes in patients with hypertrophic cardiomyopathy(HCM) with CHF progression to III-IV functional class(NYHA).
Methods: structural and hemodynamic parameters were examined in 345 unrelated patients with HCM(199 males and 146 females,age from 17 to 72 years,median age 47 years) by echocardiography,heart MRI, 24-hour ECG-monitoring.Mutation search in encoding sequences of genes CTC1, MYBPC3, MYH7, MYL2, MYL3, TNNI3, TNNT2 and TPM was carried out by next generation sequencing(NGS) for 15 patients with CHF.Revealed mutations in near relatives were identified by the method of automatic Sanger sequencing.
Results: for the observation period(median of observation 6,7 years) adverse outcomes were registered in 7 patients:lethal outcome because of the CHF progression to "terminal stage" in 6(1,7%) out of 345 patients,acute disturbance of cerebral circulation with lethal outcome in 1 patient.Event-free median of survivability was 4,3 years.Symptoms progression to III-IV functional class (NYHA) happened in 9 (2,6%) out of 345 patients for the observation period.Genotyping was carried out in all patients with lethal outcome and in 8 patients with "terminal stage".Mutations which are the cause of HCM:Glu924Lys in MYH7 gene; Arg346His, Gln1233*(in 2 patients) in MYBPC3 gene and combination of two mutations

Glu1265Val+Cys1266Arg in MYBPC3 gene - were identified in 5 out of 8 patients with lethal outcome.Next mutations:Val186Leu, Arg663His,Glu930del,Glu1356Lys in MYH7 gene;Gln1233*(in 2 patients) and rp1007fs in MYBPC3 gene;combination of two mutations Glu1265Val + Cys1266Arg (1 patient) in MYBPC3 gene - were identified in 8 patients with CHF-progression to "terminal stage".Trp1007fs mutation leading to reading frame shift in MYBPC3 gene and forming of premature stop codon was detected for the first time.Mutation search among near relatives identified both genotype-positive/phenotype positive and genotype-positive/phenotype-negative family members.Female patient with Trp1007fs mutation in MYBPC3 gene had sudden cardiac death (SCD) in family anamnesis(son with the same replacement); male patient with Val186Leu mutation also had SCD in family anamnesis (daughter).Mother of male patient with Glu1356Lys mutation in MYH7 gene had the same mutation and died in 59-year age from CHF-progression.It should be noted that Gln1233* mutation was identified in 4 patients which indicates on it association with CHF development.Combination of two mutations Glu1265Val + Cys1266Arg in MYBPC3 gene was identified in 2 patients with this pathology one of which had died in 48-year age.There were no mutations in analyzed genes in 3 out of 15 patients.
Conclusion: genetic features along with clinical factors are markers of high risk CHF-progression and can be used for adverse outcomes prognostication in patients with HCM and for early diagnostics of the disease in their near relatives.

P2253

Nosologic spectrum and differential diagnosis in primary left ventriculare hyperthrophy syndrome: results of clinic, genetic and morphological studies

O V Olga Blagova[1]; AV Nedostup[1]; EA Kogan[1]; VP Sedov[1]; YV Frolova[2]; SL Dzemeshkevich[2]; ME Polyak[2]; EV Zaklyazminskaya[2]
[1]*I.M.Sechenov I Moscow State Medical University, Moscow, Russian Federation*; [2]*Russian Research Center of Surgery, Moscow, Russian Federation*

Purpose: to study the nosological variety of primary left ventricular hyperthrophy syndrome (LVHS) and the spectrum of morphological changes during its various forms.
Methods: in this register were included 46 adult patients (25 men, 45.8 ± 15.6 years) with primary LVHS (more than 12 mm). The exclusion criteria were athletic heart, hypertensive heart disease, severe valvular disease and other causes of secondary LVHS. We performed 11 endomyocardial biopsy, 8 intraoperative biopsy, 1 study of explanted heart, 1 autopsy with virus investigation (real-time PCR) of the blood and myocardium. Mutational screening had included NGS (Ion Torrent) simultaneous sequencing of the MYBPC3, TAZ, TPM1, LDB3, MYL2, ACTC1, MYL3, MYH7, TNNI3 ? TNNT2 genes and direct Sanger sequencing of target genes. Clinical examination had included ECG, Holter monitoring, EchoCG, coronary angiography, CT / MRI (by indication).
Results: In 20 patients was diagnosis of isolated hyperthrophic cardiomyopathy (HCM) established, another 10 have a combination of HCM and noncompaction myocardium (NCM). Mutations in MYH7 and MYBPC3 genes in six cases were detected. In 13 cases (28.3%) were non-sarcomeric causes of LVHS detected. In 3 patients was Fabry disease diagnosed, in 2 - Danon disease, in 6 - amyloidosis (AL and mutant in 1), in 1 - Friedreich ataxia, in 1 - syndrome LEOPARD (mutations in X-GAL, LAMP, TTR, FXN, PTPN11 genes were detected). In 2 patients the etiology of LVHS remains unclear (HCM? amyloidosis?). The nosological diagnosis is in 28.3% of patients genetically verified. In patients with HCM were significantly more frequent asymmetric septal hypertrophy with obstruction and muscle bridges, in other forms of primary hypertrophy - right ventricular hypertrophy, low QRS voltage, QS complexes and increasing of EF (54.1 ± 13.8% vs 63.6. ± 9.1% in HCM, $p < 0.05$). The morphologic signs of myocarditis were in 36.4% of biopsy detected: in 3 patients with NCM and in 4 patients with HCM. In two cases were identified lymphocytic infiltration in the endocardium (one patient developed thrombotic endocarditis after the myotomy). The viral genome in the myocardium was in 8 patients (72.6%) detected, previously human herpes virus type 6 (it was correlation with myocarditis in 75.0%), and also parvovirus B19 (without myocarditis in 71.4%). It was not myocarditis and virus in patients with storage disease. The patients with myocarditis had the higher NYHA class (3 [1; 3] vs 2 [1; 2]), left ventricular diastolic size (5.2 ± 1.3 vs 4.8 ± 0.3 cm) and lower EF (53.0 ± 22.4 vs 58.0 ± 13.8%), $p > 0.05$. In a follow-up of 12 months 11 patients with LVHS died due to a stroke / heart hailure.
Conclusion: The spectrum of causes of the primary syndrome of myocardial hypertrophy is very wide. The frequency of associated myocarditis was 36.4%. When lower EF and heart failure in patients with HCM can be result of myocarditis, in patients with storage disease they are the result of disease itself.

P2254

Multi-parameter approach to risk stratification of sudden cardiac death for family dilated cardiomyopathy

TG Vaikhanskaya[1]; TV Kurushka[1]; LN Sivitskaya[2]; NG Danilenko[2]; OG Levdanskiy[2]; OG Davydenko[2]
[1]*Republican Scientific and Practical Center "Cardiology", Minsk, Belarus*; [2]*Institute of Genetics and Cytology, National Academy of Science, Minsk, Belarus*

Background: Risk stratification for sudden cardiac death (SCD) in family dilated cardiomyopathy (fmDCM) remains a difficult and controversial issue. The primary prevention of SCD with ICD-device therapy is effective but it is challenging to ?nd optimal candidates - patients who can benefit from it.
The aim of this research was to study the multi-parameter data in patients with fmDCM for optimization of the SCD risk stratification to accordance identified predictors of life-threatening ventricular tachyarrhythmic events.
Materials and methods. The study included 60 unrelated patients with fmDCM (aged 37.4 ± 15.9 years, 37/61.6 % male, NYHA 2.27 ± 0.75, LVEF 31.6 ± 9.12 %, follow-up 38.4 ± 7.14 months). All patients underwent dynamic studies (Intecard-7 ECG, HM, Echo, LGE-CMR). The NGS method using the Nextera XT for searching of mutations in the genes of the cardiopanel Illumina Inc (USA) was performed.
Results: Pathogen mutations were detected in 27 (45 %) patients: 6 (10%) had non-synonymous nucleotide substitutions in the LMNA gene; in 21 pts mutations identified in other genes such as a TTN (3\5 %), MYH 6 (3\5 %), MYH7 (2\3.3 %), SCN5A (2\3.3 %); and by one mutation (1.6 %) in genes DES, ACTN2, BAG3, LDB3, LAMP2, MYBPC3, NEXN, TRPM4, ACTC1, MYPN. In the three-year follow-up period, 13 (22.03 %) patients had documented episodes of stable VT/VF (including 6\10 % carriers of LMNA mutations). The following events were accepted as primary endpoints: SCD, successful resuscitation, stable VT/FF, appropriated ICD\CRT-D shock. As a result of the Spearman correlation analysis, a positive correlation revealed with carrier LMNA mutations ($p = 0.0015$), septal ECG criteria (V1-V3: Q or QS, poor R wave progression, QRS fragmentation) and interventricular septal or ventricular ?brosis by LGE-CMR ($p = 0.0025$), myocardial global longitudinal strain deformation (GLS LV average: $p = 0.003$) and unstable fast-VT (= 5 ventricular complexes with HR = 150 bpm: $p = 0.003$); a negative correlation was detected with the LV ejection fraction ($p = 0.002$). The results of ROC analysis confirmed the significance of unstable fast-VT (AUC 0.771, $p = 0.001$), LGE-CMR ventricular ?brosis (AUC 0.775, $p = 0.001$) and LMNA mutations (AUC 0.716, $p = 0.002$).
Conclusion: Family DCM patients with LMNA mutations have poor prognosis. The obtained data confirm the strategic importance of genetic research of fmDCM pts to searching LMNA mutations for early prognosis of adverse outcomes. Risk strati?cation should include the assessment of ventricular ?brosis by LGE-CMR, in addition to GLS LV or EF LV, HM ECG and the genetic pro?le of the fmDCM pts when available. This could signi?cantly improve the appropriateness of ICD therapy for fmDCM pts to the direction of personalized and precision medicine.

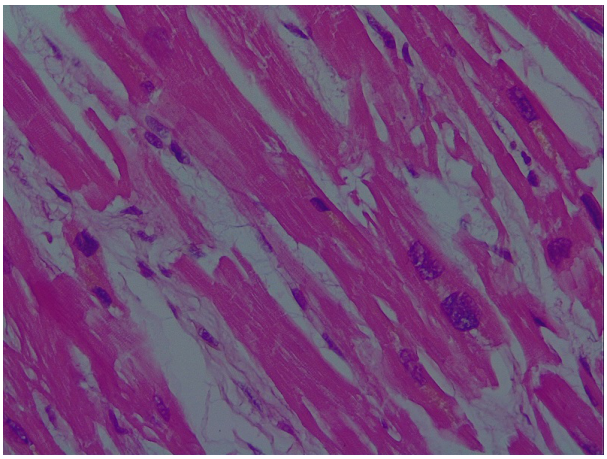
P2255

Dilated cardiomyopathy - from clinic to pathology

O Ovidiu Tica[1]; M I Popescu[2]; O A Tica[2]
[1]*University of Medicine of Oradea, Morphological Department, Oradea, Romania*; [2]*University of Medicine of Oradea, Cardiology Department, Oradea, Romania*

Introduction: Dilated cardiomyopathy (DCM) is characterized by a global heart dilation which leads to systolic impairment. More than half of primary DCM are familial in nature. Classic symptoms include paroxysmal nocturnal dyspnea, orthopnea, leg swelling, and shortness of breath. The diagnosis of DCM has been difficult to standardize given the influence of body size, athletic training, and biological heterogeneity on measurements of left ventricular volume and contractile function.
Aim: DCM is one of the most common causes of congestive heart failure with an ominous prognosis.
Methods: We performed a retrospective study were we included all deceased patients in our department with diagnosis of DCM (128 patients) during a period of 1 year (2016), excluding trauma related deaths. We examined medical charts, death certificates, autopsy reports and histopathological reports. Cardiac fragments are harvested, kept in formalin solution for minimum 24 hours, after trimming and orientation, tissue fragments undergoes processing for paraffin embedding and sectioned at a thickness of 3 to 5 μm manual microtome. The slides are stained using classical Hematoxylin-Eosin and Masson's trichrome stain.
Results: From the whole cohort (128 patients with DCM), 63 corpses were autopsied and all the organs were examined. More than 70 bodies had pulmonary complication (the most frequent was pulmonary edema) and 40 patients presented hepatic comorbidities. Generalized atherosclerosis was documented in 57 patients but the real number is consistently bigger (no documentation of atherosclerosis was made in patients who were exempt of the autopsy). Macroscopy examination reveals increased heart volume with a globular shape and a reduced tonus. In microscopy

we notice myocyte hypertrophy (enlarged, muscle fibres with hyperchromatic nuclei) and collagenous fibrosis (diffuse or extend into sub-endocardium). Interstitial cellularity is represented by scattered lymphocytes, fibrous cells, fibroblasts. Some myocardial fibres may exhibit degenerative changes and a perinuclear yellow - brown attrition pigment (lipofuscin).
Discussions: Pulmonary and systemic embolism can occur as blood stasis in dilated and hypocontractile cardiac chambers lead to activation of the coagulation cascade. Although the onset of the disease occurs with a mean age at presentation at about 50 years, in our study the main age group affected was from 61 to 80 y.o.
Conclusion: Early detection and proper treatment may improve the quality of life in these patients. When there is progressive end-stage heart failure despite maximal medical therapy and the prognosis is deemed poor, one may consider a heart transplant.



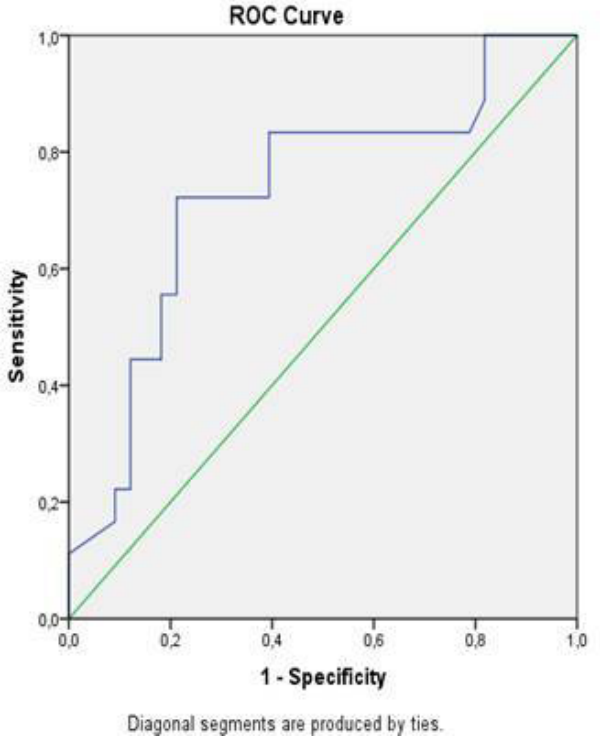
Myocite hypertrophy

P2256

Systemic ventricular longitudinal strain and NTproBNP independently predict major cardiovascular events in adult patients with congenital heart disease

A Alexandra Frogoudaki[1]; V Bistola[1]; I Pantelakis[1]; I Ikonomidis[1]; D Alexopoulos[1]; J Parissis[1]; G Filippatos[1]
[1]Second Cardiology Department, Athens University, ATTIKON University Hospital, Athens, Greece

Introduction: Global longitudinal strain (GLS) of the systemic ventricle predicts functional capacity, but its prognostic value is not established for all groups of adult patients with congenital heart disease .
Purpose: To examine the predictive value of GLS in adult patients with congenital heart disease .
Methods: We studied 57 clinically stable patients (31 men, mean age 37.1 ± 16.9) with congenital heart disease. Fourty-nine had systemic left ventricle, 5 systemic right ventricle and 3 single ventricle physiology. All patients underwent echocardiogram while NTproBNP was measured in a week interval from the echocardiogram. Off line GLS measurement of the systemic ventricle (SV) was performed (ECHOPAC GE).
All patients were followed-up by clinical visit or phone call for 782 ± 240 days and major cardiovascular events (MACE) were recorded. Death, hospitalization for heart failure, worsening functional class or cardiac intervention was defined as MACE.
Results: SVGLS significantly differed between systemic right, left and single ventricle patients
(-11.42 ± 3.37% vs -15.83 ± 4.03% vs -11.53 ± 6.13%, respectively, p = 0.025).
Median NTproBNP value was 118pg/ml (min18.7 pg/ml- max3788pg/ml).
SV GLS correlated with LogNTproBNP (r = 0.46, p < 0.001).
MACE occurred in 18 patients (30%).
NTproBNP and SVGLS independently predicted MACE (p = 0.006 and p = 0.007 respectively).
A cut-off value of NTproBNP 112pg/ml predicted MACE with a sensitivity 72% and a specificity 61%.
A cut off value of SVGLS - 14.45% predicted MACE with sensitivity 72% and specificity 79% (figure). SVGLS maintained its predictive value when adjusted for NTproBNP (HR: 1.189, 95% CI:1.047-1.349, p = 0.007)
Conclusion: Global longitudinal strain of the systemic ventricle predicted MACE in adult patients with congenital heart disease. Its predictive ability was maintained after adjustment for NTproBNP



ROC SVGLS

P2257

Does gender matter in patients with Takotsubo cardiomyopathy?

PM Pedro Azevedo[1]; B Faria[2]; R Pontes Santos[3]; N Craveiro[4]; A Marques[5]; H Antunes[6]; L Reis[7]; F Sa[8]; R Guerreiro[9]; O Azevedo[2]
[1]Faro Hospital, Cardiology, Faro, Portugal; *[2]Hospital Guimaraes, Cardiology, Guimaraes, Portugal*; *[3]Hospital Centre do Tamega e Sousa, Cardiology, Penafiel, Portugal*; *[4]Hospital of Santarem, Cardiology, Santarem, Portugal*; *[5]Hospital Garcia de Orta, Cardiology, Almada, Portugal*; *[6]Hospital Sao Teotonio, Cardiology, Viseu, Portugal*; *[7]University Hospitals of Coimbra, Cardiology, Coimbra, Portugal*; *[8]Hospital Santo Andre, Cardiology, Leiria, Portugal*; *[9]Hospital Espirito Santo de Evora, Cardiology, Evora, Portugal*

On behalf of: SUNSHINE

Introduction: Takotsubo cardiomyopathy (TC) affects primarily female patients. Some studies reported a higher mortality rate in male patients with TC, but the impact of gender in the characteristics and outcome of these patients is inconsistent throughout the literature.
Purpose: Assess the impact of gender in patients with TC.
Methods: Portuguese multicenter, prospective, descriptive and correlational study, involving 12 hospitals, in which all patients diagnosed with TC from 2004 to 2017 were included. Patients were divided in two groups based on gender: female (F) or male (M). Clinical data was compared between the groups. The primary endpoint was in-hospital mortality and the secondary endpoints were: 1) composite endpoint of in-hospital mortality, cardiogenic shock and malignant arrhythmias; 2) all-cause mortality during follow-up; 3) TC recurrence during follow-up.
Results: 240 patients were included, 24 (10%) were male with a mean age of 67.5 ± 15 years (versus 67.8 ± 11 years for females). Men were more frequently smokers (33.3% vs 11.6%, p = 0,003) and were more likely to have a previous history of myocardial infarction (8.3% s1.4%, p = 0.02). There were no differences regarding other cardiovascular risk factors and major comorbidities.
Regarding the presentation, male patients had more frequently syncope (25%vs3.2%, p < 0,001) and physical stress as a precipitant (54.2%vs14.4%, p < 0,001), while females reported more chest pain (90.7%vs58.3%, p < 0,001) and an emotional trigger (50%vs16.7%, p = 0,002).
There were no differences regarding the type of TC, Killip class and left ventricular ejection fraction (LVEF) at admission, and electrocardiographic changes, except for complete right bundle brunch block (RBBB), which was more frequent in men (23.5%vs1.2%, p < 0,001). Men were more likely to have significant coronary artery disease (CAD) (26.1%vs11.2%, p = 0,04) and stroke during hospitalization (8,3%vs0.9%, p = 0,007). There were no differences regarding LVEF recovery and LVEF at discharge.

Concerning outcome, men had higher in-hospital mortality (12.5%vs0.9%, p = 0,008) and a tendency for higher rates of the composite endpoint of death, cardiogenic shock and malignant arrhythmias (16.7%vs8.8%, p = 0.21). After adjusting for covariates in a logistic regression model, gender had no impact in in-hospital mortality. With a medium follow-up of 35.8 months, there were no differences regarding all-cause mortality and TC recurrence.
Conclusion: Men comprise 10% of patients with TC, have more frequently significant CAD, syncope, physical stress as a precipitant and RBBB at admission. In this study, in univariate analysis, men had higher in-hospital mortality and a tendency for the higher rates of the composite endpoint of death, cardiogenic shock and malignant arrhythmias. Nevertheless, in multivariate analysis, male gender was not associated with a worse outcome.

Ventricular Arrhythmias and SCD - Pathophysiology and Mechanisms

P2258
Screening for mutations in patients with arrythmogenic right ventricular cardiomyopathy using next-generation sequencing

L Hategan[1]; J Borbas[1]; A Tringer[1]; B Csanyi[1]; V Nagy[1]; T Forster[1]; Z Hegedus[2]; I Nagy[3]; R Sepp[1]
[1]2nd Department of Internal Medicine and Cardiology Center, University of Szeged, Szeged, Hungary; *[2]Institute of Biophysics, Bioinformatics Group, Biological Research Center, Szeged, Hungary*; *[3]Seqomics Biotechnology Ltd, Morahalom, Hungary*

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Background: Arrythmogenic right ventricular cardiomyopathy/dysplasia (ARVC/D) is an inherited cardiac disorder caused by mutations in the genes encoding for desmosomal cell adhesion proteins or even non-desmosomal ones. Since the right ventricular myocardium is being progressively replaced by fibrofatty tissue, patients present with severe ventricular arrhythmia and an increased risk of sudden cardiac death.
Purpose: We aimed to screen for genetic variants in ARVC causative genes in patients with definite or suspected diagnoses of ARVC.
Patients and Methods: We screened 10 patients with 'definite' ARVC (6 males, average age 46 ± 10 yrs), 1 with 'borderline' ARVC (female, aged 64 yrs) and 4 with 'possible' ARVC (2 males, average age 43 ± 15 yrs). Genotyping was performed by next-generation sequencing and validated by capillary sequencing. ARVC-related genes were targeted for sequencing.
Results: Altogether 38 rare (minor allele frequency < 1%) genetic variants, leading to amino acid or 'splice-site' change have been identified in our patients. Out of the 15 patients, 3 carried a definite pathogenic gene variant (PKP2: p.Arg79*, p.Trp123* and DSC2 p.Ser645fs). Other 5 patients carried variants of unknown significance in desmosomal genes (PKP2 p.Asn512Lys, DSG2 p.Arg292Cys, DSP p.Asp2070Asn and p.Gln1670Pro, DSC2 p.Cys559Tyr). In other 4 distinct clinically confirmed patients, putative disease-causing non-desmosomal gene variants were found: p.Ala134Val in membrane-related CAV3 gene, p.Arg343Gln in AGL gene involved in glycogen degradation, p.Glu11099del in TTN gene, and p.Ser52Leu in CTNNA3 gene, already reported to be a candidate gene for ARVC. Single mutations were detected in 3 patients, whereas the others were identified as one of multiple variants.
Conclusion: Despite the high genetic heterogeneity, desmosonal genes remain the main causative genes in ARVC. Several non-desmosomal candidate genes like ACADVL, CAV3, AGL and TTN may contribute to the phenotype.

Myocardial Disease - Clinical

P2259
Immunosuppression in lymphocytic myocarditis with parvovirus B19 presence

C Tschoepe[1]; S Sophie Van Linthout[2]; B Pieske[1]; U Kuehl[1]
[1]Charité - Universitätsmedizin Berlin, Campus Virchow-Klinikum (CVK) Kardiologie, Berlin, Germany; *[2]Berlin-Brandenburg Center for Regenerative Therapies, Berlin, Germany*

Results from the "Cortisone in parvovirus inflammatory cardiomyopathy (CaPACITY) - observational trial"
Background: Parvovirus B19 (B19V) is generally acquired in childhood and persists lifelong in 60 to 70% of the adult population The current scientific statement of the ESC recommends avoidance of the use of immunosuppression in entero- and adenoviral genome-positive patients with lymphocytic myocarditis (MC). Whether this precaution holds true for patients with B19V persistence is unknown.
Aim: We aimed to get insights in the effects of immunosuppressive treatment of B19V-positive (+) and –negative (-) patients with endomyocardial biopsy-proven MC.
Methods and Results: B19V+ (n = 43) and B19V- (n = 17) MC patients were treated with prednisolone and azathioprine in addition to standard heart failure medication. Six months after treatment, inflammatory infiltrates had resolved in all B19V- and 36 (83.7%) of B19V+ patients, by which mean viral DNA copy numbers declined. At baseline, VP1/VP2 mRNA was present in eight patients (13.3%), of which half resolved or persisted, respectively. LV-EF improved similarly in both B19V+ and B19V- groups upon treatment and stayed for at least 13 months.
Conclusion and translation: Ongoing cardiac inflammation is the most important risk factor for impaired outcome in MC. The finding that B19V replication is not aggravated under immunosuppression and patients gain a benefit from immunosuppression as do B19V- individuals is important to reduce inflammation in B19V+ MC patients. Further significance of these findings needs be proven in a phase II trial.

Pulmonary Circulation, Pulmonary Embolism, Right Heart Failure - Clinical

P2260
A propose management model of ambulatory patients recovered by acute pulmonary embolism

AB Scardovi[1]; P Petti[1]; P Coletta[2]; T Di Giacomo[1]; A Totteri[1]; G Vitaliani[1]; S Iosi[1]; R De Maria[3]; L Luca Arcari[1]; R Ricci[1]
[1]Hospital Santo Spirito, Cardiology, Rome, Italy; *[2]Hospital Santo Spirito, Medical, Rome, Italy*; *[3]CNR Institute of Clinical Physiology, Milan, Italy*

Background: Deep vein thrombosis (DVT) and pulmonary embolism (PE) are leading causes of preventable morbidity and mortality among hospitalized patients (pts). Pts who recover from acute PE are at risk of recurrent PE, chronic thromboembolic pulmonary hypertension (CHEPT) and right heart failure. Moreover DVT/PE may represent the first clinical manifestation of hidden neoplastic or autoimmune diseases. The early diagnosis of complications and sequelae of PE remains a challenge. For the delivery of quality care in the post-acute phase a dedicated cardiology clinic may be pivotal for structured ambulatory follow-up (FU) and the organization of a medical network with community cardiologists and general practitioners may be worthwile.
Methods and Results: At the Cardiology Department of our institution we have built a model of FU of pts with previous PE (shared between the Cardiology, the Medical Department and the Hospital Health Department) for risk assessment and management of anticoagulantion within 3/6 months of discharge and referral of pts with CHEPT to invasive therapies (pulmonary endarterectomy, pulmonary artery angioplasty).
Between 2014 and 2017 we enrolled 150 pts (aged 69+12 years, median 73, 59% female) in a follow-up pathway that included at entry a cardiology visit, 2nd level echocardiogram with detailed evaluation of the size and pressure of the right sections, functional capacity assessment through six-minutes walking test , cardiopulmonary test , complete blood tests including BNP and troponin assay and, in selected cases, genetic tests for thrombophilia, doppler of lower limbs veins, multidisciplinary specialist consultations. In pts at low risk of recurrent PE and/or development of CHEPT, anticoagulant therapy was withdrawn and the FU was carried on by the community medical network. In pts at intermediate risk, anticoagulation was continued, cardiological therapy was optimized and prognosis was reassessed based on the presence of perfusion deficits. High-risk pts were referred for 2nd level procedures. When anticoagulant therapy was withdrawn, the risk of relapse was monitored through serial measurement of D-dimer for the first 3 months, and long-term anticoagulation was recommended in pts with persistently high D-dimer.
We report our preliminary findings. In 40 pts (27%) early FU is still ongoing; of the remaining 110, 60 (54%) were low risk, 35 (32 %) intermediate risk, 15 (14%) were high risk; 8 (5%) pts died during FU. Outcomes were periodically reassessed by audits within the network to verify the effectiveness and efficiency of FU strategies.
Conclusions: Although crucial from the prognostic point of view, FU of pts with previous PE is not codified by the international guidelines and very little widespread in clinical daily practice. Our goal is to spread this virtuous management model.

P2261
Prevalence and clinical characteristics of adverse prognostic factors in pulmonary hipertension

A Ferro[1]; A Lescano[1]; G Damianich[1]; D Crippa[1]; HG Santa Maria[1]; A Lavalle Cobo[1]; N Gonzalez[1]; M Gonzalez[1]; H Grancelli[1]
[1]Finochietto Clinic, Buenos Aires, Argentina

Pulmonary hypertension (PH) is a multi-factorial condition associated with high morbidity and mortality. It requires for its diagnosis and treatment a multidisciplinary approach. In the past decades there have been many advances in the epidemiological, pathophysiological and therapeutic knowledge of the disease. However, there is little information available regarding clinical and prognostic factors in patients diagnosed with PH in Latin America.
Pourpose: Determine the prevalence and clinical characteristics of adverse prognostic factors in a population with recent diagnosis of PH.
Methods: Patients with recent diagnosis of PH (< 7 days) confirmed by right heart catheterization, with a mean pulmonary-artery pressure (MPAP) = 25 mm Hg (using a Swan Ganz Catheter) from three heart failure and pulmonary hypertension services were analyzed between March 2012 and December 2017. According to the recommendations of international guidelines, the following data were recorded: Personal data, PH group (G), clinical features: symptoms, functional class FC. Direct hemodynamic parameters: pulmonary pressures (PP), wedge pressure (WP), right atrium pressure (RA) and cardiac index (CI). Functional: 6 minute walk (6MW) test distance. Echocardiographic variables: right ventricle systolic function (RVSF), systolic pulmonary pressure and presence of pericardial effusion (PE). Data obtained were analyzed with BioEstat 5.3 program. Adverse prognosis factors identified were: history of heart failure (HF), syncope, advance functional class (III-IV), performance in the 6MW test < 350 m, presence of PE, RA = 12 e CI = 2,2.
Results: Multicenter, observational, descriptive, consecutive and prospective study. 131 patients where included. 73% women. Mean age was 59.8 (±19) years, 30% = 70. The mean delay in diagnosis was 22 months after the first sign or symptom recorded. PH group distribution: GI 65%, GII14%, GIII9%, GIV5% and GV6%. FC of presentation: I4%, II 40%, III35% and IV21%. History of HF in 76%, syncope in 24%. 6MW mean distance walked was 317 (±144) meters, 49 % performed = 350 meters. RHC: MPAP 48.9 (±16) mmHg, RAP 9.9 mmHG (±5,1) and = 12 mmHg 34%; CI 2,72 litres/min/mt2 (= 2,2 24%). Ecocardiographic data show: 80 % impaired FSVD (40% slight, 19% moderate and 21% severe) and PE in 25%.
Conclusions: In our population with confirmed pulmonary hypertension, with a predominance of group I, we had a high presentation in over 70 years of age. At diagnosis time a high number of patients present adverse prognosis factors. This findings remark the need to use early diagnosis and therapeutic strategies.

Hypertension - Other

P2262

Association between six-month blood pressure level and 1-year heart failure in hypertensive patients with acute myocardial infarction

S-J Joo[1]; J-G Lee[1]; K-Y Boo[1]; J-H Choi[1]; S-Y Kim[1]; K-S Kim[1]; M-H Jeong[2]
[1]Jeju National University Hospital, Cardiology, Jeju, Korea Republic of; [2]Chonnam National University Hospital, Cardilogy, Gwangju, Korea Republic of

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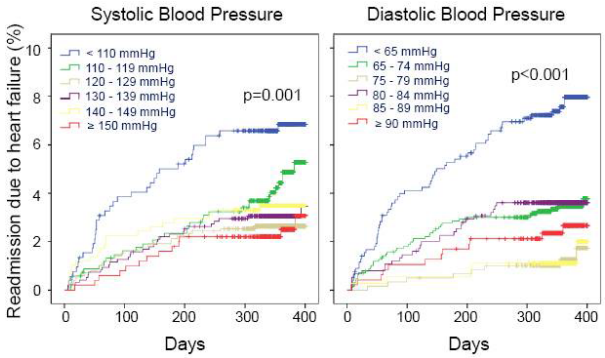
Background and purposes; There has been a long debate about "J-curve phenomenon" in the management of patients with hypertension, especially who have cardiovascular diseases. The blood pressure (BP) lower or higher than optimal level may be harmful in hypertensive patients with acute myocardial infarction (AMI). This study aimed to investigate the association between 6-month BP level and 1-year readmission due to heart failure (re-HF) in hypertensive patients with AMI.
Methods:; Among 13,104 patients who enrolled in nationwide AMI database of South Korea, the KAMIR-NIH Registry, 4,216 hypertensive patients, who survived the initial attack and had 6-month BP data, were selected in this study. They were divided into six systolic or diastolic BP groups according to BP levels (Table).
Results: Lowest 6-month systolic BP group of < 110 mmHg or lowest 6-month diastolic BP group of < 65 mmHg showed the highest re-HF at 1-year (6.9±1.1% and 8.0±1.0%, respectively) (Figure). On multivariate Cox-proportional hazard analysis, patients with lowest systolic BP (OR; 2.01, 95% CI; 1.17-3.44, p = 0.011) or lowest diastolic BP (OR; 4.04, 95% CI; 1.84-8.97, p = 0.001) had the highest re-HF at 1-year compared with optimal level of BP. Higher diastolic BP than optimal level also increased re-HF. Even after excluding patients with re-HF before 6 months, patients with lowest systolic BP (OR; 2.09, 95% CI; 1.19-3.67, p = 0.010) or lowest diastolic BP (OR; 3.98, 95% CI; 1.80-8.79, p = 0.001) at 6- month showed the greatest risk for re-HF at 1-year.
Conclusions: Systolic BP lower than optimal level, and diastolic BP lower or higher than that at 6-month, increased re-HF at 1-year in hypertensive patients with AMI.



Kaplan-Meier survival curve of HF

P2263

Features of early-diagnosed preeclampsia versus non-proteinuric gestational hypertension: a clinical and echocardiographic longitudinal study

N Patrascu[1]; LF Trasca[1]; DJ Mihalcea[1]; L Lungeanu Juravle[1]; MS Neagu[1]; M Cirstoiu[1]; D Vinereanu[1]
[1]University of Bucharest Carol Davila, Bucharest, Romania

Background: Hypertensive diseases of pregnancy are important causes of both maternal and fetal morbidity and mortality worldwide. Preeclampsia (PE) has the poorest prognosis by multiple organ damage and some data show a particular worse outcome for early-diagnosed preeclampsia (before 34 weeks). It is not known the cardiovascular evolution in these particular cases of pregnancy-induced hypertension long time after delivery.
Objectives. A clinical and echocardiographic 2 years follow-up after delivery in women diagnosed with early-diagnosed preeclampsia by comparison to non-proteinuric gestational hypertension (GHT).
Methods: 41 pregnancy-induced hypertensive women were enrolled, 18 with PE diagnosed before 34 weeks of pregnancy and 23 non-proteinuric GHT, no other cardiac disease, non-smokers and non-diabetics. We assessed by 2 D, tissue Doppler, speckle tracking and 4D echocardiography left ventricle (LV) structural parameters (wall thickness, sphericity and mass indexes); systolic global and regional function: 4D ejection fraction (LVEF), TDI S wave, radial, circumferential and global longitudinal (GL) strain and strain rate; and diastolic function by a set of spectral and TDI parameters. 19 subjects (9 former early PE) were re-examined 2 years after enrollment.

P2262 Risks of re-admission due to HF at 1-yr

SBP (mmHg)	No.	HR	95% CI	p value	DBP (mmHg)	No.	HR	95% CI	p value
<110	521	2.01	1.17-3.44	0.011	<65	779	4.07	1.84-8.97	0.001
110-119	681	1.59	0.93-2.74	0.091	65-74	1,268	2.48	1.11-5.53	0.027
120-129	988	1.00	Reference		75-79	588	1.00	Reference	
130-139	951	1.36	0.79-2.34	0.272	80-84	749	4.04	1.75-9.33	0.001
140-149	576	1.37	0.75-2.49	0.307	85-89	360	1.58	0.50-5.00	0.435
≥150	499	0.91	0.46-1.80	0.792	≥90	472	3.07	1.20-7.84	0.019

Multivariate Cox-proportional hazard analysis including age, sex, body mass index, diabetes, prior angina, prior myocardial infarction, prior heart failure, Killip class, smoking, chronic kidney disease, beta-blockers, inhibitors of renin-angiotensin system, statins, left ventricular ejection fraction, and ST-elevation myocardial infarction
DBP; diastolic blood pressure, CI; confidence interval, HR; hazard ratio, SBP; systolic blood pressure

Results: Groups were similar in terms of age (33 ± 4 vs 31 ± 6), pregnancy weeks, primi-/multiparity, systolic and diastolic blood pressure (150.3 ± 23/92.8 ± 22 vs. 157.6 ± 25/97.1 ± 24) and heart rate (90 ± 10 vs. 89.5 ± 12 bpm). At baseline, early PE group had significant lower pre-pregnancy weight (65.7 ± 11 vs 74.9 ± 15,p = 0.03), weight (76.2 ± 10 vs 85.9 ± 14 kg) and body surface area at enrollment (1.83 ± 0.1 vs 1.95 ± 0.1, both p = 0.01). No differences between all echocardiographic parameters were found. At 2 years follow up, 11 subjects (47%, 7 former early PE) were still hypertensive and treated. For all subjects, an improvement from baseline was noted only for radial strain (42.8 ± 15 vs 31.2 ± 7, p = 0.008), strain rate (2.6 ± 0.7 vs 2.1 ± 0.4, p = 0.04), GL strain (22.1 ± 2 vs 17.4 ± 3, p = 0.000) and GL strain rate (1.3 ± 0.1 vs 1.1 ± 0.2, p = 0.03) and LV sphericity index decreased (0.3 ± 0.05 vs 0.3 ± 0.1, p = 0.03). No significant changes in LV mass, LV wall thickness, S wave, LVEF or diastolic parameters were registered and there were no differences between former early PE or non-proteinuric GHT.
Conclusions: Our study showed that early-diagnosed preeclampsia women had, at baseline, a similar left cardiac systolic and diastolic function despite a significant lower weight pre-pregnancy and at enrollment time, by comparison to women with non-proteinuric gestational hypertension. However, 2 years after delivery, a significant number of women with history of early preeclampsia were still hypertensive requiring treatment. This underlines the importance of closer monitoring and management after delivery in these cases for preventing long term cardiovascular events.

P2264
Atrial electro-mechanical delay in hypertensive patients.

S Antit[1]; I Slama[1]; A Bleouer[1]; I Boussabeh[1]; M Thameur[1]; L Zakhama[1]; S Benyoussef[1]
[1]*Interior Security Forces Hospital, Department of Cardiology, Marsa, Tunisia*

Background: hypertension is the first cause of atrial fibrillation. Its onset is explained by intricate mechanisms such as atrial conduction impairment.
The aim of our study was to evaluate atrial conduction by tissue Doppler imaging in hypertensive patients compared to a control group.
Methods: This is a comparative prospective study performed in the cardiology department of the FSI hospital enrolling 55 patients with hypertension and 55 controls. All of them underwent a complete echocardiography exam with Doppler tissue imaging. We measures inter-atrial and intra-atrial electromechanical delay by Pulsed Tissue Doppler.
Results: Left ventricular mass and septal thickness were more important in the hypertensive group. Mitral A wave was greater in hypertensive group compared to controls (7.1 cm/s vs 5.6cm/s; p < 0.001; respectively). Left atrial volume was of 32.7ml ± 6.8ml/m^2 in hypertensive vs 29.5 ± 4.3ml/m^2 in controls (p = 0.006). Doppler Tissue study showed homogeneous statistically significant elongation of atrial conduction times in hypertensive patients compared to controls: inter-atrial time (16.8 ± 7.8ms vs 12.7 ± 4.2ms, p < 0.0003) and left intra-atrial (27.6 ± 8.6ms vs 19.0 ± 4.3ms, p < 0.0001) and right intra-atrial time (10.6 ± 6ms vs 6.6 ± 2.9ms, p < 0.0001) respectively for hypertensive and control subjects. There was a significant correlation between measured intra-atrial and inter-atrial electromechanical delays and duration of hypertension, indexed left atrial volume and indexed left ventricular mass (r: 0.27-0.47, p < 0.001). Conclusion: Atrial conduction time is significantly longer in hypertensive patients. Impairment of atrial conduction may be predictive of atrial fibrillation and should prompt closer follow-up to detect this arrhythmia in these patients.

Renal Failure and Cardiovascular Disease

P2265
Does right ventricle function and mechanics change in patients with end stage renal disease undergoing hemodialysis?

E Egle Tamulenaite[1]; R Zvirblyte[2]; R Ereminiene[3]; E Ziginskiene[3]; E Ereminiene[2]
[1]*Lithuanian University of Health Sciences, Kaunas, Lithuania*; [2]*Hospital of Lithuanian University of Health Sciences, Department of Cardiology , Kaunas, Lithuania*; [3]*Hospital of Lithuanian University of Health Sciences, Department of Nephrology , Kaunas, Lithuania*

Background: Right ventricle (RV) systolic dysfunction has been recognized as a predictor of cardiovascular death in many cardiovascular diseases (CVD), however the impact of end stage renal disease (ESRD) and hemodialysis (HD) on RV systolic function is still unclear.
Purpose: The aim of our study was to evaluate changes of RV systolic function and mechanics and to define predictors of RV dysfunction in patients with ESRD, undergoing HD.
Methods: 38 patients undergoing HD without known clinically significant CVD (HD group) and 32 age-matched persons with normal kidney function (GFR >90mL/min/1.73m2) (control group) were included into the study. Conventional 2D echocardiography and 2D STE offline analysis was performed and parameters of RV and LV geometry, function and myocardial deformation were evaluated. Statistical analysis was performed using SPSS version 24.0, p value < 0.05 has been considered statistically significant. Logistic regression analysis was performed to evaluate predictors of RV dysfunction (GLS>-20%) in ESRD.
Results: The groups were of the same age, gender, and body surface area. Basal diameter of RV did not differ between groups. Parameters of RV free wall longitudinal function were reduced in HD group, as well, as indices of global longitudinal RV strain, while RV fractional area change (FAC) didn't differ between groups (Table 1). PH was diagnosed in 6 (15.8%) of HD group patients. Univariate analysis showed that indices of LV geometry and function (LV myocardial mass index (OR 1.028, p = 0.031), E/e' ratio (OR 1.181, p = 0.039), LV GLS (OR 1.553, p = 0.004)) and PH (OR 15.750, p = 0.024) were associated with RV dysfunction. On multivariate analysis PH was found to be an independent predictor of RV dysfunction. (OR 24.826, p = 0.040) in HD group.
Conclusion: RV longitudinal function and deformation indices are reduced in ESRD patients undergoing HD. PH was found to be an independent predictor of RV dysfunction (GLS >-20%) in this group of patients.
Conflict of interest. None.

Table1.

Characteristic	Control group N = 32	HD group N = 38	p value
RVD1 (mm)	32.4±5.7	33.2±3.9	0.490
TAPSE (mm)	26.7±5.1	22.4±5.8	0.001
RV S' (cm/s)	15.6±1.6	12.4±3.1	<0.001
RV FAC (%)	58.1±7.5	55.7±7.4	0.191
RV GLS (%)	-25.5±2.5	-22.6±3.1	<0.001
RV GLPSS (%)	-25.1±2.4	-22.9±4.2	<0.001

RV - right ventricle, RVD1 - basal RV diameter, TAPSE - tricuspid annular plane systolic excursion, FAC - fractional area change , GLS - global longitudinal strain, GLPSS - global longitudinal peak systolic strain.

P2266
Applying of combined biomarker test in early diagnosis of acute kidney injury in patients with acute cardiac diseases

M Efremovtseva[1]; S Avdoshina[1]; S Villevalde[1]; Z Kobalava[1]
[1]*Peoples Friendship University of Russia (PFUR), Moscow, Russian Federation*

Introduction: The role of markers of structural kidney damage in diagnosis and prognosis of acute kidney injury (AKI) is widely discussed but still is unclear. Early diagnosis of AKI is especially important in acute cardiovascular diseases due to increased risk of severe adverse events associated with development of cardiorenal syndrome.
Purpose: To explore the role of biomarkers in early diagnosis of AKI and their prognostic values in patients with acute cardiac diseases.
Methods: 109 patients (51 with acute decompensated heart failure (ADHF), 58 with non-ST-elevation acute coronary syndrome (NSTE-ACS) were examined. Biomarkers of HF (NT-pro BNP in serum) and kidney damage (cystatin C in serum; neutrophil gelatinase-associated lipocalin (NGAL), kidney injury molecule-1 (KIM-1) and interleukine-18 (IL-18) in the urine) were estimated. Mann-Whitney test and multivariate logistic regression analysis were performed, p <0.05 was considered statistically significant.
Results: Patients with vs without AKI had higher levels of NGAL (344 ± 308.8 vs 37.9 ± 65.1 ng/ml, p <0.001) and KIM-1 (0.774 ± 0.36 vs 0.402 ± 0.59 ng/ml, p <0.01) in all groups. Patients with NSTE-ACS with vs without AKI had higher level of NT-proBNP (12857.1 ± 3108.8 vs 10134 ± 2479,μmol/ml, p <0.001), no difference was detected in ADHF group. In course of ROC analyses NGAL and KIM-1 showed the best prognostic values (AUC value 0.948 and 0.760). The ?ut points for NGAL >60.1 ng/ml (sensitivity 87%, specificity 92%) and KIM-1 > 0.519 ng/ml (sensitivity 87%, specificity 67%) were detected, coefficient of association f was 0,781 and 0,555 respectively. Simultaneous detection of two markers of structural kidney damage (increase of NGAL and/or KIM-1) in high-risk patients permits to diagnose 95% of AKI cases at admission. Patients with AKI and diagnostically significant levels of biomarkers had higher prevalence of CKD (p <0.01), acute heart failure, ADHF (p <0.05) vs those without increase of biomarkers, in-hospital mortality in this group was 29,8%.
Conclusions: Positive combined biomarker test is an independent and strong predictor of AKI in patients with acute cardiac diseases, and its implementation in

clinical practice may improve the early diagnostics of AKI when markers of kidney function are still at normal levels.

P2267

Risk assessment scale for detection of community-acquired acute kidney injury in patients admitted with cardiac diseases

S Avdoshina[1]; B Lobzhanidze[1]; M Efremovtseva[1]; S Villevalde[1]; Z Kobalava[1]
[1]*Peoples Friendship University of Russia (PFUR), Moscow, Russian Federation*

Introduction: Acute kidney injury (AKI) is a common and serious problem associated with poor prognosis.
Purpose: To reveal the prevalence and predictors of community-acquired AKI in patients with acute cardiac diseases.
Methods: 566 patients (278 with acute decompensated heart failure (ADHF), 288 with non-ST-elevation acute coronary syndrome (NSTE-ACS), 46% male, 71 ± 11 years (M ± SD), smokers 26%, arterial hypertension 91%, previous myocardial infarction (MI) 45%, diabetes mellitus (DM) 28%, atrial fibrillation 35%, chronic kidney disease (CKD) 46%, previous hospitalization with ADHF 36%, ejection fraction (EF) <35% 15%, blood pressure (BP) 142 ± 30/83 ± 16 mmHg were examined. AKI was diagnosed according 2012 KDIGO Guidelines. Community of hospital-acquired AKI was identified depending on time of development.
Results: Incidence of AKI in all patients, patients with ADHF and NSTE-ACS was 40, 43.5 and 37.2%. In-hospital mortality in patients with AKI was higher than in those with stable kidney function (14.9 vs 3.6%, p <0.001). Community-acquired AKI was present in 18% of patients (20.5 and 15.6% in ADHF and NSTE-ACS patients), in-hospital mortality was 16.7% (10.5 and 24.4% respectively). The risk assessment scale for community-acquired AKI was developed based on independent predictors of AKI, using binary logistic regression and ROC analysis (AUC 0.860, 95% CI 0.821-0.898).
Independent variables included in the model, and the corresponding points (pts) are listed below: clinical and demographic characteristics (male gender - 6 pts, alcohol abuse - 7 pts, DM - 1 pt), present on admission (MI - 5 pts, AHF/ADHF - 9 pts, systolic BP <120 - 10 pts, <110 - 15 pts, <90 mmHg - 27 pts; state of kidney function on admission: serum creatinine >98 and >128 mkmol/L - 14 and 22 pts, GFRCKD-EPI <45 and <15 ml/min/1.73 m2 - 7 and 14 pts; glucose level >7 mmol/L - 4 pts), outpatient intake of ACE inhibitors - 4 pts, absence of spironolactone in outpatient therapy - 1 pt. Diagnostically significant risk score for predicting AKI was >30 pts, the risk prediction model showed sensitivity 89%, specificity 66%.
Conclusions: Community-acquired AKI is common in patients in acute cardiovascular events, is associated with high mortality, and often is underdiagnosed. Usage of risk assessment scale in clinical practice may help to detect patients with high-risk of AKI on admission. Baseline kidney function and blood pressure level are main predictors of AKI in patients admitted with cardiac diseases.

P2268

Cardiorenal interrelations in patients with acute cardiac diseases: prevalence and prognosis

S Avdoshina[1]; M Efremovtseva[1]; S Villevalde[1]; Z Kobalava[1]
[1]*Peoples Friendship University of Russia (PFUR), Moscow, Russian Federation*

Introduction: Impaired renal function is a common finding in patients with cardiac diseases and confers an adverse prognosis in this population.
Purpose: to evaluate the incidence, phenotypes and prognostic value of cardiorenal interrelations in patients with acute decompensated heart failure (ADHF) and non-ST-elevation acute coronary syndrome (NSTE-ACS).
Methods: we examined 278 patients with ADHF (85.3% had anamnesis of symptomatic HF with frequent hospitalizations, 20.1% had ejection fraction <35%) and 288 with NSTE-ACS (64.9% developed myocardial infarction (MI)). In ADHF group in comparison with NSTE-ACS the patients were younger (69.7 ± 10.2 vs 72 ± 12.1 years, p <0.01), there were more men (55.4 vs 36.5%, p <0.001), smokers and alcohol abusers (47.8 and 30.6% vs 8 and 5.6%, p <0.001). The comorbidities were more typical for ADHF group: atrial fibrillation 46 vs 24% (p <0.001), obesity 55.8 vs 30.9% (p <0.001), anemia 40.6 vs 25.3% (p <0.001), diabetes mellitus 33.1 vs 23.3% (p <0.01).
Chronic kidney disease (CKD) and acute kidney injury (AKI) were diagnosed according to KDIGO 2012 Guidelines. AKI phenotypes were identified depending on time of development (community- or hospital-acquired), persistency (transient or persistent), history of CKD (AKI de novo or AKI on CKD).
Results: Incidence of CKD in patients with ADHF and NSTE-ACS was 45 and 46.5%, CKD was first diagnosed on admission in 57.6 and 64.2% of patients respectively. In 7.6% cases of ADHF and 14.2% of NSTE-ACS groups the duration of impaired kidney function was unknown. No associations of existing CKD and in-hospital mortality were detected.
Incidence of AKI in ADHF and NSTE-ACS groups was 43.5 and 37.2%. The hospital-acquired AKI, AKI on CKD and persistent AKI were found in 52.9, 47.9 and 46.3% of ADHF patients with AKI, and in 57.9, 58.9 and 50.5% in NSTE-ACS with AKI group respectively. In-hospital mortality was higher in patients with AKI in ADHF and NSTE-ACS groups (12.4 vs 5%, p <0.01 and 17.8 vs 3.3%, p <0.001). Mortality in patients with ADHF and hospital-acquired persistent AKI de novo and community-acquired persistent AKI on CKD was 41 and 29%, and in community-acquired transient AKI on CKD in the NSTE-ACS group - 29%.
Conclusions: Different cardiorenal interrelations were revealed in 75.2% of patients with ADHF and in 61.8% with NSTE-ACS. In patients with acute cardiac diseases high in-hospital mortality is tightly associated with phenotypes of hospital-acquired persistent AKI de novo and community-acquired persistent AKI on CKD in ADHF, and in community-acquired transient AKI on CKD in the NSTE-ACS.

P2269

Predictors of acute heart failure in patients with ST-segment elevation myocardial infarction of the electrocardiogram after PCI

E Mezhonov[1]; Y Vyalkina[2]; K Vakulchik[2]; S Shalaev[1]
[1]*GBUZ TO "Regional clinical hospital", Tyumen, Russian Federation*; [2]*Tyumen State Medical University, Tyumen, Russian Federation*

Background: Despite the PCI in patients with ST-segment elevation myocardial infarction (STEMI) the development of acute heart failure (AHF) Killip = II is associated with a poor prognosis.
Purpose: To identify predictors of the development of AHF and the prognostic value of AHF in patients with STEMI after PCI. Methods. In a prospective study, which lasted 6 months, included 233 patients (average age of 62.1 ± 10.89 years, 73.4% of men) admitted to the hospital due to the development of STEMI who underwent PCI. The endpoint was defined as the death from cardiovascular causes. Statistical processing of the results was carried out using the statistical packages of the programs "SPSS Statistics 17.0".
Results: During the follow-up observation from 1 day to 6 months (median follow-up of 5.2 months), 25 patients (10.7%) reported the onset of the endpoint, including 20 cases during the index hospitalization. AHF Killip = II during indexed hospitalization developed in 25 patients (10.7%). Independent predictors of Killip = II were: GFR < 60 ml/min initially on admission to hospital (OR 95% 5.690 (2.082-15.551), p = 0.001), anemia (OR 95% 5.317 (1.957-14.448), p = 0.001), EF < 40% (OR 95% 6.686 (1.291-34.628), p = 0.024). OR of the development of Killip = II increased with a decrease in GFR initially when admitted to the hospital: GFR 45-59 ml/min (OR 95% 6.167 (1.432-26.563), p = 0.015), GFR 30-44 ml/min (OR 95% 13.704 (2.795-67.187), p = 0.001), GFR 15-29 ml/min (OR 95% 32.889 (4.967-217.770), p < 0.001). The development of AHF Killip = II was associated with an increase in the frequency of the onset of the endpoint (7.2% and 40%, respectively, p < 0.001), increasing with the increase in the class Killip (I 7.2%, II 0%, III 55.6%, IV 83.3%, p < 0.001). In patients with AHF Killip = II, the incidence of acute kidney injury (AKI) increased (20.2% and 40%, respectively, p = 0.025). Killip = II increases the OR of development of AKI by 2.6 times (OR 95% 2.635 (1.105-6.282), p = 0.029). In the case of the development of both the AHF Killip = II and AKI, the OR of the onset of the endpoint increased many times (OR 95% 40.704 (8.990-184.283), p < 0.001), while the AHF Killip = II without AKI increased the OR fourfold (OR 95 % 4.361 (1.041-18.268), p = 0.044). Conclusion. In patients with STEMI the development of the AHF Killip = II is associated with a poor prognosis, the development of AKI in patients with AHF Killip = II aggravates this prognosis.

P2270

Combination of extracorporeal membrane oxygenation and continuous renal replacement therapy

R G Yarosh[1]; N S Piatrovich[1]; L G Shestakova[1]; Y P Ostrovsky[1]
[1]*Republican Scientific and Practical Centre of Cardiology, Department of extracorporeal blood circulation, Minsk, Belarus*

Objective: Acute renal injury is observed in 60-85% of patients within 48 hours after the beginning of ECMO. The main mechanisms of kidney damage on ECMO are related to the development of a systemic inflammatory response, the extent of the renal failure is determined by the duration of the procedure.
Purpose: To analyze the combined usage of extracorporeal membrane oxygenation (ECMO) and continuous renal replacement therapy (CRRT) in cardiac surgery.
Methods: A retrospective single-center analysis of 14 patients who who recieved combined treatment(ECMO and CRRT) during the period 2010-2017. The criteria for inclusion were: 1) Patients older than 18 years, 2) The combination of the use of ECMO and CRRT. The exclusion criteria was a duration of CRRT the background of ECMO less than 24 hours. Medical protocols of cardiovascular interventions, anesthetic management, conducting of CPB, ECMO and CRRT corresponds to all standards which are accepted for our centre.

Results: The duration of CRRT ranged from 3 to 15 days. By the second day of the combined treatment (CRRT and ECMO)we observed a significant decrease in urea and creatinine serum 2-fold to 9.1 mmol / l (p = 0,034) and 133.5 mmol / l (p = 0,007) respectively, as well as the restoration of acid-base status (p = 0.004).
Conclusions: The combination of two extracorporeal methods ECMO and CRRT is an effective combination. Integration of two physiological circuits ECMO and CRRT avoids cannulation of central or peripheral veins, thus provide an opportunity to avoid additional risks and complications associated with this type of intervention.

Autoimmune/Chronic Inflammatory Disorders and Heart Disease

P2271
Prevalence, factors associated and prognostic effects of preoperative anemia on short-and long-term mortality in patients undergoing Transcatheter Aortic Valve Replacement

E Munoz-Garcia[1]; M Munoz-Garcia[1]; A J Antonio Jesus Munoz Garcia[1]; JM Garcia-Pinilla[1]; F Carrasco-Chinchilla[1]; AJ Dominguez-Franco[1]; JH Alonso-Briales[1]; JM Hernandez-Garcia[1]; MF Jimenez-Navarro[1]; E De Teresa-Galvan[1]
[1]*University Hospital Virgen de la Victoria, Department of Cardiology, Malaga, Spain*

There is little information on the prevalence and factors associated with preoperative anemia in patients undergoing Transcatheter Aortic Valve Replacement (TAVR).
The aim of study was to analyze the prevalence and factors associated with preoperative anemia and the prognostic effects in mortality in patients with aortic stenosis undergoing TAVR.
Methods: 553 patients with aortic stenosis who underwent TAVR were included. Anemia was defined by the World Health Organization criteria (hemoglobin < 12.0 g/dl in women and < 13.0 g/dl in men).
Results: Before TAVR procedure, 367 patients (66.4%) were classified as anemic with a mean hemoglobin of 10.7 ± 1.1 g/dl vs. 13.3 ± 1.05 g/dl in the non-anemia group, p <0.001.Anemic patients were required more frequently blood transfusion (41.3% vs. 8.7%,p <0.001) after procedure. At discharge, the value mean of hemoglobin levels was 10.6 ± 1.5 g/dl in group anemic vs. 11.5 ± 1.3 g/dl, p = 0.015 in the non-anemia group.
The patients with anemia had more comorbidities compared with non-anemia group: Charlson index 3.5 ± 1.8 vs. 2.9 ± 1.4, p < 0.001; Karnosfky index 59 ± 18 vs. 66 ± 15, p < 0.001), Logistic EuroSCORE 18.4 ± 13 vs. 15.5 ± 9, p <0.001 and lower left ventricular ejection fraction 58.7 ± 15 vs. 62.8 ± 15%, p = 0.02.
Preoperative anemia was associated with total mortality 36.5% vs. 27.6% [OR= 1.511 (95% CI 1.027-2.223) p= 0.036] but not associated with 30-days mortality, 3% vs. 1.1%, p = 0.161. The predictors of anaemia were: chronic kidney injury (adjusted Odds ratio [OR]: 2.829 (95% CI: 1.680 to 4.764), p = 0.001, treatment with diuretics [OR= 3.104 (95% CI 1.676-5.749), p = 0.001] and anticoagulant treatment [OR= 1.989 (95% CI 1.006-3.936), p = 0.048].
Conclusions: the presence of anaemia is a frequent co-morbidity in patients with aortic stenosis who underwent TAVR, and it was associated with increase in overall death.

P2272
Insulin resistance, adiponectin level, endothelial function in rheumatoid arthritis females with heart failure with preserved ejection fraction

O Oksana Sirenko[1]; O Kuryata[1]; T Lysunets[2]
[1]*Dnipropetrovsk State Medical Academy, Dnipropetrovsk, Ukraine*;
[2]*Dnipropetrovsk Regional Clinical Hospital, Dnipropetrovsk, Ukraine*

Rheumatoid arthritis (RA) are associated with higher risk for cardiovascular mortality and developing of heart failure with preserved ejection fraction (HFpEF). Endothelial dysfunction, insulin resistance, adipose tissue exchange disorders may play important role in RA females with HFpEF.
We aimed to evaluate insulin resistance, adiponectin level, endothelial function in RA females with HFpEF.
44 females with HFpEF and low disease activity (DAS28 <3.2) comorbid RA (mean age - 55,7 [51,3; 60,5] years) were enrolled. Control subgroup made HFpEF females without RA (n = 29). All patients received stable therapy more than 6 months. ?atients with verified diagnosis of ischemic heart disease and diabetes haven't included in the study. The levels of adiponectin, insulin were measured using ELISA kit test, insulin resistance (IR) was estimated using HOMA2 index. Endothelial-dependent flow mediated vasodilatation (EDVD) by D. Celermajer method was performed. Statistical analysis included non-parametric methods with p value < 0.05.
Endothelial dysfunction was established in the majority of HFpEF females with RA - 32 (72.7%). The level of EDVD was significantly lower in this pts compare to controls - 4.5 [2.6; 6.4] % and 7.3 [5.3; 8.8] % respectively (p < 0.05). In multivariate analysis remaining factors for endothelial dysfunction in HFpEF females with RA were RA disease duration>10years (OR 3.4, 95%CI 1.4-8.8), ESR>16mm/h (OR 2.3, 95%CI 1.1-5.3), GFR < 90ml/min/1.73m2 (OR 2.8, 95%CI 1.1-6.1) and seropositive RA (OR 4.2 95%CI 2.1-7.7). Insulin resistance was estimated in 35 (79.5%) main group pts, elevated serum adiponectin level - in 17 (38.6%). HFpEF females with RA had significantly higher adiponectin, insulin, insulin resistance levels compare to control (p <0.05). Risk factors for IR in RA females with HFpEF were BMI = 30 kg/m2 (OR 7.4, 95%CI 4.3-15.8), RA-duration>10years (OR 2.6, 95%CI 1.2-5.8), EDVD <10% (OR 4.8, 95%CI 1.1-18), glucocorticoid therapy > 3 months (OR 6.4, 95%CI 2.1-16) and increased serum adiponectin level (OR 5.9, 95%CI 2.8-14.7).
HFpEF females with comorbid RA are characterized by significantly higher frequency of endothelial dysfunction, insulin resistance, adipose tissue disorders that should be taken in account in management of this group of pts.

Cardiovascular Nursing - Other

P2273
Remote patient telemonitoring in heart failure care. Experiences and perception of nurses and physicians in the Nordic Baltic region

I T Aamodt[1]; E Lycholip[2]; J Celutkiene[2]; A Stromberg[3]; D Atar[4]; R Sorum Falk[5]; T Von Lueder[6]; R Helleso[7]; T Jaarsma[8]; I Lie[9]
[1]*Oslo University Hospital, Centre for Patient centered heart and lung research, University of Oslo, Oslo, Norway*; [2]*University Hospital Santariskiu Klinikos, Clinic of Cardiac and Vascular diseases, Centre of Cardiology and Angiology, University of Vilnius, Vilnius, Lithuania*; [3]*Linkoping University, Department of Medical and Health Sciences, Linkoping, Sweden*; [4]*Oslo University Hospital, Department of Cardiology B and University of Oslo, Faculty of Medicine, Oslo, Norway*; [5]*Oslo University Hospital, Oslo Centre for Biostatistics and Epidemiology, Oslo, Norway*; [6]*Oslo University Hospital, Department of Cardiology B, Oslo, Norway*; [7]*University of Oslo, Department of Nursing Science, Oslo, Norway*; [8]*Linkoping University, Department of Social- and Welfare studies, Linkoping, Sweden*; [9]*Oslo University Hospital, Centre for Patient centered heart and lung research, Department of Cardiothoracic surgery, Oslo, Norway*

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Background: Remote patient telemonitoring (RTM) may improve heart failure patients' symptom management at home, and reduce the high rehospitalisation rate. Research reveal patients' need for knowledge on symptom monitoring, access to heart failure services and support from health care professional (HCP). HCPs experience and implementation of RTM in daily clinical practice are unknown in Norway and Lithuania.
Objective: Our aims were (1) to explore HCPs experience of and perception to use RTM in heart failure care in Norway and Lithuania, and (2) to identify characteristics of HCP considering RTM to be relevant in clinical practice.
Methods: Physicians and nurses (n = 784) working with heart failure patients either on a hospital ward or outpatient clinic at 100 hospitals, were enrolled into this cross-sectional study. Data from a 43-items questionnaire with closed and open-ended questions were collected between September and December 2016. To explore the impact on HCP considering RTM to be relevant in clinical practice, univariate logistic regression analyses with 15 variables of HCPs characteristics, including their competency with information and communication technology, was performed. Variables significant at a 5 % level were included in the multivariable analyses. Analyses of quantitative data included using SPSS. Text data from open-ended questions were qualitatively analyzed using summative content analyses.
Results: RTM is not a part of routine clinical practice in heart failure care in Norway or in Lithuania with none of the responding HCPs using telemonitoring as of today. The majority, 69% [536/784] of HCPs in Norway and in Lithuania responded to the questionnaire. The mean age of HCPs in Norway was 46 years (SD 11.2), Lithuania 48 years (SD 10.9) and the length of experience in clinical practice in Norway was 18.3 years (SD 10.5) and 24.8 years (SD 11.4) in Lithuania. The multivariable logistic regression analyses on characteristics of HCPs that found RTM relevant to implement in daily heart failure care revealed a significant interaction between country and education, and significant effect of hospital level (OR 2.6, 95 % CI 1.48-4.56). "How many years of postgraduate experience do you have" was forced to be included due to clinical relevance (OR 1.0, 95 % CI .958-1.00). As for the most challenging categories for implementing RTM in clinical practice, HCP responded (a) financing of RTM from different levels of health care authorities and (b) patients' limitations: mental and physical, knowledge and compliance issues.
Conclusion: RTM is not a part of routine heart failure care in Norway or Lithuania. Additional funding from health care authorities and targeting of heart failure patients, may improve use of RTM. Moreover, to support leaders and health care authorities

in the process of implementation of RTM at home, key HCP are characterised by level of education, working at a university hospital and their country.

P2274

Heart failure nurses education: theory and practise. implementation of the heart failure nurse curriculum in local cardiovascular education for nurses. a substudy of the interact-in-hf study

K Karolien Baldewijns[1]; HP Brunner-La-Rocca[2]; L De Maesschalck[1]; A Deville[3]; J Boyne[2]
[1]Thomas More Mobilab, Mobilab , Geel, Belgium; *[2]Maastricht University Medical Centre (MUMC), Department of Cardiology, Maastricht, Netherlands*; *[3]Thomas More Kempen, Inclusie, Geel, Belgium*

Background: According to the ESC guidelines, Heart Failure nurses (HFN) are an essential part of successful Heart Failure (HF) management programs. Due to the complexity of HF, HFN need specific competences to deliver high quality care. The heart Failure Association (HFA) of the European society of cardiology (ESC) has developed the Heart Failure nurse curriculum, yet little is known about its' implementation in additional local cardiovascular education (CE) in ESC-member states.
Purpose: To describe to which extent CE programs in Belgium, the Netherlands and Germany correspond with the HFA-curriculum.
Methods: A case study design was used to obtain an in-depth understanding of the implementation of the HFA-curriculum within three CE in three ESC-member states. Although some member states offer more than one CE, for this purpose we chose CE organised by the national cardiovascular nursing societies.
Representatives of these CE programs shared their curricula including the learning objectives, which we compared with the HFA-curriculum. This methodology corresponds with the method of structured focused comparison as defined by George (1979).
Results: All studied CE aim to provide HFN or cardiovascular nurses with essential knowledge, skills and professional behaviour to enable them implementing evidence-based and guideline derived care. It has been found that every CE has different areas of attention:
CE in Belgium discusses aspects of all core learning objectives of the HFA-curriculum. Within the HFA curriculum learning objectives consist of knowledge, skills and professional behaviour aspects necessary for competent HF-care. CE in Belgium primarily emphasizes knowledge aspects of HF-care, whereas skills and professional behaviour are less emphasized.
CE in the Netherlands concentrates on aspects of chronic diseases in general, and pays limited attention specifically to HF. Elaborate attention is paid on patient education, support in self-care and to manage the effective use of pharmacological and device therapies.
CE in Germany particularly pays attention to recognise patients with suspected HF, patient education, support in self-care, to manage the effective use of pharmacological and device therapies, palliative care and the importance of comorbidities. However, very little attention is paid to acute HF, and monitoring signs and symptoms of HF.
All studied CE pay some attention to the optional learning objectives of the HFA-curriculum i.e. management of advanced heart failure, and leadership in HF-Nursing.
Conclusion: All compared CE adopt certain aspects of the HFA- curriculum, but none of them adopts the curriculum as a whole.

P2275

Construction and validation of protocol for nursing consultation in pediatric cardiac transplantation

MGV Sobral[1]; V L Vera Lucia Pessoa[1]; RS Florencio[1]; VRF Cestari[1]; LC Souza[1]; DL Salles[1]; TMM Moreira[2]; JCS Santiago[3]; SR Braga[1]; WM Barroso[1]; KL Penaforte[1]; LR Menezes[1]; JNC Bento[1]
[1]HOSPITAL DE MESSEJANA DR CARLOS ALBERTO STUDART GOMES, Fortaleza, Brazil; *[2]State of Ceara University, Nursing Graduation, FORTALEZA, Brazil*; *[3]Federal University of Ceara, FORTALEZA, Brazil*

The pediatric heart diseases have been gaining a significant increase in society and are classified as congenital and acquired. The multidisciplinary team has a key role in the care of these heart diseases, especially the nursing professional, since it provides care to these inpatients during the whole day and in outpatient consultations. This study was intended to develop a technology to guide the outpatient follow-up consultation to the children and adolescents who underwent heart transplantation. This is a methodological study, which was developed in two steps: in the first, we drew up a protocol based on the existing literature; the second consisted of the process of validating the content and suitability of the material by expert judges. In this step, the evaluation of the quality of the protocol was performed by five judges, using the Appraisal of Guidelines for Research and Evaluation (AGREE II) instrument. This instrument is composed by 23 items divided into 6 domains, in addition to a global evaluation. In the present work, the following items 05,13, 18,21, 22 e 23 were excluded because they did not comply with the research. The scores assigned by the judges were calculated and analyzed according to the guidelines of the instrument itself and presented through tables and charts, which were produced

PROTOCOL DOC

in Microsoft Excel, version 2016. The calculation of Pearson's coefficient of variation was performed by domains; and the average by items of AGREE II. The expert judges have an average time of training of six years, four of whom have practical experience in the field of pediatric heart transplantation. Concerning the evaluation of the quality of the protocol, domain 2 (Stakeholders' engagement) received the highest score from the judges (94.3%), whilst domain 1 and domain 4 maintained a percentage equal or higher than 80%. The lowest percentage fell on domains 3 and 5, which had percentages of 76.30% and 78.60%, respectively. The analysis of PCV showed that all domains had low PCV indexes, which demonstrates the high homogeneity in the scores given by the judges to each evaluation item. When analyzing PCV, we observed that the highest degree of dispersion of the evaluation percentages was in domain 3 (8.70%), due to the greater variation of the scores assigned by the judges. The domains that presented the lowest values were domains 2 (3.00%) and 5 (5.80%), since the scores assigned to the items of these domains by the judges were mostly 6 and 7. The percentage of quality of the global evaluation of the protocol was 77.1%, and all judges pointed out the use of the protocol, but with amendments. After validation of the protocol for the nursing consultation to transplanted children and adolescents, we evaluated that its development has achieved a significant success. We hope that this protocol may subsidize the nursing practice.

P2276

Attitude toward advance directives and heart failure prognosis among patients with heart failure: a pilot study

MS Mi-Seung Shin[1]; J Kim[2]; S Heo[3]; M An[4]
[1]Gachon University Gil Medical Center, Incheon, Korea Republic of; *[2]Gachon University, College of Nursing, Incheon, Korea Republic of*; *[3]University of Arkansas for Medical Sciences, College of Nursing, Little Rock, United States of America*; *[4]Chonnam National University, College of Nursing, Gwangju, Korea Republic of*

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Background: Advance directives (ADs) are initially addressed in palliative care of patients with heart failure (HF) in Korea.
Objective: The purpose of this study was to explore values, treatment wishes, and proxy of patients with HF using a Korean-Advance Directive (K-AD) model and to explore associations of AD attitude and HF prognosis.
Methods: Patients with HF participated in this pilot test and completed surveys to explore the feasibility of K-ADs, attitude toward ADs, and HF prognosis.
Results: Of 24 patients (mean age, 67 years; men, 58.3%; ejection fraction, 35.88%), 62.5% completed the K-ADs. The major reason for incomplete K-ADs was knowledge deficit. Patients valued "comfortable death" the most (45.4%), followed by "giving no burdens to their family" (13.6%). Among treatment wishes, hospice care (66.7%) was preferred by the majority, while cardiopulmonary resuscitation (CPR) (31.8%) was selected less frequently. A child (50.0%) was mostly appointed as a proxy, followed by a spouse (33.3%). Patients with HF showed moderately positive AD attitude, with their completion rate of the K-AD of 70.0%. The 5-year survival estimation was 69.2%, with patients who wished for CPR having a higher survival (70.6% vs. 68.5%) and patients who wished for hospice care having a lower survival than their counterparts (70.7% vs. 75.2%).
Conclusion: The findings support the feasibility of the K-AD model, with a high acceptance in the two-thirds of the sample. Further studies are warranted to investigate whether treatment wishes are associated with AD attitude and HF prognosis in larger samples.

Digital health

P2277
Effects of telemedicine on depressive symptoms in ambulatory patients with chronic heart failure

J Kohler[1]; *A Stengel[2]; T Hofmann[3]; SD Anker[4]; K Koehler[5]; O Deckwart[5]; F Koehler[5]; M Rose[3]; U Laufs[6]
[1]Universität Leipzig - Faculty of Medicine, Leipzig, Germany; [2]University Hospital Tübingen, Department of Psychosomatic Medicine and Psychotherapy, Tuebingen, Germany; [3]Charité - Universitätsmedizin Berlin, Charité Center for Internal Medicine and Dermatology, Department for Psychosomatic Medicine, Berlin, Germany; [4]Charité - Universitätsmedizin Berlin, Division of Cardiology and Metabolism; Department of Cardiology, Berlin, Germany; [5]Charité - Universitätsmedizin Berlin, Department of Cardiology and Angiology, Center for Cardiovascular Telemedicine, Berlin, Germany; [6]Universitätsklinikum Leipzig, Klinik und Poliklinik für Kardiologie, Leipzig, Germany

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*equal contribution
Background/Introduction: Depressive symptoms are highly prevalent in patients with chronic heart failure (CHF) and associated with increased morbidity and mortality. CHF events such as hospitalisations worsen depressive symptoms. Evidence-based treatment options for depression in CHF patients are scarce. However, in most telemedical studies depression is an exclusion criterion.
Purpose: We investigated the effect of telemedicine on depressive symptoms in CHF-patients.
Methods: Our investigation represents a sub-analysis of the Telemedical Interventional Monitoring in Heart Failure (TIM-HF) Study. In this randomised, controlled, interventional trial (NCT 00543881), 710 CHF-patients were randomly assigned to either a group receiving usual care (UC) or a group that received a telemedical intervention (TM) consisting of a daily remote device that monitored the electrocardiogram, blood pressure and body weight. Depressive symptoms were evaluated by the 9-item Patient Health Questionnaire (PHQ-9) every three months in the first year and every six months in the second year. The analyses included only patients, who completed every item of the PHQ-9 at baseline. The cut-off for depression was set at = 10 points. Follow-up was 24 months.
Results: 158 patients presented clinically relevant depressive symptoms with a PHQ-9 score at = 10, independently, whether all or only some items were completed (TM: 80, UC: 78). 145 patients (TM: 73, UC: 72) completed every item of the PHQ-9, of whom 28 died within the study period (TM: 17, UC: 11, p = 0,22). Baseline characteristics did not differ between TM and UC group. Functional class III, dyspnoe at exertion, hospitalisation within the last 12 months prior randomisation, living alone and a prescription of antidepressants or antiarrhythmic agents were significantly associated with higher PHQ-9 levels at baseline (p <0.05). Higher PHQ-9 scores were also correlated with higher NT-proBNP levels (r = 0,141, p <0.05). After 24 months follow-up, the survivors with depressive symptoms at baseline who received telemedical care showed clinically meaningful improvements of PHQ-9 scores compared to the UC group by 32% from 12.7 ± 3.3 to 8.7 ± 5.6, (p <0.001). The improvement was consistent over the 24-month study period. The UC group showed no changes in PHQ-9 scores over time (13.1 ± 3.1 vs. 11.8 ± 5.5, p = 0.12).
Conclusion: The results of this study suggest that a subgroup of patients with significant depression symptoms at baseline shows improvement in depressive symptoms over a period of 24 months when successfully enrolled in a long-term telemedical care programme. Further studies are needed to confirm these results.

Basic Science - Cardiac Diseases

P2278
The biomarker sst2 is an independent predictor for acute kidney injury in patients with st segment elevation myocardial infarction

IR Vyshnevska[1]; YV Hilova[1]; OV Petyunina[1]; MP Kopytsya[1]
[1]Government institution"L.T. Malaya Therapy National institute of the National academy of medical sci, Kharkiv, Ukraine

The development of acute kidney injury (AKI) in patient with ST segment elevation myocardial infarction (STEMI) significantly associated with the adverse prognosis. In order to diagnose this condition in time the search for biomarkers is going. ST-2 is a novel and promising biomarker in the evaluation prognosis for STEMI patients with AKI.
Purpose: to determine the role of various markers in the development of AKI in patients with STEMI.
Methods: 103 STEMI patients were screened (75 male and 28 female), mean age was 61,85 ± 12,23 years. All patients had to undergo baseline investigations, including the level of serum creatinine; the glomerular filtration rate (GFR) was estimated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula. Accordingly, to the result, a group of patients has been selected (n= 59), their creatinine level was determined during the first 24 hours and after 48 hours. All patients were divided into two groups according to acute kidney injury network classification (AKIN): 27 patients in the first group with negative dynamic (1st stage AKIN and higher), 32 patient in the second group without creatinine dynamic. In addition, during the first day of hospitalization the sST2 and N-terminal pro-brain natriuretic peptide (NT-pro BNP) were determined.
Results: the analyses of biomarkers interconnection (NT pro-BNP, sST2) and GFR showed significant difference of estimated parameters in both groups as well (? = 0.02; ? = 0.03, respectively). Also, correlation of high and medium strength was found between biomarkers (sST2, NT pro-BNP) and GFR (? = 0.0001, p = 0.001). For identification of the main risk factor for reduced kidney function, we have used logistic regression method and found NT-pro BNP (area under curve (AUC) 0.7; p <0.05; 95% confidence interval (CI): 0.52 - 0.8; sensitivity (Se) 63%, specificity (Spe) 71%), sST2 (AUC 0.63; p <0.02; 95% CI: 0.52 - 0.74; Se 83%, Spe 41%) were main risk factors for predicting AKI formation.
Conclusions: changes in sST2 and NT-pro BNP level independently predict development of AKI in patients with STEMI.

Poster session 4 - Basic Science

Basic Science - Cardiac Biology and Physiology

P2279

The effects of exercise modality on myosin heavy chain isoform remodeling in the infarcted heart

JQ Zhang[1]; JR Cruger[1]; E Chung[1]
[1]*University of Texas at San Antonio, San Antonio, United States of America*

Funding Acknowledgements: UTSA Faculty Research Grant

Following myocardial infarction (MI), myosin heavy chain (MyHC) isoform expression shifts from a-MyHC to ß-MyHC, which associates with contractile dysfunction. The purpose of this study was to evaluate the effects of resistance training (RT) and endurance training (ET) on the MyHC isoform shift in rats with MI. MI was induced via surgical ligation of the left descending anterior coronary artery (LAD) in six-week-old male rats. Sham-operated rats underwent identical surgical procedures, only without LAD ligation to serve as non-MI controls. Rats were assigned to 4 groups: Sham (no MI, no exercise; n = 7), MI-Sed (MI, no exercise; n = 7), MI-RT (MI+ resistance training; n = 7), and MI-ET (MI+ endurance training; n = 7). Exercise training began 1-week after surgery for the MI-RT and MI-ET groups and continued for 10 weeks. MI-RT training consisted of progressively weighted ladder climbs on a 1m ladder with 2cm grip steps inclined at 85°, 3 days per week. MI-ET exercise entailed 10-16m/min running on a rodent treadmill inclined to 5° for 50 minutes per day, 5 days per week. Results showed significant increases in highly contractile a-MyHC cardiac isoforms in both the MI-RT and MI-ET groups compared to MI-Sed ($P < 0.05$). Furthermore, echocardiographic assessments revealed improvements in percent fractional shortening for both exercise groups which positively correlated with increases in a- to ß-MyHC isoform ratios ($P < 0.05$, $R2 = 0.535$). These results indicate beneficial effects of both RT and ET exercise modalities on post-infarct myocardial remodeling.

P2280

The relationship between metabolic shifts and cardiomyocyte structure alterations in heart failure and ischemic heart disease

T Tatiana Kulikova[1]; O Stepanova[1]; M Valikhov[1]; A Voronova[1]; V Sirotkin[1]; V Masenko[1]; R Akchurin[1]
[1]*Russian Cardiology Research and Production Complex, cardiology department, Moscow, Russian Federation*

Introduction: It is still unknown metabolic shifts in substrate utilization in the heart may be considered a cause or consequence in the pathogenesis of contractile dysfunction and heart failure (HF). A direct causal relationship between contractile abnormalities and metabolic dysregulation remains elusive. In HF there is a decrease in fatty acid mitochondrial oxidation concomitant with an increased reliance on carbohydrates for oxidative energy metabolism. Experimental studies, in addition to the tight coupling between cardiac work and oxidative metabolism, have demonstrated a direct causal relationship between shifts in substrate utilization and contractile dysfunction. Cardiomyocytes differ from other cells in that they contain sarcomeres which are essential for the contraction of the heart. Sarcomere is a main contractile unit of the heart. We propose that metabolic dysregulation in HF is connected with contractile dysfunction and cardiac metabolic alterations may lead to cardiomyocyte structure alterations, changes in sarcomere apparatus and impaired contraction of cardiomyocytes. The aim of the work is to study the relationship between metabolic shifts in HF and cardiomyocyte structure alterations.
Methods: In our study the expression levels of PPAR alpha as main regulator of cardiac metabolism were determined in left atrial appendages from patients with ischemic heart disease (IHD, n = 10) and HF and human non-diseased myocardium autopsy specimens (n = 5) using real time qPCR. Transmission electron microscopy was used for myocardial tissue studying.
Results: PPAR alpha expression level decrease was detected in the myocardial samples of patients with HF and IHD in comparison with expression level of PPAR alpha in the myocardial samples without cardiovascular pathology. These data indicate the occurrence of metabolic disorders in IHD - an energy metabolism shifting from cardiac fatty acid mitochondrial oxidation as primary energy source to glucose oxidation. In the same samples cardiomyocytes were evaluated by electron microscopy. Revealed cardiomyocytes have such features as sarcomere disorganization, obvious disruption of the sarcomere apparatus, enhanced glycogen content, mitochondria disposition, limited perinuclear mitochondria localization. It is well noticeable that mitochondria, which produce the basic energy for cardiac contraction in the normal heart and are localized along sarcomeres, depart from the disassembled sarcomeres in HF and IHD.
Conclusions: The results of our study have shown cardiac metabolic alterations and changes in structure of mitochondria - major energy station of cardiomyocytes - such as sparse mitochondrial infrastructure with immature cristae in HF and IHD. Mitochondria depart from contractile machinery of cardiomyocytes - sarcomeres, which become disassembled that lead in turn to impaired contraction of cardiomyocytes and to the decrease in cardiac contraction in HF.

P2281

Oxidative stress-induced changes in mitochondrial dynamics of cardiomyocytes in cell culture

O Orsolya Horvath[1]; L Deres[1]; K Eros[2]; K Ordog[1]; T Habon[1]; B Sumegi[3]; K Toth[1]; R Halmosi[1]
[1]*University of Pecs, Division of Cardiology and Angiology, 1st Department of Medicine, Medical School, Pecs, Hungary*; [2]*University of Pecs, Szentagothai Research Center, Pecs, Hungary*; [3]*University of Pecs, MTA-PTE Nuclear-Mitochondrial Interactions Research Group, Pecs, Hungary*

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Introduction: Oxidative stress induces imbalance in mitochondrial fusion and fission processes finally leading to cell death. Previous studies demonstrated the beneficial effect of two antioxidant molecules, BGP-15 and L2286 on mitochondrial functions and on cellular oxidative stress response. In this work, we studied the effects of these compounds on the processes of mitochondrial quality control.
Methods: We used H9c2 cardiomyoblast and isolated neonatal rat cardiomyocytes (NRCM) for the experiments. The concentration of stressors and antioxidants was determined with MTT test. We applied MNNG in 125 μM, 400 μM and 800 μM concentrations for 4 and 8 hours on H9c2 cells. H2O2 was used in 150 μM and 300μM concentration for 0.5 and 4 hours on both models. L2286 was applied in 10 μM, while BGP-15 in 50 μM doses. Cellular levels of proteins playing role in mitochondrial dynamics were measured in Western blot samples. For the analysis of mitochondrial network we applied electron microscopy and immunocytochemistry.
Results: Due to MNNG treatment the level of fusion proteins (OPA1, MFN2) decreased, while the level of fission protein DRP1 increased markedly. The levels of fusion proteins increased in L2286 and BGP-15-treated cells. During the 8 hour treatment, the level of DRP1 also increased in the treated cells ($p < 0.05$).
In H2O2 stressed cells, administration of L2286 increased the level of OPA1 in both H9c2 and NRCM cells. MFN2 levels in NRCMs raised considerably due to BGP-15 treatment ($p < 0.05$). L2286 treatment decreased the DRP1 level in H9c2 cells ($p < 0.05$). We observed that the H2O2-induced mitochondrial fragmentation could be decreased by L2286 treatment ($p < 0.05$).
Discussion: Our results indicate that the PARP-inhibitor L2286 has beneficial effect on mitochondrial dynamics during oxidative stress, and also in the case of directly induced DNA damage. We can make similar.
Conclusions: in the case of BGP-15, which, via reducing ROS accumulation, propagates fusion processes, preserving cellular viability.

P2282

Identifying the role of fat body-specific lipolysis for heart function using Drosophila melanogaster

A Blumrich[1]; A Foryst-Ludwig[1]; J Grune[1]; B Hoeft[1]; U Kintscher[1]
[1]*Charité - Universitätsmedizin Berlin, Institute of Pharmacology, CCR/German Center for Cardiovascular Research, Berlin, Germany*

Funding Acknowledgements: DZHK (German Centre for Cardiovascular Research)

Background: Adipose tissue lipolysis has recently been identified as a crucial regulator of cardiac function. To clarify the underlying mechanisms, we analyzed the

role of the ATGL (adipose triglyceride lipase) ortholog in D. melanogaster, Brummer (Bmm), which was also found to be the key enzyme for fat body lipolysis in flies.
Methods: The cardiac phenotype of male flies with fat-body specific RNAi-mediated Bmm knockdown (fbBmm-KD) was analyzed using high-speed video imaging (semi-automated optical heartbeat analysis (SOHA)).
Results: fbBmm-KD was validated by confirmation of significantly reduced Bmm mRNA expression and subsequently increased triglyceride levels due to decreased lipolytic rates. Two-week-old fbBmm-KD flies showed no changes of cardiac parameters such as fractional shortening or heart rate (HR), compared to control flies. Challenging fbBmm-KD flies with starvation (1% agar) for 48 h slightly reduced cardiac output (CO) mediated by decreased HR in the presence of preserved stroke volume. Determination of heart diameters revealed a significantly smaller diastolic and systolic diameter in fbBmm-KD flies compared to controls. Interestingly, extension of the starvation duration to 72 h led to significantly augmented decrease of CO and HR only in fbBmm-KD flies, but not in control flies. In addition, a compensatory increase of stroke volume was observed in fbBmm-KD flies compared to controls.
Conclusion: In summary, we found that fbBmm-KD affects heart function during starvation by reducing CO mediated mainly through a decrease in HR. These data suggest that adipose tissue lipolysis, which occurs not only during starvation but also during chronic heart failure, affects HR regulation. This process likely involves cardiac actions of fatty acids or glycerol released from adipose tissue during lipolysis.

P2283
Specific cleavage of cardiomyopathy associated mutant DES by CRISPR-Cas9

A Ruppenstein[1]; A Brodehl[1]; A Gaertner-Rommel[1]; J Gummert[1]; AV Marakhonov[2]; MY Skoblov[2]; H Milting[1]
[1]Heart and Diabetes Center NRW, Ruhr University Bochum, Erich & H. Klessman Institute for Cardiovasc., Bad Oeynhausen, Germany; [2]Research Centre for Medical Genetics, & Moscow Institute of Physics and Technology (Dolgoprudny), Moscow, Russian Federation

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Background: Mutations in the gene DES, encoding the intermediate filament protein desmin, cause skeletal and cardiac myopathies. Desmin filaments are formed in a stepwise protein assembly process of dimers, tetramers and unit length filaments. Most DES mutations are small missense or in-frame deletion mutations spread over the whole sequence of the ROD domain. They are inherited in a dominant mode. At the cellular level, the majority of DES mutations cause cytoplasmic protein aggregates consisting of wild-type and mutant desmin. However, no molecular treatment is available for patients carrying DES mutations.
Purpose: Recent studies established reliable genome editing technologies used for the development of molecular therapies of different diseases in vitro and in animal models. Therefore, we tested if genome editing using Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)-Cas9 could be applied in vitro to degrade the mutant desmin with high specificity.
Methods: We inserted two different small in-frame deletion mutations into plasmids containing the DES-cDNA via site-directed mutagenesis. Guide RNAs (sgRNAs) were generated by in-vitro transcription and the specificity of all generated sgRNAs was tested by in vitro digestion using recombinant Cas9.
Results: Confocal microscopy using transfected SW13 cells demonstrated for one DES deletion mutation a cytoplasmic protein aggregation. The cleavage assays revealed for both deletion mutations the specificity of the designed sgRNAs. Whereas the wild-type desmin plasmid could not be cleaved by Cas9 in combination with the sgRNAs, the mutant forms were efficiently recognized and digested.
Conclusion: In our study, we designed and applied sgRNAs leading in combination with Cas9 to a specific cleavage of mutant DES-cDNA without affecting the wild-type form. In future, we will apply this approach to investigate in cell culture if the expression of the mutant desmin could be inhibited which might has relevance for the development of efficient therapies for patients with DES mutations.

P2284
FTO polymorphism influences risk of rejection in heart transplant patients

D Dana Dlouha[1]; JA Hubacek[1]; J Vymetalova[2]; V Lanska[3]; I Malek[3]
[1]Institute for Clinical and Experimental Medicine (IKEM), Centre for Experimental Medicine, Prague, Czech Republic; [2]Institute for Clinical and Experimental Medicine (IKEM), Cardiocentre, Prague, Czech Republic; [3]Institute for Clinical and Experimental Medicine (IKEM), Statistical Unit, Prague, Czech Republic

On behalf of: Centre for experimental medicine
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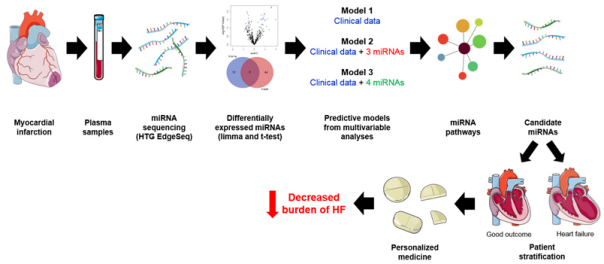
Background: Although a significant progress achieved by modern immunosuppressive therapy, acute coronary rejection is the important obstruction on the way to the long-term survival of heart transplant patients. Risky alleles of the first intron polymorphisms within the FTO (fat mass and obesity-related gene, OMIM acc No. 610966) are the important risk factors associated with a wide list of noncommunicable diseases.
Materials and Methods: In our study, we have genotyped a unique set of 396 adult patients (aged 55.5 ± 11.9 years, 79% of males) who underwent heart transplantation at Institute for Clinical and Experimental Medicine, Prague, between January 2005 and December 2015, together with their donors. DNA was isolated from aortic tissue samples. Genotyping was performed using TaqMan technology on an AB 7300.
Results: No significant differences in FTO genotype frequencies between donors, recipients and the general population have been detected in our study. Recipient FTO genotypes were not associated with either type of rejection, or with the presence of one or two rejections. In contrast, donor TT genotype was significantly more prevalent in subjects where both types of rejections were detected (50%), than in subjects with just one (28.8%) or in subjects without the history of rejection (28.1%). The significant difference (P = 0.02) was reached for dominant model (TT vs. G allele carriers comparison; OR, 95% CI ? 2.53; 1.16 - 5.49).
Conclusions: The results of our study suggest that a donor, but not recipient FTO genotype could be a significant predictor of acute organ rejection in heart transplant patients.

P2285
Identification of circulating microRNAs from HTG EdgeSeq sequencing to predict outcome after acute myocardial infarction

C Pedrosa Da Costa Gomes[1]; E Schordan[2]; L Zhang[1]; D Attar[3]; H Firat[2]; Y Devaux[1]
[1]Luxembourg Institute of Health, CVRU, Strassen, Luxembourg; [2]Firalis SAS, Huningue, France; [3]Oslo University Hospital, Oslo, Norway

On behalf of: Cardiolinc™ network (www.cardiolinc.org)

Background: Numerous patients develop heart failure (HF) after acute myocardial infarction (AMI), representing a leading cause of mortality worldwide. Early intervention is important to prevent left ventricular remodelling that leads to heart failure. There is an urgent need for stratification of patients since, to date, no highly reliable biomarker-based tests are available for early risk assessment.
Purpose: Identify microRNAs (miRNAs) in plasma of post-AMI patients associated with left ventricular remodelling and HF that increment the value of clinical tests.
Methods: Plasma samples were collected from 82 and 87 post-AMI patients at two-time points, 12 hours after AMI (early) and 72 hours after AMI (late), respectively. Patients were assessed by echocardiography after 1 month (early) or 4 months (late), and were classified in 3 groups according to ejection fraction (EF): reduced (HFrEF), midrange (HFmrEF) and preserved (HFpEF). Plasma samples were analysed by HTG EdgeSeq followed by a bioinformatics approach to identify miRNAs differentially expressed between EF groups ($p < 0.05$ and $|log2FC| > 0.5$). Multivariable ordinal regression analyses were conducted to generate predictive models using clinical data and miRNAs. Comparison of the Akaike information criterion (AIC) of the models with the likelihood ratio test allowed to determine the incremental predictive value provided by miRNAs. The AIC rather than the area under the curve was used to avoid model overfitting due to the multiplication of predictive variables.
Results: Two lists of candidate miRNAs were obtained, one for the early and one for the late samples, with one miRNA in common between them. Nine miRNAs were differentially expressed between HFrEF/HFpEF and HFrEF/HFmrEF groups in the early samples, and 25 miRNAs in the late samples. These miRNAs, known to be enriched in cardiomyopathy relevant pathways, were used to generate predictive models with clinical data. In both early and late samples, the models involving clinical data and miRNAs more robustly risk stratified patients compared to the model with clinical data only. In the early samples, addition of panels of 3 or 4 miRNAs to the clinical model had a significant incremental predictive value as attested by a decrease of the AIC ($p < 0.001$). The improvement of prediction provided by panels of 3 or 4 miRNAs was also highly significant in the late samples ($p < 0.001$).
Conclusion: We identified 2 panels of miRNAs that significantly increment the value of clinical parameters to risk stratify AMI patients, at an early (12h) or late (72h) stage after AMI. These findings may help moving forward personalized healthcare of AMI patients. Further independent validation in large patient groups is needed.



Figure

P2286

The genetic basis of end-stage hypetrophic cardiomyopathy in heart transplant recipients

M Franaszczyk[1]; J Poninska[1]; A Podgorska[1]; M Dabrowski[2]; P Kolsut[3]; M Jasinska[4]; M Kusmierczyk[3]; M Sobieszczanska-Malek[5]; T Zielinski[5]; J Rozanski[3]; R Ploski[6]; A Witkowski[2]; ZT Bilinska[7]; A Lutynska[1]; M Klopotowski[2]
[1]Institute of Cardiology, Department of Medical Biology, Warsaw, Poland; *[2]Institute of Cardiology, Department of Interventional Cardiology and Angiology, Warsaw, Poland*; *[3]Institute of Cardiology, Department of Cardiac Surgery and Transplantology, Warsaw, Poland*; *[4]Institute of Cardiology, Department of Anesthesiology, Warsaw, Poland*; *[5]Institute of Cardiology, Department of Heart Failure and Transplantology, Warsaw, Poland*; *[6]Medical University of Warsaw, Department of Medical Genetics, Warsaw, Poland*; *[7]Institute of Cardiology, Unit for Screening Studies in Inherited Cardiovascular Diseases, Warsaw, Poland*

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Background: A heart transplant (OHT) is performed on patients with end-stage heart failure when other medical or surgical treatments have failed. End-stage hypertrophic cardiomyopathy (HCM) indicates progression to left ventricle remodeling and systolic dysfunction. It is associated with a poor prognosis and affects 2.4-15.7% of cases of HCM. Mortality in this group of patients reaches 11%.
Purpose: Sarcomeric mutations are found in 30-65% of patients with HCM. However, most of the studies on HCM genetic background did not take into account the end-stage form, mainly due to its low prevalence in the HCM population. On the other hand, studies conducted in groups with end-stage HCM focused mainly on sarcomeric genes. In this study patients who underwent heart transplantation in the course of end-stage HCM were investigated using next generation sequencing for genetic background of the disease.
Methods: Nineteen unrelated patients (6 male, 31.6%) who underwent heart transplantation in the course of end-stage HCM were investigated for genetic background of the disease. Two approaches of next generation sequencing were used: TruSight Cardio panel by Illumina (n = 14) that provides coverage of 174 genes with known associations to 17 inherited cardiac conditions including cardiomyopathies, or custom panel of 35 cardiomyopathies genes (n = 5). Mean age of OHT were 44.2 ± 12.2 (range 17-63), 43.8 ± 18.3 in males (range 17-58) and 44.4 ± 9.1 in females (range 32-63).
Results: Thirteen probands (68.4%) had a single mutation in one of the sarcomeric genes: MYH7 (n = 7, 36.8%), MYBPC3 (n = 3, 15.8%), TNNT2 (n = 2, 10.5%), TNNI3 (n = 1, 5.3%) and one proband (5.3%) was compound heterozygote (MYH7 + MYBPC3). In 5 patients (26.3%), genetic examination did not reveal a pathogenic mutation. All mutations in MYH7 were missense variants and all mutations in MYBPC3 were truncating variants. The youngest OHT recipient (male, OHT at 17 y) had known pathogenic mutation in TNNT2 gene. Mean age of OHT in MYH7 carriers was 44.4 ± 10.7 and in MYBPC3 was 49 ± 4.4. The carrier of double mutation had OHT at 57.
Conclusion: The high prevalence of sarcomeric mutations with majority cases of MYH7 and MYBPC3 in OHT recipients confirms that genetic background of typical HCM and end-stage HCM is similar. The finding only truncating variants in MYBPC3 gene may suggest the stronger impact on the course of the disease. Surprisingly, the double mutation carrier has undergone OHT later than the average for the study group. Despite a small study group, our results suggest that the specific gene mutation may be related to the age of receiving a heart transplant. Also, more than 1/4 unsolved cases suggests that in some cases whole exome/genome sequencing might be needed to recognize the pathogenic mutation.

P2287

The polymorphic variant rs2070744 of NOS3 gene is associated with the functional state of the myocardium in patients with coronary artery disease and type 2 diabetes mellitus

E F Muslimova[1]; T YU Rebrova[1]; T G Nonka[1]; S A Afanasiev[1]; A N Repin[1]
[1]Cardiology Research Institute, Tomsk National Research Medical Center, Russian Academy of Sciences, , Tomsk, Russian Federation

Coronary artery disease (CAD) is one of the most socially significant cardiovascular diseases, commonly resulting in chronic heart failure (CHF). It is important to carry out fundamental research aimed at finding predictors of pathological changes in the myocardium. The range of candidate genes of cardiovascular pathology is large. Among them, a clinical importance is attached to the NOS3 gene, which encodes endothelial nitric oxide synthase. Polymorphism T-786C (rs2070744) of this gene is particularly distinguished.
Aim: The association of polymorphism T-786C of the endothelial NO-synthase gene NOS3 with the functional state of the left ventricle (LV) was studied among residents of the West Siberian region with CAD and CHF, including that combined with type 2 diabetes mellitus (DM2).
Methods: The work followed the ethical principles set forth in the 1975 Helsinki Declaration, revised in 1989 in Hong Kong. All patients gave their informed consent for participation in the study. The sample consisted of 198 male patients (58 (52; 63) years of age) with chronic CAD. CHF was diagnosed in 190 (96.0%) patients. DM2 was identified in 56 (28.3%) patients; their glucose level was 6.4 (5.9; 7.4) mmol/L; the level of glycated hemoglobin 6.4 (5.7; 7.2)%. Amplification was carried out by allele-specific polymerase chain reaction using the commercial kit.
Results: In the total sample of patients, the frequencies of genotypes of polymorphism T-786C of gene NOS3 were as follows: 786TT, 69 (34.8%); 786TC, 97 (49.0%); 786CC, 32 (16.2%). The distribution complied with the Hardy–Weinberg equilibrium (p = 0.830). The frequency of allele –786C was 41%. Among patients without T2DM, the carriers of genotype –786TT were characterized by the largest LV ejection fraction (p = 0.012). In a pairwise comparison, statistically significant differences were found between –786TT and –786TC groups (p = 0.024). This dependence was not revealed in the group of patients with CAD combined with DM2. In the group with genotype –786TC, the frequency of left ventricular hypertrophy was higher among patients with DM2 than patients without it (p = 0.025). But there was no association between NOS3T –786C polymorphism and the severity of functional class of heart failure in both the groups.
Conclusion: The risk of development and progression of CAD and CHF is caused by numerous factors, among which genetic predictors play a significant role and in combination with metabolic disorders and specific environmental influences form a wide clinical variability of these diseases.

P2288

THE effect of Pex14 RNA interference on cardiomyocytes under anoxia-reoxygenation

I Tetjana Drevytska[1]; E Gonchar[1]; L Tumanovska[1]; D Klionsky[2]; V Dosenko[1]
[1]Bogomoletz Institute of Physiology, Department of general and molecular pathophysiology, Kiev, Ukraine; *[2]University of Michigan, Life Sciences Institute, Michigan, United States of America*

As a step toward understanding the homeostasis of peroxisomes in mammalian cells, we investigated a role of PEX14 RNA interference on the culture of neonatal in response to anoxia-reoxygenation. Selective autophagy is the significant process in cardioprotection and has beneficial and detrimental roles to cardiomyocytes depending on the level of autophagy and another circumstance. Proteins of pexophagy, and in particular, Pex14p plays a pivotal role in pexophagy via direct interaction with LC3-II.
Ventricular myocytes were isolated from 2-days-old Wistar rats by enzymatic digestion. 2 μg of expression plasmid mixtures were electroporated into isolated neonatal cardiomyocytes with a Nucleofector™ device using a Rat Cardiomyocytes Neo Nucleofector Kit (USA). For establishing the number of living and necrotic cells after 48-hours of cultivation we used fluorescence microscopy with hoechst and propidium iodide staining of cardiomyocytes. To identify signs of autophagy cardiomyocytes were stained with dansylcadaverine. Peroxisome labelling was assessed by a SelectFX Alexa Fluor 488 Peroxisome Labeling Kit with primary antibody directed against peroxisomal membrane protein 70 (PMP 70) according to manufacturer's protocol. For monitoring autophagy degradation, we quantified the number of the p62-staining aggregates protein in each cell using ImageJ software. RNA isolation was performed using phenol-chloroform extraction with guanidine isothiocyanate. cDNA was synthesized by reverse transcription. Real-time PCR was for quantitative evaluation of PEX14 and PINK1 mRNA. Data are present as means ± SE. The analysis of variance was performed using one-way ANOVA.
We found that the application of antiPEX14 siRNA significantly decreased the level of PEX14 mRNA (4.9x compared to the scrambled group, P < 0.01) confirming the

effectiveness of PEX14 RNA-interference. It was shown that PEX14 decreased the cell viability and led to an increase in the amount of propidium-positive cells at anoxia-reoxygenation (AR) modelling compared to scrambled. The AR modelling led to a decrease in peroxisomes quantity compared to control. The PEX14 RNA interference increase of peroxisomes quantity compared to the scrambled group with anoxia-reoxygenation modelling. Level of p62 was higher in culture with antiPEX14 siRNA application in contrast with scrRNA application at AR modelling. Thus, it is shown that the interference of the PEX14 at the modelling of AR led to an increase of the number of peroxisomes, which is accompanied by the suppression of autophagy, accumulation of the protein p62, and downgrade of the survival of cells. Taken together, these results suggest that peroxisomal proteins such as PEX14 are necessary to ensure pexophagy and, as a consequence, to protect the heart in a number of pathological conditions, such as, for example, myocardial infarction. The intensity of pexophagy can be a target for the development of future cardioprotective drugs.

P2289

Pharmacological and genetic aspects of RAAS genetic polymorphisms in patients with chronic heart failure

S U Volkova[1]; KA Tomashevich[2]; MY Soloboeva[3]; EV Panteeva[1]; AU Efanov[4]
[1]Tyumen State Medical University, Tyumen, Russian Federation; *[2]"Neftyanic" hospital, Tyumen, Russian Federation*; *[3]Tyumen Regional Hospital, Tyumen, Russian Federation*; *[4]Tyumen Department of the South-Ural Scientific center RAMS, Tyumen, Russian Federation*

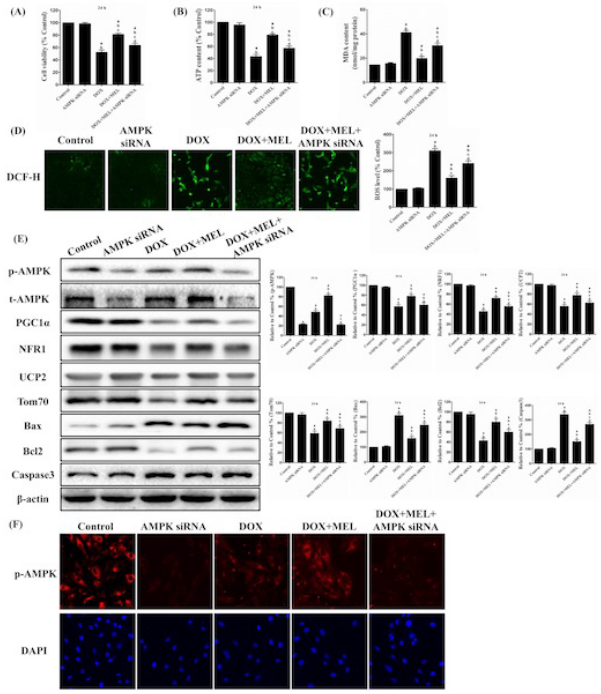
Aim: To estimate influence of different medicine classes intake on disease issues in patients with chronic heart failure (CHF) in dependence of RAAS genetic polymorphism.
Materials and Methods: 51 patients have been investigated (27 women, 24 men, mean age 73.1+11.3 years old) with congestive heart failure, who had been hospitalized in "Neftyanik" hospital. All patients received standard therapy according to National guidelines. Using PCR genome DNA analyses "SNP-express" followed by electrophoretic detection we estimated polymorphisms ofA1166C angiotensin II receptor type I (AGTR1),T174M and M235T angiotensinogen gene (AGT), angiotensin converting enzyme (ACE) gene. We estimated the end point (lethal issue) within 4 years of surveillance (mean period 325.8+291.5 days) in these patients and analyzed pharmacological and genetic correlation for all medicine classes, used for CHF treatment: ACE-inhibitors, beta-blockers, aldosterone antagonists, digoxin, calcium channel blockers.
Results. RAAS genotypes were matched with clinical issues in patients with CHF. Kaplan-Meier method showed no correlation of RASS genetic polymorphisms with lethal issues. Significant pharmacological and genetic correlation and their influence on survival were detected for ACE gene Del allele in patients taking ACE inhibitors (? <0,06), and for T174M –AGT polymorphisms.Kaplan-Meier method for AA showed more cumulative survival among patients, who didn't have 174?et AGT gene allele, compared to the ones, who had this allele ($p = 0.012$). Similar data were obtained for T174M –AGT polymorphisms in patients, taking beta blockers. The cumulative survival was higher in patients, who didn't have 174?et AGT gene allele compared to the ones, who had this allele ($p = 0.004$). In all the cases the survival curves diverged from the first weeks of surveillance. For diuretics, digoxin, calcium channel blockers in our research we found no pharmacological and genetic associations.
Conclusion: Results of our research (obtained even on a small population of patients) showed that it is preferable to take into account RAAS genetic polymorphism when prescribing CHF medical therapy. This would certainly have significance for long-term prognosis in these patients.

P2290

AMPK/PGC1 activation by melatonin attenuates acute doxorubicin cardiotoxicity

D Dong Liu[1]
[1]Fuwai Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Cardiology, Beijing, China People's Republic of

Doxorubicin (DOX) is a highly effective antineoplastic anthracycline drug; however, the adverse effect of the cardiotoxicity has limited its widespread application. Melatonin, a highly conserved molecule that is mainly produced by the pineal gland, is well known for its free radical scavenging and anti-oxidative roles. The aim of this study was to investigate the possible protective effects of melatonin against DOX-induced cardiomyopathy. We preliminarily established DOX-induced cardiotoxicity models in H9c2 cells, and C57 mice, which clearly showed cardiac dysfunction and injury, oxidative stress, and apoptotic damage. Treatment with melatonin obviously attenuated the DOX-induced cardiac dysfunction and pathological changes. The anti-oxidative stress activity of melatonin was achieved via reduced generation of reactive oxygen species through regulation of AMPK and PGC1a signaling. Its anti-apoptotic activity was shown by reductions in the number of TUNEL-positive cells and DNA fragments along with a decreased ratio of Bax/Bcl-2 expression. In a further mechanistic study, melatonin exerted improvement on the cardiac function, oxidative stress, and apoptosis were inhibited by Compound C treatment or AMPK/PGC1a siRNA. The present work demonstrates for the first time that melatonin obviously prevented DOX-induced cardiotoxicity via the suppression of oxidative stress and apoptosis through the AMPK/PGC1a signaling pathway.



P2291

Detailed hemodynamic characterization of a transgenic rat strain stably expressing the calcium sensor protein GCaMP2

T Radovits[1]; A Olah[1]; BT Nemeth[1]; M Ruppert[1]; TI Orban[2]; A Apati[2]; B Sarkadi[2]; B Merkely[1]
[1]Semmelweis University, Heart and Vascular Center, Budapest, Hungary; *[2]Hungarian Academy of Sciences, Research Centre for Natural Sciences, Institute of Enzymology, Budapest, Hungary*

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Background: Calcium homeostasis and signaling has been object of intensive investigations in various tissues. A novel transgenic rat strain has recently been generated that stably expresses the genetically engineered calcium sensor protein GCaMP2 (containing a calmodulin-based calcium sensor and a fluorescent protein) in different cell types including cardiomyocytes (Sci Rep 2015;5:12645). This animal model offers a unique possibility to directly examine calcium signaling in cells, tissues and organs, thus it might be a useful tool for assessing the effects of drugs and pathophysiological states on cardiac calcium homeostasis. In order to investigate whether the expression of the GCaMP2 protein itself affects cardiac function, in the present work we aimed at characterizing in vivo hemodynamics by left ventricular (LV) pressure-volume analysis in the GCaMP2 transgenic rats strain.
Methods: GCaMP2 transgenic rats (GCaMP2 group, $n = 10$) and age-matched Sprague-Dawley control animals (Co group, $n = 10$) were investigated. In vivo hemodynamic characterization was performed by LV pressure-volume analysis, obtaining both conventional hemodynamic parameters as well as sensitive, load-independent functional indices.
Results: Post-mortem heart weight data showed increased heart weight in the GCaMP2 group compared to controls (heart weight to tibial length ratio: 0.26 ± 0.01 GCaMP2 vs. 0.23 ± 0.01g/cm Co, $p < 0.05$), suggesting myocardial hypertrophy. We detected elevated mean arterial pressure (MAP: 138 ± 3 GCaMP2 vs. 128 ± 3mmHg Co, $p < 0.05$) in transgenic rats. LV systolic function was not altered in transgenic rats as indicated by conventional parameters (ejection fraction, stroke volume, dP/dtmax) and load-independent, sensitive indices (end-systolic pressure-volume

relationship, preload recruitable stroke work). Regarding diastolic function we found a marked deterioration of LV active relaxation in GCaMP2 animals (Tau: 16.8 ± 0.7 GCaMP2 vs. 11.7 ± 0.6ms Co, p <0.001; dP/dtmin: -9641 ± 247 GCaMP2 vs. -10781 ± 420mmHg/s Co, p <0.05). Parameters of LV stiffness were found to be unchanged in transgenic rats.
Conclusions: Our data indicated myocardial hypertrophy, arterial hypertension and impaired LV active relaxation along with unchanged systolic performance in the heart of transgenic rats expressing the GCaMP2 fluorescent calcium sensor protein. Myocardial expression of this genetically engineered calcium sensor protein might interfere with physiological calcium handling, resulting in the observed characteristic changes in the heart. While there were no significant changes in calcium handling in primary cardiac cell cultures (Sci Rep 2015;5:12645), special caution should be taken when using this rodent model in cardiovascular pharmacological and toxicological studies. In addition, this rat may be a useful model for studying calcium handling in cardiac hypertrophy.

P2292
Totally percutaneous model with echoguidance of ischemic mitral regurgitation in the pig

OUAFA Hamza[1]; A Kiss[1]; AM Kramer[1]; K Tillmann[1]; BK Podesser[1]
[1]Ludwig Boltzmann Cluster for Cardiovascular Research, Center for Biomedical Reasearch, Vienna, Austria

Background: Development of translational animal models of cardiovascular disease is crucial to understand the disease mechanism and pathophysiology and provide a unique platform to test novel therapies and devices. The European heart survey showed that 49% of patients with severe symptomatic mitral regurgitation were denied surgery. This patient population was characterized by one particularly recurrent parameter: Secondary mitral regurgitation. Surgical treatment of secondary mitral regurgitation remains a subject of controversy and still doesn't show a clear impact on the mortality. In addition, there is unmet need to establish less invasive approaches in patients with secondary mitral regurgitation. Aims: therefore, the aim of the present study was to establish a clinically reliable large animal model of mitral valve regurgitation.
Methods: Young female domestic pigs were used for this model extablischement (n = 9). The induction of mitral valve regurgitation was performed by localized posteromedial papillary muscle (PMPM) myocardial infarction. The PMPM irrigating branches are first identified by selectively injecting contrast media in the circumflex branches while performing echocardiography. Then a 2ml of pure Ethanol are injected in the identified branches. The evaluation of the mitral valve regurgitation and cardiac function was assessed by echocardiography.
Results: 7 pigs survived during the 6 weeks follow up period. One pig was euthanized after 3 weeks and another after 2 because of refractory pulmonary edema. Ethanol injection resulted in postero-inferior wall and PMPM dyskinesia. Significant left ventricle enlargement was noticed (End diastolic diameter at baseline: 50,04 ± 4.34mm vs at 6 weeks 62,12 ± 3.92mm; p < 0.001) as well as left atrium enlargement (left atrium area at baseline: 7.75 ± 0.95 vs at 6 weeks 17.65 ± 3.2mm; p < 0.001). Mitral regurgitation jet area significantly increased over the 2 weeks follow up period (jet area at baseline 0.03 ± 0.015 cm^2 vs at 6 weeks 3.22 ± 0.53). A significant tenting area developed over the follow up period (Tenting area at baseline 0.35 ± 0.21cm^2 vs 2.17 ± 0.63cm^2 at 6weeks; p < 0.001)
Conclusion: Our results clearly provided significant evidence about a totally percutaneous clinical relevant model of ischemic mitral valve regurgitation in pigs.

P2293
Comparison of the anti-remodeling effect of pharmacological soluble guanylate cyclase activation with pressure unloading in pathological myocardial left ventricular hypertrophy

M Mihaly Ruppert[1]; T Radovits[1]; S Korkmaz-Icoz[2]; S Li[2]; P Brlecic[2]; BT Nemeth[1]; A Olah[1]; CS Matyas[1]; K Benke[1]; EM Horvath[3]; B Merkely[1]; M Karck[2]; G Szabo[2]
[1]Semmelweis University Heart Center, Budapest, Hungary; *[2]University of Heidelberg, Department of Cardiac Surgery, Heidelberg, Germany*; *[3]Semmelweis University, Department of Physiology, Budapest, Hungary*

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Background: Pressure unloading induces the regression of left ventricular myocardial hypertrophy (LVH). Recent findings indicate that pharmacological activation of the soluble guanylate cyclase (sGC) - cyclic guanosine monophosphate (cGMP) pathway may also exert anti-remodeling properties in the myocardium.
Purpose: Therefore, we aimed to investigate the effects of the sGC activator cinaciguat in a rat model of LVH and compare it to the "gold standard" pressure unloading therapy.
Methods: Abdominal aortic banding was performed for 6 or 12 weeks. Sham operated animals served as controls. Pressure unloading was induced by removing the aortic constriction after week 6. The animals were treated from week 7 to 12, with 10 mg/kg/day cinaciguat or with placebo p.o. respectively. Cardiac function and morphology were assessed by left ventricular pressure-volume analysis and echocardiography. Additionally, key markers of myocardial hypertrophy, fibrosis, nitro-oxidative stress, apoptosis and cGMP signaling were analyzed.
Results: Pressure unloading effectively reversed LVH (heart weight to tibial length ratio [HW/TL]: 0.57 ± 0.02 AB-Co vs. 0.40 ± 0.01g/cm Debanded, p < 0.05), decreased collagen accumulation and provided protection against oxidative stress and apoptosis. Regression of LVH was also associated with a full recovery of cardiac function. In contrast, chronic activation of the sGC enzyme by cinaciguat only slightly influenced the pre-established hypertrophy (HW/TL: 0.57 ± 0.02 AB-Co vs. 0.48 ± 0.03g/cm AB-Cin, n.s.). However, it led to increased PKG activity and had a significant impact on myocardial fibrosis (Masson's score: 1.71 ± 0.11 AB-Co vs. 1.12 ± 0.18 AB-Cin, p < 0.05), nitro-oxidative stress and cardiomyocyte apoptosis. The inhibition of pathological processes resulted in improved systolic (cardiac contractility, ejection fraction) and diastolic (myocardial stiffness) function.
Conclusion: Our results indicate that both cinaciguat treatment and pressure unloading evoked anti-remodeling effects and improved LV function, nevertheless in a different manner.

P2294
FGF23 induces local angiotensin II signaling in cardiomyocytes

K N Ketaki Mhatre[1]; P Wakula[1]; O Klein[1]; E Bisping[2]; J Volkl[1]; B Pieske[1]; F Heinzel[1]
[1]Charite - Campus Virchow-Klinikum (CVK), Experimental Cardiology, Berlin, Germany; *[2]Medical University of Graz, Cardiology, Graz, Austria*

Heart failure (HF) manifestation and progression are driven by systemic activation of neuroendocrine signaling cascades, such as the renin-angiotensin aldosterone system (RAAS). Fibroblast growth factor 23 (FGF23), an endocrine hormone, is linked to HF and cardiovascular mortality. It is also a mediator of left ventricular hypertrophy (LVH). FGF23 is proposed to trigger pathological signaling by involving Ca2+-regulated transcriptional pathways. In vivo, high circulating levels of FGF23 are associated with an altered systemic RAAS response. In the present study, we investigated Ca2+-dependent signaling of FGF23 in ventricular cardiomyocytes and its association with angiotensin II (ATII).
Neonatal rat ventricular cardiomyocytes (NRVMs) were isolated and cultured for 5 days. ATII (1μM) or FGF23 (25ng/ml) were used as hypertrophy stimuli. Cell surface area and ATII levels were studied by immunostaining. Gene expression was accessed by qPCR. Ca2+ transient (CaT) amplitude (F/F0peak at 1Hz; Fluo-4 AM) and CaT area under the curve (AUC) were quantified in cytosol and nucleus. A subset of NRVMs was treated with losartan (1 μM), Aminoethoxydiphenyl borate (2-APB, 5μM) 30 min before agonist stimulation. Mass spectrometry analysis was carried out to detect secreted ATII.
In neonatal rat ventricular myocytes (NRVMs), both ATII and FGF23 induced hypertrophy as reflected by cell area and hypertrophic gene expression. In Ca2+ imaging experiments, an increase of cytoplasmic (2.4folds ± 0.3) and nuclear (1.9folds ± 0.3) CaT amplitude was observed on acute treatment with FGF23 (p < 0.01) similar to ATII. CaT AUC too was augmented significantly by both the treatments in cytoplasm and nucleus. The study with inositol 1, 4, 5-triphosphate (IP3) inhibitor 2-APB showed that FGF23– like ATII– induced IP3-dependent Ca2+ release from the nucleoplasmic Ca2+ store, associated with cellular hypertrophy.
Interestingly, ATII receptor antagonist losartan significantly attenuated FGF23-induced changes in Ca2+ homeostasis and cellular hypertrophy suggesting the involvement of ATII receptor-mediated signaling. Furthermore, FGF23 increased intracellular ATII expression (4.2folds ± 0.5) at 24h as well as on acute 90mins treatment (2.2folds ± 0.1) vs. control (p < 0.01), suggesting ATII involvement. Moreover, the mass spectra (m/z range: 1044-1054) of the supernatant collected from FGF23 treated NRVMs clearly showed the presence of a peak of ATII peptide (m/z 1046.562), confirming ATII secretion. However, the ATII peak was absent in the supernatant collected from untreated NRVMs.
In conclusion, FGF23 and ATII share a common mechanism of IP3- and Ca2+-dependent cardiomyocyte hypertrophy. FGF23-mediated cellular hypertrophy is associated with increased production and secretion of ATII by cardiomyocytes. These findings indicate a pathophysiological role of the cellular angiotensin system in FGF23-induced hypertrophy in ventricular cardiomyocytes.

P2295
Beta-adrenergic effect on calcium cycling is potentiated in autophagy-deficient mouse cardiomyocytes

S Kraler[1]; M Abdellatif[1]; S Ljubojevic[1]; S Simon Sedej[1]
[1]Medical University of Graz, Graz, Austria

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Background: Autophagy is a cytoprotective process required for the maintenance of physiological homeostasis of virtually every organ, including the heart. Chronic ß-adrenergic stress causes a profound left ventricular cardiac dysfunction and increases cardiomyocyte death in autophagy-deficient hearts. We tested the hypotheses that loss of autophagy causes dysfunctional subcellular calcium homeostasis early in life and that these alterations are potentiated in response to acute ß-adrenergic activation. Such early alterations of intracellular calcium homeostasis may contribute to the development of contractile dysfunction and functional remodeling of autophagy-deficient cardiomyocytes.
Methods: Ventricular myocytes were isolated from adult (14-16 weeks old, male and female) cardiomyocyte-specific autophagy-deficient mice (Atg5-/-; N = 4) and their control littermates (Atg5+/+; N = 4). Nucleoplasmic and cytoplasmic calcium transients were recorded using line-scan confocal imaging in electrically stimulated cells (1 Hz, steady-state, room temperature) loaded with Fluo-4/AM (8 μM) and perfused with normal Tyrode solution containing 1 mM CaCl2 (control) followed by acute exposure to the ß-adrenergic agonist isoprenaline (10 nM). Sarcoplasmatic reticulum calcium content was assessed as calcium released during rapid caffeine application (30 mM) at the end of each experiment. Data were analyzed using two-way RM ANOVA and are reported as mean ± S.E.M..
Results: At baseline, Atg5-/- cardiomyocytes had significantly increased time for 50% relaxation from peak of the cytosolic calcium transient (RT50: 242 ± 17ms vs. 204 ± 10ms; n = 13-16 cells, P < 0,02), while cytosolic calcium transient amplitude, time to peak and time for 90% relaxation from peak of the cytosolic calcium transient (RT90) were not different. Autophagy-deficient cardiac myocytes also showed markedly prolonged time to peak of nucleoplasmic calcium transient compared to control cells (235 ± 14ms vs. 172 ± 14ms; P < 0,01). As expected, administration of isoprenaline profoundly increased calcium transient amplitude and reduced decay time of the calcium transient in cytosol as well as nucleus in both groups. In Atg5-/- cells, however, isoprenaline increased cytosolic calcium transient amplitude to a significantly higher level as compared to Atg5+/+ cells (by 149% vs. 74% of control, P < 0,01; respectively). In addition, RT50 and RT90 were reduced by a greater extent in Atg5-/- cells than relaxation times from Atg5+/+ cells (32% vs. 20% and 33% vs. 24% of control; P < 0,01 and P < 0,03, both respectively). Upon isoprenaline administration the sarcoplasmatic reticulum calcium load was comparable between groups.
Conclusion: Autophagy-deficient ventricular cardiomyocytes display increased susceptibility to ß-adrenergic activation underlying potentiated cytosolic and nuclear calcium cycling. Our results suggest that intact autophagy plays a protective role in the intracellular calcium handling during ß-adrenergic stress.

P2296

Beneficial effects of repeated remote ischemic conditioning on left ventricular function following chronic myocardial infarction in rats

A Kiss[1]; B Bodi[2]; P Pilz[1]; H Ouafa[1]; M Lang[1]; D Santer[1]; A Toth[2]; Z Papp[2]; BK Podesser[1]
[1]*Medical University of Vienna, Center for Biomedical Research, Vienna, Austria*; [2]*University of Debrecen, Faculty of Medicine, Department of Cardiology, Division of Clinical Physiology, Debrecen, Hungary, Debrecen, Hungary*

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Introduction: Repeated remote ischemic conditioning (RIC) is considered as a potential clinical approach to improve cardiac function following myocardial infarction (MI).
Purpose: To clarify the impact of RIC on: 1) hemodynamic function following chronic MI; 2) the regulation of myocardial Ca2+-dependent force production
Methods: MI was induced by permanent ligation of the left coronary artery in male Sprague-Dawley rats (10-12 weeks old). At 4 weeks after MI, rats were allocated into the untreated control (n = 6) and RIC-treated groups (n = 6). RIC treatment was performed by 3 cycles of 5 min unilateral hindlimb ischemia and 5 min of reperfusion once a day for 2 weeks. Echocardiography was used to asses left ventricular (LV) ejection fraction (LVEF). 6 following MI, hemodynamic function was monitored by an invasive method involving the determination of LV systolic pressure (LVSP) and the rate of LV pressure development (+dP/dt). Tissue samples were collected from the remaining anterior and a remote non-infarcted inferior LV areas to: 1) assess Ca2+ regulated force production in permeabilized isolated cardiomyocytes and 2) to determine site-specific phosphorylation statuses of cardiac troponin-I (cTnI) by Western Immunoblotting and cardiac myosin-binding protein C (cMyBP-C) by a ProQ Diamond phosphoprotein staining kit.
Results: 4 weeks after MI LVEF decreased from 82 ± 1% and 81 ± 1% to 54 ± 2% and 51 ± 4% in the control and RIC groups, respectively. However, at 6 weeks after MI LVEF was markedly imporved in the RIC group (57 ± 4%; P <0.05) than that at 4 weeks, while it was unchanged in controls (50 ± 1%). These differences were accompanied by higher LVSPs (96 ± 3 vs. 87 ± 2 mmHg, P <0.05) and +dP/dt values (5226 ± 96 mmHg/s vs. 4622 ± 142 mmHg/s, P <0.05) in rats with RIC than in controls. In addition, the Ca2+ sensitivity of cardiomyocyte force production was significantly lower both at the anterior (pCa50: 5.93 ± 0.02 vs. 6.05 ± 0.03, P <0.05) and the non-infarcted LV areas (pCa50: 6.01 ± 0.03 vs. 6.10 ± 0.02, P <0.05) in the RIC groups than in controls, respectively. Furthermore, RIC enhanced cTnI phosphorylation levels at Ser(22) both in the infarcted (1.09 ± 0.04 in the RIC group; 0.78 ± 0.05 in controls, P <0.05, in relative units) and non-infarcted LV areas (1.08 ± 0.08 in the RIC group; 0.82 ± 0.02 in controls, P <0.05). cTnI phosphorylation at the Thr(143) site showed difference only in the infarcted region between the groups (1.0 ± 0.07 in the RIC group; 0.58 ± 0.06 in controls, P <0.05). Similarly, phosphorylation of cMyBP-C was enhanced by RIC in the infarcted region of LV (0.97 ± 0.06 vs. 0.65 ± 0.04 in controls, P <0.05).
Discussion: RIC limited LV hemodynamic impairment following MI via a mechanism possibly involving cTnI and cMyBP-C phosphorylations in infarcted rat hearts. These findings implicate the preservation of ß-adrenergic responsiveness during repeated RIC evoked cardioprotection, and provide support for RIC as a therapeutic approach for improve post-infarct cardiac depression.

P2297

Repeated remote ischemic conditioning enhances Neuregulin-1/ErbB2/3/4 expression following myocardial infarction in rats

P Pilz[1]; M Lang[1]; O Hamza[1]; C Kaun[2]; J Wojta[2]; BK Podesser[1]; A Kiss[1]
[1]*Medical University of Vienna, Center for Biomedical Research, Vienna, Austria*; [2]*Ludwig Boltzmann Cluster for Cardiovascular Research, Department of Internal Medicine II, Medical University of ViennaCluster for Cardiovascular Research, Vienna, Austria*

Introduction: Adverse left ventricle (LV) remodelling following myocardial infarction (MI) plays an important role in the progression of congestive heart failure (HF). Recombinant human Neuregulin-1 (rhNRG-1) has been demonstrated to improve LV ejection fraction (LVEF) and coronary microcirculation in patients with HF. Repeated remote ischemic conditioning (RIC) is considered as a potential clinically approach to improve cardiac function following MI, however the mechanisms are not fully elicited.
Purpose: The aim of the present study was to (1) clarify the effects of a brief period of RIC on LV hemodynamic function and coronary flow and (2) to assess the expression of NRG-1, ErbB2/3/4 expression following MI.
Methods: Male Sprague-Dawley rats were subjected to permanent left coronary artery (LCA) occlusion and allocated to two groups: (1) Myocardial infarction (MI; n = 7) and (2) MI+RIC; n = 5). Repeated RIC was started at the 3rd day after MI once a day for 5 days by 3 cycles of 5 min of unilateral hindlimb ischemia and 5 min of reperfusion. Cardiac functional parameters were assessed by transthoracic echocardiography at baseline and at days 3 and 8 following MI. Coronary flow (CF) and LV systolic pressure (LVSP) were evaluated on an isolated erythrocyte-perfused working heart model at day 8 following MI. The alterations in coronary flow primarily reflect alterations in coronary resistance, allowing evaluation of microvasculature function in this experimental set up. The expression of plasma level of NRG-1 was measured by ELISA and mRNA expression of ErbB2/3/4 was accessed by RT-qPCR.
Results: RIC enhanced LVEF as compared to MI group (63 ± 1% vs. 58 ± 2% on day of 8th following the induction of MI, p = 0.074). This was accompanied by preserved LV systolic function in rats with RIC as compared with MI (LVESD: 5.9 ± 0.06 mm and 6.4 ± 0.2 mm, p = 0.064). Results were obtained from the isolated working heart system showed that CF and LVSP were markedly enhanced in rats with RIC as compared to MI (CF: 4.3 ± 0.2 vs 3.1 ± 0.2 ml/g heart weight and LVSP: 109 ± 2 mm Hg vs 119 ± 4; mm Hg; p <0.01, respectively). Both plasma and tissue expressions of NRG-1 were significantly elevated by RIC in comparison to MI group (plasma: 10.6 ± 1.7 μg/ml vs 19.4 ± 3.3 μg/ml and LV tissue: 0.53 ± 0.09 vs. 3.16 ± 0.9 1/18S; p <0.05). Similarly, the mRNA expression of ErbB2/3/4 showed at least part in significant differences between the groups (ErbB2: 1.0 ± 0.2 vs. 2.08 ± 0.4 1/18S, p <0.05; ErbB3: 1.07 ± 0.3 vs. 2.4 ± 0.4 1/18S, p <0.05; ErbB4: 0.46 ± 0.12 vs. 0.64 ± 0.23 1/18S; n.s) in LV tissue samples were taken from the infarcted zone.
Discussion: RIC preserves systolic LV function and markedly enhances basal coronary flow following MI in rats. These results were accompanied by with a marked increase in NRG-1 levels in plasma and myocardial tissue samples indicating enhanced cardioprotection. Therefore, repeated remote RIC is a potential therapeutic approach for improved post-MI remodeling.

P2298

Acute effects of palmitoleic acid, an obesity-related free fatty acid, on ventricular cardiomyocyte Ca signaling

T Tim Guthof[1]; I Betz[2]; D Bode[1]; F Hohendanner[1]; A Foryst-Ludwig[2]; U Kintscher[2]; B Pieske[1]; F Heinzel[1]
[1]*Charite - Campus Virchow-Klinikum (CVK), Department of Cardiology, Berlin, Germany*; [2]*Charite - Campus Mitte (CCM), Institute of Pharmacology, Center for Cardiovascular Research, Berlin, Germany*

Background: Obesity plays an important role in the development of heart failure and is associated with alterations of fatty acid metabolism and elevated free fatty acids. Previously, we have found palmitoleic acid (PE16:1) to be involved in heart failure with reduced ejection fraction in mouse and human.
Purpose: We tested the hypothesis that palmitoleic acid has an acute effect on the intracellular calcium (Ca2+) homeostasis in ventricular cardiomyocytes.
Methods: Freshly isolated rat ventricular cardiac myocytes were incubated with PE 16:1 and the respective BSA concentration (Control) for 30 minutes. Cells were stimulated in an electric field and confocal line scan images were recorded (Fluo-4). Ca2+ transients (CaT, 1-5 Hz) were examined by the calculation of CaT amplitude (F/F0), time to peak (TTP), the time to half maximal release (TF50) and the time constant of decay (Tau). The amplitude of the caffeine response was used to estimate the asarcoplasmic reticulum (SR) Ca2+ load and the respective time constant of Ca2+ decay was used to estimate the NCX function.
Dyssynchrony of Ca2+ release was assessed by calculating the percentage of the local early Ca2+ release (local TF50 < 5 ms) compared to the control group. To further investigate the causes of the dyssynchrony the probability of early release and the propagation velocity of spontaneous waves were calculated.
Results: Myocytes incubated with PE 16:1 (30 min) showed a normal CaT amplitude but prolongation of global TF50 (control: 5.4ms vs. PE 16:1: 9.4ms, $p < 0.05$) and global TTP (26.7ms vs. 41ms, $p < 0.05$). Cytosolic Ca2+ removal was significantly slowed (Tau: 97ms vs. 156ms, $p < 0.05$), but SR Ca content was significantly increased with PE 16:1. Slowed decay of the caffeine-induced Ca transient (Tau: 606ms vs. 1353ms, $p < 0.05$) suggested reduced forward mode Na/Ca exchanger activity.
Moreover, intracellular Ca2+ release was more dyssynchronous with significantly less early release sites (control: 50%; PE 16:1: 25%, $p < 0.05$) and increased time to half maximal release (TF50) of late release sites (9ms vs. 15ms, $p < 0.05$). The probability of local early Ca2+ release was lower (0.71 vs. 0.61, $p < 0.05$) and the propagation velocity of waves slower (150.4 μm/ms vs. 120.4 μm/ms ; $p < 0.05$). The cells incubated with PE16:1 showed more sparks (159 /100μm/ms vs. 814 /μm/ms, $p < 0.05$) but a lower wave to spark ratio (0.61 vs. 0.30, $p < 0.05$). The average wave count was higher but statistically not significant (2.1 vs. 3.5, $p = 0.08$).
Conclusion: In cardiomyocytes palmitoleic acid acutely reduces the synchrony and global kinetics of Ca homeostasis and at the same time increases arrhythmogenic Ca release. These acute changes precede and may trigger cardiomyocyte remodeling leading to adipositas-related cardiac contractile dysfunction and heart failure.

P2299

Oxidative stress signalling through ASK1 and p38-MAPK regulates cardiomyocyte gene expression and induces hypertrophy

KA Rostron[1]; DN Meijles[2]; JJ Cull[1]; S Shaw[1]; PH Sugden[1]; A Angela Clerk[1]
[1]University of Reading, Reading, United Kingdom; *[2]St George's University of London, London, United Kingdom*

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Background: Stress-regulated mitogen-activated protein kinases (SR-MAPKs; i.e. p38-MAPKs and JNKs) are activated in the heart by various stresses. They cause cardiac dysfunction and cardiomyocyte death, so pathway components are potential therapeutic targets for heart failure. Cardiac ischemia is associated with increased oxidative stress that is further enhanced on reperfusion (I/R). Oxidative stress (e.g. H2O2) activates SR-MAPKs in cardiomyocytes and perfused hearts but, while ischemia activates p38-MAPKs, JNKs are only activated by I/R. SR-MAPKs are activated by specific MAPK kinases, but the upstream MAP3Ks that initiate the signal in different conditions are not well-defined. ASK1 is an oxidative stress-responsive MAP3K for SR-MAPKs and is required for cardiac hypertrophy, but its specific role in ischemia or I/R is not clear.
Purpose: Our aims were to determine if ASK1 signals selectively to p38-MAPK in the heart, particularly during ischemia, and establish downstream consequences of ASK1 signalling in the heart.
Methods:/Results: We confirmed that H2O2 activated SR-MAPKs in rat neonatal cardiomyocytes by immunoblotting with antibodies to the phosphorylated (activated) kinases. The concentration-dependence for ASK1 phosphorylation by H2O2 was bell-shaped, with maximal activation at 1 mM and reduced activation >1 mM H2O2. Rat hearts were perfused ex vivo in the Langendorff mode and subjected to ischemia (15 min) or I/R (15/45 min). ASK1 was activated only during ischemia, consistent with moderate levels of oxidative stress being required. We did not detect activated ASK1 with I/R. Selonsertib (1 μM), a highly selective ASK1 inhibitor, suppressed p38-MAPK, but not JNK, activation by H2O2 in cardiomyocytes or perfused hearts, or hearts subjected to ischemia or I/R. Thus, ASK1 signals selectively to p38-MAPK. The effects of 4 mg/kg/d selonsertib on mouse hearts (male C57Bl6; 10 weeks) in vivo were assessed with/without 0.8 mg/kg/d angiotensin II (AngII), a hypertensive model associated with increased oxidative stress (7 d; n = 6-8). Echocardiography was used to assess cardiac function/dimensions. Selonsertib alone had no effect on any of the variables studied. AngII promoted cardiac hypertrophy with increased diastolic and systolic left ventricular posterior wall thickness. This was significantly inhibited by selonsertib indicating ASK1 is required in AngII-induced cardiac hypertrophy.
Conclusions: ASK1 is an oxidative-stress responsive MAP3K that signals selectively to p38-MAPK in cardiomyocytes in the context of moderate stress during ischaemia. High level oxidative stress as occurs on reperfusion does not activate ASK1 to a significant degree. Moreover, ASK1 activation in hypertension contributes to the hypertrophic response. By dissecting upstream activators of p38-MAPK and JNKs, it will become increasing apparent which may be targeted under specific conditions to manipulate p38-MAPK and/or JNK signalling for the management of heart failure.

P2300

The effects and mechanisms of Pyridostigmine on cell proliferation and fibrosis of human cardiac fibroblasts

S Lishui[1]; L Xiaoli[2]; S Guilin[2]; D Guoming[2]; C Dong[2]
[1]Zhejiang Hospital, cardiovascular department, Hangzhou, China People's Republic of; *[2]anji people's hospital, cardiovascular department, huzhou, China People's Republic of*

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Objective To investigate the effects and mechanisms of Pyridostigmine(PYR) on cell proliferation and fibrosis in human cardiac fibroblasts(HCFs). Methods The model of fibrosis in HCFs was induced by transforming growth factor beta. After the intervention of PYR, the content of collagen I(COL1) was observed by measuring the hydroxyproline concentration. The cell cycle of HCFs was screened by Flow cytometry. The mRNA levels of Connective tissue growth factor(CTGF) and Smad3 were examined by real-time PCR analysis.The relative expressions of CTGF, Smad3, pSmad3 were examined by Western blot. Results Compared with the TGF-ß group, the TGF-ß+PYR group had lower proportion of S/G2 phased cells[(30.8 ± 1.4) % vs (48.6 ± 3.5)%], less synthesis of COL1 [(0.95 ± 0.15) vs (1.25 ± 0.18)]and fewer expressions of CTGF mRNA [(1.73 ± 0.10) vs (2.92 ± 0.12)]and CTGF protein[(1.23 ± 0.42) vs (2.36 ± 0.62)], the difference was statistically significant($P < 0.05$). However, the expressions of Smad3 mRNA[(1.50 ± 0.06) vs (1.55 ± 0.08)] , Smad3 protein [(2.85 ± 0.45) vs (2.98 ± 0.47)] and pSmad3 protein[(2.39 ± 0.32) vs (2.51 ± 0.52)] between these two groups showed no significant difference($p>0.05$). Conclusion Pyridostigmine significantly alleviated cell proliferation and collagen synthesis in HCFs induced by TGF-ß, and its mechanism was related to the inhibition of CTGF expression rather than blocking the TGF-ß/Smads signaling pathway.

The cell cycle of HCFs in each group

Group	G1(%)	S(%)	G2(%)	S/G2(%)
Control	65.3±3.5	20.6±1.8	10.2±1.1	30.8±1.6
PYR	64.2±1.6	18.1±2.1	11.4±1.1	29.5±1.9 *
TGF-β1	43.2±2.6	33.0±4.1	15.6±2.2	48.6±3.5 #
10ng/ml TGF-β1+50uM PYR	58.3±3.7	25.0±4.2	9.6±1.5	34.6±3.4 Δ?
10ng/ml TGF-β1+100uM PYR	61.3±4.1	20.8±2.0	10.0±1.2	30.8±1.4 Δ
10ng/ml TGF-β1+200uM PYR	58.0±6.8	24.1±3.6	11.9±2.1	36.0±2.8 Δ?
10ng/ml TGF-β1+400uM PYR	58.7±2.9	23.2±3.3	10.3±1.7	33.5±2.1 Δ?

Table 1. Effect of PYR on cell cycle of HCFs induced by TGF-ß1(mean ± s,n = 6). *P>0.05 versus Control group,# P < 0.05 versus Control group;?P < 0.05 versus TGF-ß1 group;?P < 0.05 versus 10ng/ml TGF-ß+100uM PYR group.

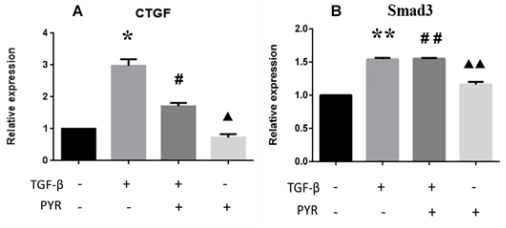


Figure 1. The relative expressions of CTGF mRNA and Smad3 mRNA in each group. The results were expressed as the mean±SD, n=6. ▲P>0.05 versus Control group，▲▲P>0.05 versus Control group, *P<0.05 versus Control group，**P<0.05 versus Control group；#P<0.05 versus TGF-β group，##P>0.05 versus TGF-β group

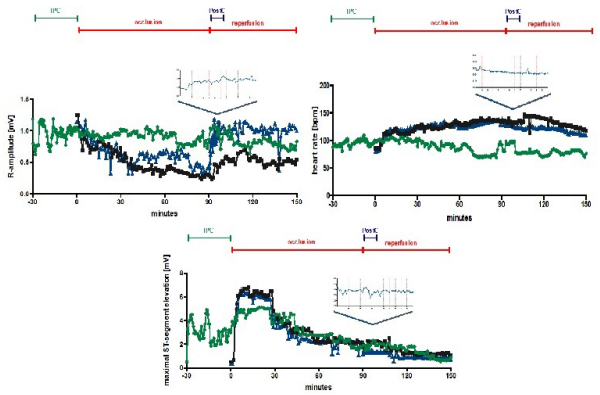
The expressions of mRNA in each group

P2301

Real-time measurement of intraventricular ECG changes in ischemic pre- and postconditioning

A Andreas Spannbauer[1]; RM Riesenhuber[1]; TD Traxler[1]; GA Gugerell[1]; ML Mandic[1]; WJ Winkler[1]; ZK Zlabinger[1]; LD Lukovic[1]; PN Pavo[1]; GM Gyongyosi[1]
[1]*Medical University of Vienna, Internal Medicine II (Cardiology), Vienna, Austria*

Background: An important contributor to the development of heart failure is ischemia-reperfusion (I/R) injury sustained after revascularized acute myocardial infarction (AMI). A potential treatment strategy for I/R injury is ischemic conditioning. In Ischemic Preconditioning (IPC), a short period of ischemia prior to AMI can protect the heart from I/R injury. In ischemic Postconditioning (PostC) short periods of ischemia immediately after reperfusion of AMI are supposed to decrease I/R injury. The electrophysiological consequences of ischemic conditioning are scarcely understood. Here, we have used an electrophysiological mapping catheter to record intraventricular ECG changes in real-time.
Methods: Domestic pigs were split into 3 groups: IPC-AMI (n = 6), AMI-PostC (n = 4) and AMI-control (n = 5) (Fig.1). IPC was performed with 3 cycles of 5 min I/R using a balloon catheter in the mid LAD prior to infarction. Myocardial infarction was induced via inflation of a balloon in the mid LAD for 90 minutes (Fig. 2). PostC was accomplished by inflating and deflating the balloon for 6x30 second cycles of I/R immediately after infarction. A NOGA endocardial mapping catheter was positioned in the left ventricle to measure a single point of myocardium for the entire procedure. Infarct size and LV function were assessed with cardiac MRI + late enhancement at 1-month follow-up. Intraventricular R-Amplitude, ST-Elevation, QRS width, Heart Rate (HR) and QT time were measured in every minute.
Results IPC led to a significantly lower max. ST-Elevation during ischemia (at 20 minutes, Median(IQR), IPC 5.00 (3.40 - 5.10) mV vs. PostC 6.10 (4.90 - 6.30) vs. AMI 6.30 (4.70 - 6.75) mV $p < 0.001$) at 60 minutes after reperfusion, there was no significant difference between the groups. Both IPC and PostC led to higher R-Amplitudes after reperfusion (at 60 minutes, Median(IQR), IPC 0.82 (0.57-1.01) vs. AMI-PostC 0.98 (0.90-1.31) vs. AMI 0.49 (0,33-0,89), Median(IQR), mV, $p= < 0.001$) (Fig. 1). IPC reduced HR significantly throughout the entire procedure compared to AMI-PostC and AMI (Mean ± SD, IPC 89 ± 12 vs. PostC 123 ± 5 vs. AMI 129 ± 12). MRI+LE resulted in significantly better LV ejection fraction and smaller infarct size in group IPC-AMI compared to AMI-control and AMI-PostC groups.
Conclusion IPC significantly reduced maximum ST-Elevation during ischemia. At follow-up, IPC showed the smallest infarct area and best ventricular function. Both IPC and PostC led to higher R-Amplitudes after reperfusion, possibly indicating preserved electrophysiological function of myocardial cells. IPC significantly reduced HR throughout the entire procedure, possibly contributing to its protective effect.



ECG Parameters

P2302

The human H2 receptor as a possible target for treatment of acute heart failure

J Joachim Neumann[1]; M Mahnkopf[1]; N Misslinger[1]; H Wache[1]; F Bergmann[1]; U Gergs[1]
[1]*Martin Luther University of Halle-Wittenberg, Halle, Germany*

In experimental animals, anthracycline-induced heart failure also involved release of histamine and this heart failure could be attenuated by pretreatment of animal with histamine H2 receptor antagonists. This is similar to the beneficial effects of ß1-adrenoceptor blockade chronic human heart failure, because both receptors signal through Gs proteins and cAMP induced protein phosphorylation. To study the hypothesis that histamine H2 receptors might be a novel target to treat heart failure, we have generated transgenic mice (TG) which overexpress the human H2 receptor in cardiomyocytes via the alpha myosin heavy chain promoter. In isolated perfused hearts (Langendorff technique) from transgenic mice (TG) but not in hearts from wild type litter mates (WT), histamine induced positive inotropic effects, positive chronotropic effects and increased phospholamban phosphorylation in frozen hearts from these perfused hearts. This mouse model was used here to get data on the relevance of histamine in a model of cardiac failure. To this end, LPS (lipopolysaccharides) were injected intraperitoneally at 30 µg/g (or isotonic sodium chloride: NaCl) body weight in TG and WT. Thereafter, the time course (1,3,7 h) of LPS-action was followed by echocardiography in isoflurane-anaesthetized mice. LPS led to a time dependent reduction in left ventricular ejection fraction (n = 6-9). EF was less in TG than in WT at 7 h after LPS injection (n = 8 each). Finally, hearts were obtained used for Western blotting or RNA isolation and reverse transcription - quantitative polymerase reaction (RT-PCR) . A LPS- induced increase in IL-6 or IkBalpha was less pronounced in TG than in WT. Moreover, in NaCl-treated TG levels of IL-1b were much smaller than in NaCl-treated TG. Finally, LPS increased CD14-levels only in TG but not in WT. Hence, TG are more sensitive to LPS-induced acute heart failure which might suggest a possible detrimental role of H2 at least in acute heart failure.

P2303

The role of the endocardial endothelium in the inotropic effects of the histamine and metabolism modifiers of cyclic nucleotides on the contractility of rat's right heart ventricle.

S Sonja Smiljic[1]
[1]*Medical faculty, Deaprtment of Physiology, Kosovska Mitrovica, Serbia*

Background: Endocardial endothelium synthesize endothelial mediators, it has receptors, acts as blood-heart barrier and has complex influence on cardiomyocytes.
Objective. The aim of the research was to determine effect of histamine and metabolism modifiers of cyclic nucleotides to heart contractility with intact and removed endocardial endothelium.
Methods: Adult rats, of both sexes, type Wistar albino were used in this experiment. Experimental model consisting of twelve experimental groups was divided into six subgroups with endocardial endothelium and six without endocardial endothelium. During the experiment, the following inotropic effect of pharmacological substances was investigated: histamine, theophylline, imidazole, dibutiril cyclic adenosine monophosphate (dbcAMP), pyrilamine and cimetidine. The stabilization period for the isolated right ventricle in the water bath, stimulated by electrical impulses, was 30 minutes. After this time, the test substance was added and its inotropic effect was monitored over the next 60 minutes.
Results: The contractility of the right ventricle of the rat's heart with the removed endothelium was 60% lower than in the heart with the intact endocardial endothelium. Inotropic effect of the histamine (1x10-4 mol/l) is significantly larger when there is no endocardial endothelium ($p < 0.05$). Theophylline (1x10-2 mol / l) had manifested a positive inotropic effect on the heart, independently of the presence of endocardial endothelium. Modulating role of the endocardial endothelium on the inotropic effect of imidazole (1x10-4 mol/l) was significant ($p < 0.05$). A significantly higher inotropic response of cardiomyocyte to dbcAMP (1x10-6 mol/l) was obtained in the absence of endothelium. Modulating role of the EE on the effects of pyrilamine (1x10-6 mol/l) was significant and a positive inotropic effect was obtained in the absence of endothelium. Cimetidine (1x10-4 mol/l) achieved a discrete inotropic effect in the case of the preserved endocardial endothelium, and when the EE was removed, the contraction amplitude was increased by 29%.
Conclusion: Our results show the definite significance of the modulating role of the endocardial endothelium in achieving the effects of the tested substances. The influence of the endocardial endothelium is of major importance in achieving cardiac performance.

P2304

The value of receptor tyrosine kinase (axl) expression in myocardial infarction: relationship with apoptotic parameters.

A Tsipis[1]; AM Athanassiadou[2]; E Petrou[1]; G Agrogiannis[2]; P Athanassiadou[2]; G Athanassopoulos[1]; N Kavantzas[2]
[1]*Onassis Cardiac Surgery Center, Division of Cardiology, Athens, Greece*;
[2]*University of Athens, Department of Pathology, Athens, Greece*

Introduction: The AXL is a membrane receptor tyrosine kinase, correlates with poor survival in patients with cancer. Also, AXL is expressed in myocardium. Hypoxia activates AXL signalling and the direct transcription of hypoxia inducible factors. The aim of the present study was to investigate the expression of AXL in myocardial infarction and the relation with apoptotic proteins.

Methods: We studied myocardial samples of hearts with histological findings of acute myocardial infarction, old myocardial infraction and normal myocardium. An immunohistochemical method was performed with the use of AXL, Bax, Bcl-2 antibodies.
Results: The immunoreactivity of AXL was low in normal myocardium and increased positive expression was noted from acute myocardial infarction (12,4%) to old myocardial infraction (62,5%). Also, AXL was associated with worse prognosis in heart failure. High concordance of AXL and Bax (pro-apoptotic protein) expression was detected in old myocardial infarction (82% of cases).
Conclusions: Increased levels of AXL were associated with intense expression of proapoptotic bax protein in old myocardial infraction. Decreased levels of AXL and intensive expression of anti-apoptotic bcl-2 were found in cases of acute myocardial infraction. The increased expression of AXL and Bax in old myocardial infraction is associated with the progressive loss of myocytes by apoptosis.

P2305

New role of Kv4.3 ion channel with HMGB1 in the the heart

V Viktoria Szuts[1]; F Otvos[2]; ZS Hamari[3]; J Jarabin[4]; JG Kiss[4]; L Rovo[4]; G Czifra[5]; CS Vagvolgyi[3]; K Halasy[6]; ZS Szegletes[2]
[1]University of Szeged, Faculty of Medicine, Department of Pharmacology & Pharmacotherapy, Szeged, Hungary; *[2]Hungarian Academy of Sciences, Center for Biological Research, Szeged, Hungary*; *[3]Department of Microbiology, Faculty of Science and Informatics, University of Szeged, Szeged, Hungary*; *[4]University of Szeged, Department of Otorhinolaryngology–Head and Neck Surgery, Szeged, Hungary*; *[5]University of Debrecen, Department of Anatomy and Histology, Debrecen, Hungary*; *[6]Szent Istvan University, Department of Anatomy and Histology, Budapest, Hungary*

The voltage-dependent transient outward currents (Ito) are major early repolarization currents and determined by Kv4.2 and Kv4.3 ion channels with synapse-associated protein 97 (Sap97) proteins. High-mobility group B1 plays a major role in the DNA replication and may be involved in the activation of proinflammatory pathways and known as a pathological factor in heart diseases. HMGB1 effects are depending of its concentration in heart. Once released into the extracellular milieu, HMGB1 activates inflammatory responses, serving as a late mediator of systemic inflammation. Contrasting actions of this cytokine are seen as it mediates both regeneration of damaged tissue. The Kv4.3 type channels associate with in the complex and maybe modulating the kinetic properties of Ito. Ophiobolins are important members of the family of phytotoxic metabolites, and they can modulate activities of kv4.x ion channels. The hypothesis was that HMGB1 is mainly localizes in the nuclear and associates with Kv4.3 ion channels but the HMGB1 cytokine effects can modulate the distribution of Kv4.x ion channels in the cardiomyocytes. In this work, we have examined the action of HMGB1 as a cytokine on the Kv4.3 channel distribution in cardiomyocytes. The microscope figures validate first the spatial difference localization of Kv4 channels. Ophiobolins A (OPA) served as an external stress agents on Kv4.x ion channels with different OPA concentrations. Our result were demonstrated that acute treatment by HMGB1 or OPA injured the structure of cells after 24 hours marking and altered the distribution of Kv4.x proteins in cell organs. Because HMGB1 is associated directly to the Kv4.3 ion channel this can be hearted directly the K+ ion homeostasis in high concentration of OPAs.

P2306

Reference values of segmental evaluation of longitudinal deformation of left ventricular myocardium in healthy individuals

A Alexey Kuchmin[1]; EP Galova[1]; DA Galaktionov[1]; AA Kazachenko[1]; AO Gergel[1]; MY Yaroslavtsev[1]; YV Epelshtein[1]; AA Shevelev[1]
[1]The Kirov Military Academy, St-Petersburg, Russian Federation

Background: Evaluation of longitudinal deformation is recognized as a reliable, reproducible and highly informative method in the diagnosis of cardiovascular diseases. However, the limiting factor for the wide use of the technique is the absence of recognized segmental norms of longitudinal deformation of the left ventricular myocardium.
Purpose: Determination ofthe level reference values of the segmental deformation of the myocardium in middle aged healthy individuals.
Methods: 56 volunteers without signs of cardiovascular pathology, 48 men and 8 women were examined. The mean age was 33.6 ± 9.3 years. All patients underwent an echocardiographic study using the GE "VividE95" device, (USA) in accordance with the recommendations of the European echocardiographic association and the American echocardiographic society. The analysis of longitudinal deformations of the myocardium was carried out, which was determined by the percentage of shortening of the fibers in each segment of the left ventricle, and was visualized on the device with the help of the "bull's eye" technique.
Results: Data of echocardiographic structures of the left and right heartsectors in all examined patients were within the limits of normal values, violations of systolic and diastolic function or valve apparatus was not detected.
In assessing the deformation of the left ventricular myocardium, it was revealed that the most values of deformations are the median anterior, lower-septal and lower (8, 9, 10 segments) and all apical segments: (13-17 segments). Based on the results obtained, the reference values for each segment are calculated: the mean plus / minus two standard deviations. Calculated reference values of LV segments: 1 - 11,3-22,9%, 2 - 12,7-21,1%, 3 - 11,6-18,8%, 4 - 12,9-20,9 %, 5 - 11,1-21,5%, 6 - 10,9-19,7%, 7 - 15,1-24,3%, 8 - 15,9-24,7%, 9 - 15,5-23,9 %, 10 - 15,6-24,0%, 11 - 12,0-23,2%, 12 - 12,7-21,1%, 13- 17,4-31,0%, 14 - 20,6-29,8%, 15 - 17,7-30,9%, 16 - 15,9-28,7% and 17 - 18,5-29,3%.
Conclusions: The obtained reference values of the segmental longitudinal deformation can be used as an approximate norm in persons of the Caucasian race when making a comparative evaluation of the changes in longitudinal deformation in different cardiovascular pathologies on GE devices "Vivid E95".

P2307

Dipeptidyl peptidase-4 activity plays a critical role in the pathogenesis of experimental autoimmune myocarditis

Y Yasuhiro Maejima[1]; Y Shiheido-Watanabe[1]; N Tamura[1]; Y Ito[1]; K Hirao[1]; M Isobe[2]
[1]Tokyo Medical And Dental University, Cardiovascular Medicine, Tokyo, Japan; *[2]Sakakibara Heart Institute, Tokyo, Japan*

Funding Acknowledgements: JSPS KAKENHI Grant-in-Aid for Scientific Research (C) (26461126); Grant for research collaboration with TMDU and Boehringer Ingelheim Japan, Inc.

Background: Autoimmune myocarditis is the most common cause of heart failure among young adults and is a major precursor of dilated cardiomyopathy. We have shown previously that dipeptidyl peptidase-4 (DPP-4) plays an important role in the development of experimental autoimmune myocarditis (EAM) in mice. However, the precise mechanism how DPP-4 aggravates EAM remains to be elucidated.
Purpose: The aim of this study is to explore the role of DPP-4 in the pathogenesis of EAM in mice.
Methods: & **Results:** Mouse EAM models were given normal diet (CONT group), or a diet mixed with linagliptin, a DPP-4 inhibitor (3mg/kg/day)(LINA group). Left ventricular ejection fraction after 21-day of EAM induction was significantly higher in LINA-group than in CONT-group (72.6 ± 6.6%* vs. 60.1 ± 9.2%, *P < 0.05). Immunohistochemical analyses demonstrated that the number of ROR?t-positive Th17 cells, a subset of T-lymphocytes expressing high level of enzymatically active DPP-4, infiltrated to EAM myocardium was significantly smaller in LINA-group than in CONT-group (46.9 ± 2.4 RFU* vs. 116.8 ± 8.6 RFU, *P < 0.05). Consistently, the DPP-4 activity in EAM myocardium was significantly lower in LINA-group than in CONT-group. Mass spectrometry analysis using lysates from EAM myocardium co-immunoprecipitated with Flag-DPP-4 recombinant protein and co-immunoprecipitation-western blot analysis demonstrated that DPP-4 bound to cathepsin-G(CTSG), a plasma membrane-bound serine protease, in the EAM heart. The activity of CTSG in EAM myocardium was significantly higher in EAM mice compared to those in untreated mice, and administration of linagliptin effectively suppressed the CTSG activity in the EAM hearts. We also found that DPP-4 significantly suppressed the activity of a1-antichymotrypsin, a protease which can catalyzes CTSG and is activated in response to EAM. Finally, we revealed that the of angiotensin II, a product catalyzed by CTSG, in the EAM heart was markedly decreased in LINA-group than in CONT-group.
Conclusion: These results suggest that DPP-4 physically interacts with CTSG, thereby enhancing CTSG activity through suppressing a1-antichymotrypsin, which, in turn, promoting angiotensin II accumulation in the EAM hearts. Thus, DPP-4 derived from Th17 cells would aggravate cardiac dysfunction during EAM.

P2308

Evaluation of PD-1 and PD-L1 expression as potential diagnostic and therapeutic targets in ischemic cardiac injury - preliminary results of a translational approach

K Hess[1]; R Rouven Berndt[2]; K Huenges[2]; R Rusch[2]; B Panholzer[2]; J Cremer[2]; M Albrecht[3]; A Haneya[2]
[1]University Medical Center, Institute of Neuropathology, Münster, Germany; *[2]University Medical Center of Schleswig-Holstein, Cardiovascular surgery, Kiel, Germany*; *[3]University Medical Center of Schleswig-Holstein, Department of Anesthesiology and Intensive Care Medicine, Kiel, Germany*

Background: Programmed cell death 1 (PD-1) and programmed cell death ligand 1 (PD-L1) are transmembrane molecules with a wide range of immunoregulative functions. Latest experimental results indicate influence of PD-1/PD-L1 expression

on the extent of cardiac ischemic injury. The aim of this study was to investigate the expression of PD-1 and PD-L1 in ischemic myocardial tissues.
Methods: Cardiac tissue samples from patients with acute myocardial infarction (n = 24), chronic ischemic cardiomyopathy (n = 18) and a control group (n = 14) were collected during cardiac surgery. Immunohistochemically staining was performed for PD-L1 and PD-1 and analyzed in a blinded manner. Clinical, demographic and echocardiography data of all patients were evaluated retrospectively and correlated with PD-L1 and PD-1 expression. Cell culture experiments with human iPSC-derived cardiomyocytes under hypoxia were performed to examine the hypoxia-depend expression of PD-L1 and PD-1.
Results: Low or absence of PD-1 and PD-L1 expression levels were detected in cardiac tissue without hypoxic injury. Acute myocardial injury was associated with a significantly increased inflammatory infiltrate, mostly consisting of PD-1 positive T-lymphocytes. In respond to chronic hypoxia in tissues from ischemic cardiomyopathy, cardiomyocytes displayed a significantly increased PD-L1 expression and showed negativity for PD-1. PD-1 expression was restricted to low levels of T-lymphocytes. Cox regression for six months follow-up after cardiac surgery demonstrated a significant higher cardiac-related morbidity and mortality in patients with enhanced PD-L1 expression. Cell culture experiments revealed a hypoxia-depend expression rate of PD-L1 in cardiomyocytes.
Conclusion: The present results demonstrated a hypoxia associated expression of PD-L1 in human cardiomyocytes whereas the expression of PD-1 was low and restricted to T-lymphocytes. Expression of PD-L1 in chronic ischemic cardiac tissue was significant correlated with higher mortality what makes PD-L1 a potential diagnostic and therapeutic target in cardiac ischemia.

P2309

Analysis of cytomegalovirus-specific T-cell responses in patients with hypertension: comparison of assay methods and antigens

JC Youn[1]; SK Lee[1]; SW Choi[1]; S Han[1]; KH Ryu[1]; S Park[2]; EC Shin[3]
[1]Dongtan Sacred Heart Hospital, Hallym University, Division of Cardiology, Hwaseong, Korea Republic of; *[2]Yonsei University College of Medicine, Division of Cardiology, Severance Cardiovascular Hospital, Seoul, Korea Republic of*; *[3]Korea Advanced Institute of Science and Technology, Laboratory of Immunology and Infectious Diseases, GSMSE, Daejeon, Korea Republic of*

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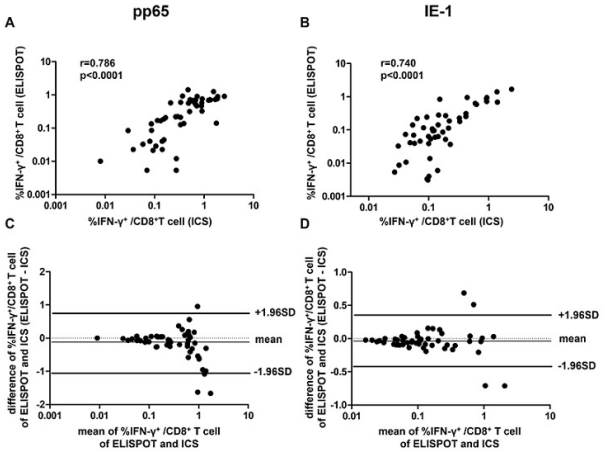
Background: Recent studies suggest an association between cytomegalovirus (CMV) infection and hypertension. In the present study, we used a variety of antigens and different assay methods to investigate the relationship between CMV-specific T-cell responses and arterial stiffness in patients with hypertension.
Methods: To evaluate arterial stiffness, pulse wave velocity (PWV) was measured in 207 hypertensive patients (average age, 63 ± 8 years). To measure CMV pp65 and IE-1-specific T-cell responses, we performed intracellular cytokine staining (ICS) and enzyme-linked immunospot (ELISPOT) assays. We also analyzed CMV-specific T-cell responses against 10 different CMV antigens using ELISPOT assays.



Results: In patients with hypertension, senescent CD8+ T-cell frequencies were significantly correlated with arterial stiffness. Moreover, arterial stiffness was independently associated with CMV pp65-specific CD8+ T-cell responses as measured by ICS. CMV-specific CD8+ T-cell responses measured by ICS and ELISPOT assays showed good agreement and significant correlation with each other. ELISPOT analyses against 10 different CMV antigens revealed a consistent response pattern irrespective of age, gender, and diabetes.
Conclusions: CMV pp65-specific CD8+ T-cell responses were independently correlated with arterial stiffness in patients with hypertension. Additionally, the results of ICS and ELISPOT assays showed a significant correlation and good agreement with each other. These findings are important for guiding choices regarding the broad clinical application of CMV-specific T-cell response assays in this patient population.

P2310

The role of complement-complex (c5b-c9) expression and apoptosis in myocardial infract area and in infract border zones

A Tsipis[1]; AM Athanassiadou[2]; E Petropoulou[3]; P Athanassiadou[2]; G Athanassopoulos[1]; N Kavantzas[2]
[1]Onassis Cardiac Surgery Center, Division of Cardiology, Athens, Greece; *[2]University of Athens, Department of Pathology, Athens, Greece*; *[3]IASO General Hospital, Department of Cardiology, ATHENS, Greece*

Introduction: Although increasing experiment data suggest that necrosis and apoptosis occur in myocardial infarction, it is less clear the relation between the two conditions and the relevant pathophysiological mechanism. The terminal complement pathway (C5b-9) inserts into the cell membrane and induces cell lysis. Complement complex (C5b-9) may also play a key role in cell apoptosis, by regulating the apoptotic proteins Bax, bcl-2 and by involving the mechanism of caspase cascade.
The aim of the present study was to investigate the expression of C9 in myocardial infarction and the relation with apoptotic proteins.
Methods: We studied myocardial samples of hearts with histological findings of acute myocardial infarction (group A, n = 100), old myocardial infraction (group B, n = 100) and myocardial samples of normal heart (control group, n = 20). An immunohistochemical method was performed with the use of C9, Bax, Bcl-2 antibodies, in order to investigate the expression of C9 and apoptosis-related proteins in ischemic cardiac disorders.
Results: The immunoreactivity of complement component was intensive at infract areas and low at infract border zones of samples with acute myocardial infarction. In old myocardial infraction the complement expression was decreased. Anti-apoptotic protein Bcl-2 is high expressed in cardiomyocytes at the risk areas of acute myocardial infarction. High concordance of complement component and proapoptotic protein Bax expression was detected at infracts areas. In old myocardial infraction the bcl-2 positive samples demonstrated weak staining as in the control group.
Conclusions: Increased levels of complement component were associated with intense expression of proapoptotic bax protein at infracts areas and decreased levels of complement component were associated with intense expression of antiapoptotic bcl-2 protein at infract border zones. Apoptosis as a consequence of complement-mediated cell damage may provide an explanation for the presence of apoptotic proteins in inflammatory processes, but the increased expression of anti-apoptotic procedure represents a possible compensatory mechanism of salvaged myocytes and a defense mechanism against myocardial ischaemia.

P2311

Role of dynamin-related protein 1 in sepsis-induced myocardial inflammation: conversion of cardiomyocytes into a proinflammatory phenotype

WEIPENG Jiang[1]; KS Li[1]; Y Bai[1]; YX Jiang[2]; T Rui[3]
[1]University Hospital of Heidelberg, Department of Experimental Heart Surgery , Heidelberg, Germany; *[2]University Hospital of Heidelberg, Department of Radiology , Heidelberg, Germany*; *[3]University of Western Ontario, Critical Illness Research, Lawson Health Research Institute, London, Canada*

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Background: Sepsis is a systemic inflammatory response syndrome (SIRS) caused by a severe local infection, and further develops to multiple organ dysfunction syndrome (MODS). It is one of the major causes of death in clinical setting. One of the reasons of the myocardial dysfunction in sepsis is the cardiomyocytes converted to proinflammatory phenotype. Dynamin-related protein 1 (Drp1) is a regulator of mitochondrial fission.. However, little is known to date that whether inhibition of Drp1 could prevent the conversion of cardiomyocytes into a proinflammatory phenotype in sepsis.
Objective: To determine whether Drp1 plays a role in sepsis-induced conversion of cardiomyocytes into a proinflammatory phenotype.
Method: In vivo: Rat model of sepsis was induced by intraperitoneal (i.p.) injection of fecal material (180 mg/mL) at a dose of 3 g/kg body weight. Rat received normal saline (NS) served as control (sham). Some rats were pretreated with Mdivi-1 (25 mg/kg, i.p.) 1h before induction of sepsis.. Six hours after the induction of sepsis, rat plasma was isolated and hearts were harvested for myocardial myeloperoxidase

(MPO) and neutrophil infiltration assay. In vitro: Isolated rat cardiomyocytes were challenged with either septic plasma (from septic rat), or sham plasma (from sham rat), Drp1 activation was evaluated with inhibitory Drp1 S637 (serine 637) phosphorylation and mitochondria translocation. Proinflammatory phenotype of cardiomyocytes was determined by measuring chemokine (LIX and KC) expression.
Results: Rats with sepsis incurred increased myocardial MPO activity and myocardial polymorphonuclear neutrophil (PMN) accumulation as compared to control animals (P <0.05). Treatment of the septic rat with Mdivi-1(25 mg/kg) attenuated the sepsis-induced increase in myocardial MPO activity(P <0.05)and myocardial PMN accumulation(P <0.05). Challenge of cardiomyocytes with septic plasma activated Drp1 and promoted Drp1 mitochondria translocation(P <0.05), and resulted in conversion of cardiomyocytes into a proinflammatory phenotype as indicated by increase in LIX and KC expression(P <0.05). Mdivi-1(10 μmol/L) pretreatment prevented the increase in LIX and KC production in cardiomyocytes with septic plasma(P <0.05)and the dephosphoration of Drp1 at S637(P <0.05) and the Drp1 translocation to mitochondria(P <0.05).
Conclution: The activation of Drp1 plays a pivotal role in conversion of cardiomyocytes into proinflammatory phenotype in sepsis.

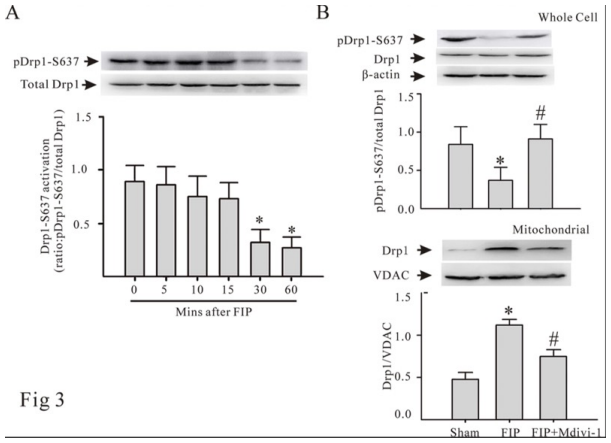


Fig 3

pDrp1-S637 Figure.3

P2312

Fingolimod can play important role in prevention of heart failure induced by ischemia reperfusion injury during heart transplanatation

N Ahmed[1]; GEBRIE Mebratu[2]; MAHYM Mansoor[3]; M Mansoor[4]; MAHAK Mansoor[3]; A Rungatscher[2]
[1]University of the Punjab, , Faculty of Health Sciences, Lahore, Pakistan; *[2]University of Verona, Cardiac Surgery Division, Verona, Italy*; *[3]King Edward Medical University, Internal Medicine, Lahore, Pakistan*; *[4]Punjab Institute of Cardiology, Cardiology, Lahore, Pakistan*

Background: Heart failure followed by Ischemia-Reperfusion Injury is a major issue in heart transplantation. During last decade, multiple strategies have been used to control this important problem. It is well known that fingolimod, a Sphingosine 1-Phosphate receptor modulator may cause anti-inflammatory, antioxidant and T-lymphocyte depletion leading to lymphopenia. Thus, it leads to a reduction in ischemia-reperfusion injury and ultimately, prevention of heart failure
Purpose: The main purpose to investigate the preoperative effect of fingolimod was to evaluate cardioprotective role in heterotopic heart transplantation experimental model in comparison of placebo administration.
Methods: Male Sprague–Dawley (SD) rats (300-350 g) (n = 30); treated with either fingolimod (1 mg/kg total body weight) or normal saline solution. Ischemia was applied for 60 minutes and reperfusion was followed for 24 hours and 1 week. Post heterotopic heart transplantation at 24 hours and 2 weeks all surviving rats were sacrificed. Blood and myocardial tissue were collected for analysis of myocardial biomarkers, inflammatory markers, oxidative stress, and signaling pathways. Myocardial fibrosis was investigated using Masson's trichrome staining and Fluorescein-activated cell sorting (FACS) to measure T-lymphocyte.
Results: Following 60 minutes of ischemia, neither saline treated nor vehicle treatment showed significant protective effects on long-term survival after Heterotopic Heart Transplantation.In fingolimod treated group, reduction of inflammation and oxidative stress have been observed as compared to saline-treated or vehicle group. FACS analysis showed a significant T-lymphocyte depletion in peripheral blood after fingolimod treatment, which was not observed after saline or vehicle treatment.
Conclusion: The long-term survival improved in this study might be due to a cardioprotective role of fingolimod to prevent ischemia reperfusion injury in heterotopic heart transplantation model, which may be mediated by decreaed inflammation, reactive oxygen species and the lymphocyte depletion shown in the FACS analysis.

P2313

Cardiac microdomains in cyclic nucleotide signalling: role of popeye domain-containing (Popdc) proteins

N K Navneet Kaur Bhogal[1]; Z Dong[1]; A Alvarez-Laviada[1]; R F R Schindler[1]; P Sarathchandra[1]; E Ioannou[1]; A V Glukhov[2]; J Gorelik[1]; T Brand[1]
[1]Imperial College London, National Heart and Lung Institute , London, United Kingdom; *[2]University of Wisconsin, Wisconsin, United States of America*

Funding Acknowledgements: British Heart Foundation

Cardiac microdomains recruit components of the various signalling pathways including cAMP signalling. cAMP is stimulated by β-adrenergic receptors (βAR) in response to catecholamines to elicit physiological and pathophysiological responses. In the heart, Popdc1 and Popdc2 are expressed highly in the cardiac conduction system and have a high affinity-binding site for cAMP localized to the cytoplasmic region of the protein. Popdc genes encode transmembrane proteins, which are localized to the plasma membrane and transverse-tubules (TT). Work in model organisms and patients have indicated an important role of Popdc for controlling expression and membrane localization of scaffolding proteins as well as membrane trafficking of Nav1.5 and TREK-1 electrogenic proteins. Therefore, Popdc could well be involved in the structural and functional applications of cardiac microdomains, where loss-of-function mutations in Popdc have been associated with cardiac arrhythmia and pacemaking abnormalities. The aim of this study is to correlate findings between single cell and tissue work, by investigating mouse atrial myocytes (AMs) to understand the way in which cAMP is modulated by cardiac microdomains, and to understand how Popdc1-/- and Popdc2-/- null mutants alter electrophysiological characteristics of the atria and the structure of AMs.
Pacemaking and atrial conduction were studied in Popdc1, Popdc2 -null and wild type mice using high spatial and temporal resolution optical mapping of the isolated atrial preparations stained with the voltage-sensitive dye di-4-ANNEPS, both, at baseline and after isoproterenol (non-selective βAR agonist; 1-300 nM) stimulation. Both premature and skipped beats were captured resulting in heart rate variability in both mutants, in response to isoproterenol. Both mutants demonstrated slower atrial conduction propagation. Popdc1-/- presented increased fibrosis levels, which is a potential substrate for re-entrant activity and AF. To determine how these responses are controlled at a cellular level left and right AMs were structurally imaged, using confocal microscopy. Three subgroups were recorded from control AMs: (a) organized, (b) disorganized, and (c) sparse TT structures. Preliminary data from Popdc1-/- AMs suggests a higher proportion of AMs with a disorganised TT structures. To understand the functional role of βARs in single AMs Förster resonance energy transfer (FRET) measured the cAMP response. So far, control AMs produced a higher cAMP response from ß1AR stimulation compared to ß2AR stimulation. However, inhibiting PDE4 during ß2AR stimulation demonstrated right AMs have a stronger cAMP response compared to left.
In conclusion, PDE4 is important for cAMP modulation in AMs and specifically in right AMs. In addition, the loss of Popdc1 proteins causes a disorganisation of the TT structure in AMs with pacemaking and atrial conduction abnormalities at a tissue level, which significantly raises the risk of developing AF.

P2314

The effect of infliximab on time course changes of hemodynamic parameters and heart tissue injury in isoproterenol-induced post myocardial infarction heart failure in the rat

A Garjani[1]; N Maleki Dizaji[1]; M Mohamadi[1]; S Mousavi[1]; H Vaez[1]
[1]Tabriz University of Medical Sciences, Department of Pharmacology, Tabriz, Iran (Islamic Republic of)

Funding Acknowledgements: Tabriz University of Medical Sciences

Inflammation and cytokine production contribute to wound healing and cardiac remodeling after a myocardial infarction (MI). However, excess inflammation can lead to more injury, infarct expansion, and adverse ventricular remodeling and thereby propagate heart failure development. We have shown that the serum and heart tissue levels of pro-inflammatory cytokines are elevated in isoproterenol-induced myocardial infarction and the serum levels of TNFa are positively correlated with the degree of coronary luminal stenosis in patients with stable angina. It seems that immunosuppressant and anti-inflammatory therapeutic strategies may have potential beneficial effects in the treatment of post MI heart failure. However, several studies show that immunosuppressant and anti-inflammatory treatments after heart attack is controversial. In a rat model of isoproterenol-induced MI we demonstrated that early administration of infliximab, a TNFa monoclonal antibody,

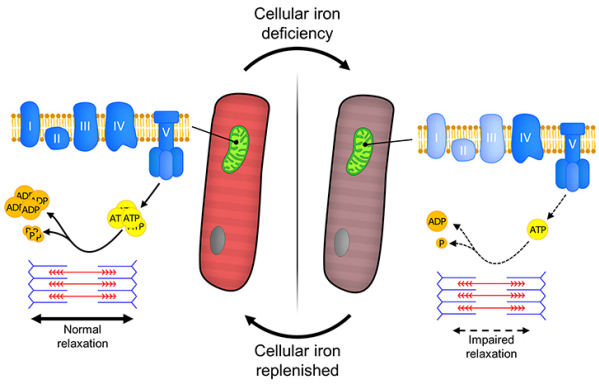
along with the MI induction despite early protection against myocardial inflammation and tissue injury (24 and 48 hours after MI) had no protective effects against the myocardial dysfunction. Even, in the long run (after 96 hours) it exacerbated the development of tissue damage from endocardium to myocardium and led to heart failure by decreasing the left ventricular systolic pressure, contractility, and relaxation and by increasing the left ventricular diastolic pressure. Heart tissue remodeling and restoration appear to be suppressed by TNFa inhibition. It is suggested that, anti-inflammatory strategies to reduce inflammation in heart after myocardial infarction should be carefully balanced as they might interfere with the tissue repair and healing.

P2315

Iron deficiency impairs contractility of human cardiomyocytes through decreased mitochondrial function.

MF Hoes[1]; N Grote Beverborg[1]; JD Kijlstra[1]; J Kuipers[2]; DW Swinkels[3]; BNG Giepmans[2]; RJ Rodenburg[4]; DJ Van Veldhuisen[5]; RA De Boer[5]; P Van Der Meer[5]
[1]University Medical Center Groningen, Department of Experimental Cardiology, Groningen, Netherlands; *[2]University Medical Center Groningen, Department of Cell Biology, Groningen, Netherlands*; *[3]Radboud University Medical Centre, Department of Laboratory Medicine, Nijmegen, Netherlands*; *[4]Radboud University Medical Centre, Department of Pediatrics, Nijmegen, Netherlands*; *[5]University Medical Center Groningen, Department of Cardiology, Groningen, Netherlands*

Aims: Iron deficiency is common in patients with heart failure and associated with a poor cardiac function and higher mortality. How iron deficiency impairs cardiac function on a cellular level in the human setting is unknown. This study aims to determine the direct effects of iron deficiency on mitochondrial function, contractility and morphology of human cardiomyocytes, and to assess whether repletion of iron levels restores cardiomyocyte function.
Methods and Results: Human embryonic stem cell-derived cardiomyocytes were depleted of iron by incubation with the iron chelator deferoxamine (DFO). Mitochondrial respiration was determined by Seahorse Mito Stress test, and contractility was directly quantified using video analyses according to the BASiC method. Detailed cellular morphology was studied using electron microscopy. The activity of the mitochondrial respiratory chain complexes were examined using spectrophotometric enzyme assays.
Four days of iron depletion resulted in an 84% decrease in ferritin ($p < 0.0001$) and significantly increased gene expression of transferrin receptor 1 and divalent metal transporter 1 (both $p < 0.001$). Mitochondrial function was reduced in iron deficient cardiomyocytes, in particular ATP-linked respiration and respiratory reserve were impaired (both $p < 0.0001$). Iron depletion affected mitochondrial function through reduced activity of the iron-sulfur cluster containing complexes I, II and III, but not complexes IV and V. Furthermore, mitochondria in iron-deficient cardiomyocytes appeared swollen and contained inclusion bodies. Iron deficiency reduced cellular ATP levels by 73% ($p < 0.0001$) and reduced contractile force by 43% ($p < 0.05$). The maximum velocities during both systole and diastole were reduced by 64% and 85% respectively (both $p < 0.001$). Supplementation of transferrin-bound iron recovered functional and morphological abnormalities within 3 days.
Conclusion: Iron deficiency directly affects human cardiomyocyte function, impairing mitochondrial respiration, and reducing contractility and relaxation. Restoration of intracellular iron levels can reverse these effects.



P2316

A novel mode of Ca regulation of the cardiac sodium channel by calmodulin

C N Johnson[1]; F Potet[2]; A M Glazer[1]; B K Knollmann[1]; A L George Jr[2]; W J Chazin[1]
[1]Vanderbilt University, Nashville, United States of America; *[2]Northwestern University, Chicago, United States of America*

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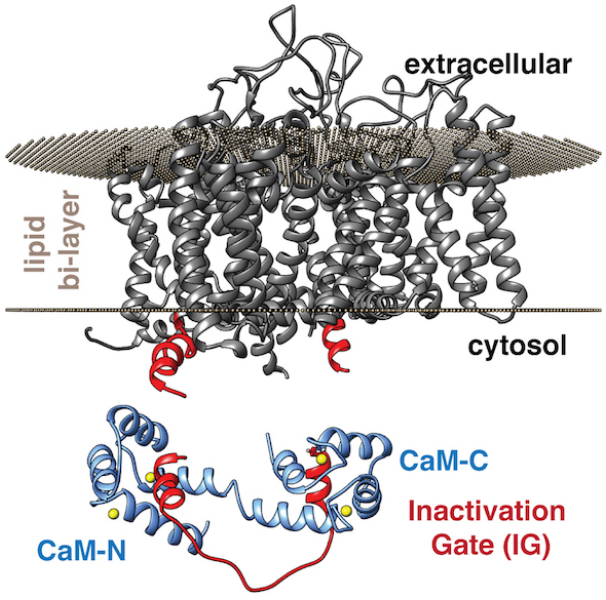
Purpose: The human cardiac sodium channel (NaV1.5) is essential for the generation and propagation of action potentials in the heart. Genetic mutations in both NaV1.5 and the accessory proteins cause channel dysfunction and are associated with life threatening cardiac conditions. Despite much investigation, treatment options for patients suffering from NaV1.5 dysfunction are lacking. Identification and development of novel therapeutic targets and improvements to existing treatments are hindered by a lack of understanding the atomic underpinnings governing channel function and regulation.
Methods: The atomic structure of CaM bound to the NaV1.5 inactivation gate was determined using a unique combination of X-ray crystallography, NMR spectroscopy and small angle X-ray scattering. A homology model of the NaV1.5 alpha subunit was created based on the atomic structure of the functional CaV1.1 channel using Rosetta. The NaV1.5 model was oriented in a lipid bi-layer using the Orientations of Proteins in Membranes database. Using strategic structure guided mutations we evaluate channel function in the absence and presence of an impaired CaM-IG interaction by whole cell patch clamp electrophysiology.
Results: Here we present the structure of a Ca dependent interaction between the Ca sensing protein Calmodulin (CaM) and the NaV1.5 channel inactivation gate (IG). CaM binds to two independent sites on the channel IG in an antiparallel manner using an unanticipated structural mode. Importantly CaM engages the IG with a high affinity that has not been previously recognized. Incorporating our structure into a homology model of the full-length channel reveals a mechanism for how CaM directly modulates NaV1.5 function in response to changes in Ca. We find that in the presence of Ca, the CaM-IG interaction promotes recovery from inactivation while impeding the kinetics of inactivation. Based on our structural findings we predict the importance of disease associated mutations contained within the channel inactivation gate and we validate perturbations to CaM binding by NMR.
Conclusions: Our results identify and characterize a new high affinity CaM interaction that forms the basis of a novel mode of Ca regulation of the NaV1.5 channel, where Ca activates CaM to engage the channel IG and facilitate re-opening. Structural investigations of disease associated mutations contained in both CaM and the NaV1.5 IG suggest new potential mechanism(s) for the cause of arrhythmia.



Model of NaV1.5 CaM Interaction

P2317

Cardiac myocyte-specific loss of the lncRNA Malat-1 protects against pathological hypertrophy and induction of pro-apoptotic genes

E L Emma Louise Robinson[1]; N Bitsch[2]; B Schroen[2]; H L Roderick[1]
[1]KU Leuven, Cardiovascular Sciences, Leuven, Belgium; *[2]Cardiovascular Research Institute Maastricht (CARIM), Department of Cardiology, Maastricht, Netherlands*

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Purpose: Reprogramming of the cardiac myocyte (CM) transcriptome underlies maladaptive pathological remodelling in cardiac hypertrophy and heart failure. Long non-coding RNAs (lncRNAs) are emerging as key regulators of gene expression in cellular development, homeostasis and pathology.
The lncRNA Malat-1 is of particular interest as it is involved in regulation of mRNA splicing, ERK/MAPK signalling, regulation of myogenic differentiation, histone lysine methylation and miR-133 activity - processes established as having important functions in cardiac hypertrophic remodelling.
Methods: CMs are outnumbered 1:3 by non-CMs in the adult heart. To study gene expression specifically in CMs from intact postmortem human and rodent hearts, we employed a powerful method involving fluorescence-assisted cell sorting to selectively isolate CM nuclei (based on positive labelling for PCM-1). RNA was isolated from PCM-1+ve nuclei and CM gene expression analysed by RT-qPCR or RNA-seq.
A CM-specific and inducible Malat-1 knockout mouse was created by crossing C57BL/6J Malat-1fl/fl mice with CM-restricted (Myh6 promotor) tamoxifen-inducible MerCreMer expressing mice to generate Malat-1fl/fl;Tg(Myh6-MCM) mice. Littermate Malat-1fl/fl mice were used as controls. Pathological hypertrophy was induced by transverse aortic constriction (TAC) on 8-10 week old mice (males and females). Control mice were sham operated. Tamoxifen (40 mg/kg) was administered one week pre-operative by a single intraperitoneal injection, to avoid transient cardiomyopathy by repetitive tamoxifen administration. Mice were sacrificed 4 weeks post-surgery.
Results: Profiling of the transcriptome in healthy and failing human CMs identified an increase in Malat-1 expression, which was also observed in rodent pathology. Pressure overload induced pathological remodelling invoked by TAC was attenuated with CM-specific genetic ablation of Malat-1 compared with controls. CM-specific loss of Malat-1 prevented the TAC-associated increases in left ventricular mass and posterior wall thickness and decrease in ejection fraction. Absence of reactivation of the cardiac foetal gene programme also indicated protection from pathological remodelling.
Probing the CM transcriptome revealed downregulation of pro-apoptotic genes in Malat-1 KO mice. Notably, the initiator caspases 8 and 9 were downregulated in Malat-1 KO CMs, genes which were otherwise upregulated in CMs with TAC in control mice. CM death is associated with pathological hypertrophy and heart failure, which was reflected by a drop in the fraction of CM nuclei measured during flow sorting in controls mice with TAC, that was not seen with TAC in Malat-1fl/fl;Tg(Myh6 MCM) mice. Suppression of CM apoptosis induced by TAC in Malat-1 KO mice was validated using the TUNEL assay.
Conclusion: Loss of Malat-1 in CMs protects against maladaptive cardiac hypertrophy through a mechanism that may involve attenuation of initiation of apoptosis.

P2318

A new form of inherited cardiomyopathy leads to to changes in heterochromatin structure in man and mice

B Gerull[1]; N Abdelfatah[2]; R Chen[1]; J Gross[1]; C Fielding[2]; H Duff[2]
[1]Comprehensive Heart Failure Center (CHFC), Internal Medicine , Wurzburg, Germany; *[2]Libin Cardiovascular Institute of Alberta - University of Calgary, Calgary, Canada*

Introduction: Nuclear envelope proteins have been shown to play an important role in the pathogenesis of inherited dilated cardiomyopathy (DCM). We recently discovered a novel homozygous mutation (p. L13R) in the inner nuclear membrane (INM) protein LEMD2 causing juvenile onset of arrhythmic cardiomyopathy and bilateral cataract. LEMD2 has been implicated in several important roles such as stabilization of the nuclear membrane and chromatin organization. However, its role in cardiac development and disease remains unknown.
Purpose: To determine the effects of mutant LEMD2 in human cells and heart tissue, in vitro cell culture and an in vivo knock-out mouse model.
Methods: Heart tissue of a deceased homozygous mutation carrier, affected fibroblasts as well as transfected cells expressing wildtype and mutant LEMD2 were investigated by histology, immunohistochemistry, electron microscopy (EM) and different assays regarding cell senescence and apoptosis. Additionally, a knock-out mouse model (KO) was generated by CRISPR/Cas9 technology and initially characterized.
Results: Histology of affected heart tissue showed myocyte disarray and extensive interstitial fibrosis. EM revealed extensive changes of myocyte nuclei, including extensive elongation and bizarre shapes with clumping of peripheral heterochromatin. However, immunohistochemistry demonstrated regular nuclear membrane localization of mutant LEMD2 in affected cardiac tissue as well as in dermal fibroblasts from patients and transfected C2C12 cells. Next, we investigated proliferation, apoptosis and cell senescence in age and passage matched patient fibroblasts and controls as well as transfected cell lines. Mutant cells showed decreased proliferation, increased cell senescence, but no increased apoptosis compared to controls. To unravel the role of Lemd2 in vivo a KO was created. Homozygous KO mice were not viable and died between embryonic day 9.5 and 10.5. Histology of E10.5 embryos showed ventricular wall thinning and abnormalities of the outflow tract. Furthermore, EM of hearts revealed extensive changes of myocyte nuclei, including bizarre shapes with clumping of peripheral heterochromatin as similar seen in cardiac tissue from patients. Abnormal heterochromatin formation may suggest inactivation of chromatin and DNA damage. Therefore, we looked at phosphorylated H2AX, a molecular marker for DNA-damage and premature aging and found in KO animals remarkedly reduced expressed gH2AX as well as repair foci compared with wildtype animals ($p < 0.00001$). Even heterozygous embryos showed a significant reduction of gH2AX levels.
Conclusion: Mutant LEMD2 leads to remarkable changes in nuclei with abnormal heterochromatin formation in mice and man. Disturbed H2AX phosphorylation, cellular senescence and reduced proliferation capacity may suggest an involvement of LEMD2 in chromatin remodeling processes and premature aging.

P2319

Endothelial mineralocorticoid receptors control macrophage properties in cardiac remodeling

A Achim Lother[1]; L Deng[1]; I Hilgendorf[2]; T Kehl[1]; T Schnick[1]; M Moser[2]; C Bode[2]; L Hein[2]
[1]Albert-Ludwig University of Freiburg, Institute of Experimental, Clinical Pharmacology & Toxicology, Freiburg, Germany; *[2]University of Freiburg, Heart Center, Department of Cardiology and Angiology I, Freiburg, Germany*

Funding Acknowledgements: Else-Kröner-Fresenius-Stiftung, ESAC Germany, Dresdener Herz-Kreislauf-Tage

Introduction:
Inflammation is recognized as a key driver for the development of cardiac remodeling and dysfunction. Chronic pressure overload increases the number of CD45+ leukocytes in the heart. Leukocyte migration and activity is closely regulated by endothelial cells. Mineralocorticoid receptor antagonists, an established therapy of chronic heart failure, have anti-inflammatory properties. The aim of this study was to investigate the impact of endothelial mineralocorticoid receptors on cardiac inflammation and remodeling.
Methods and Results: In order to assess to role of endothelial mineralocorticoid receptors on cardiac inflammation and remodeling we generated mice with endothelial cell-specific deletion of the mineralocorticoid receptor (MRCdh5Cre) using the Cre/loxP system. MRCdh5Cre and Cre-negative littermates (MRwildtype) underwent transverse aortic constriction (TAC, $n = 5$-7 per group). After pressure overload, the number of CD45+ CD11b+ leukocytes was similarly increased in the hearts of both genotypes (MRCdh5Cre 3840 ± 443 vs. MRwildtype 4051 ± 385 /mg tissue, n.s.). However, subtype analysis revealed a higher proportion of inflammatory Ly6Chigh F4/80low monocytes in the heart of MRwildtype after TAC (TAC 20 ± 6 vs. sham 4 ± 1 %, $P < 0.05$) but not of MRCdh5Cre mice (TAC 6 ± 2 vs. sham 3 ± 1 %, n.s.).
CD45+ CD11b+ F4/80high Ly6Clow macrophages from pressure overloaded vs. sham treated hearts were isolated by fluorescence-assisted cell sorting and showed marked differences in gene expression as determined by RNAseq. Expression of 185 genes was differentially regulated ($q < 0.05$) in macrophages from MRwildtype hearts after pressure overload but restored by MR deletion from endothelial cells.
Cardiac hypertrophy (ventricle weight 143.2 ± 5.2 vs. MRwildtype 167.3 ± 6.7 mg, $P < 0.001$) and interstitial fibrosis (sirius red stained area 8.2 ± 4.7 vs. MRwildtype 13.5 ± 4.5 %, $P < 0.05$) after pressure overload were attenuated in MRCdh5Cre mice. mRNA expression levels of atrial natriuretic peptide (Nppa), the pro-fibrotic molecule galectin 3 (Lgals3) and the monocyte marker C-C chemokine receptor type 2 (Ccr2) were determined by qRT-PCR and confirmed these findings. The attenuated cardiac inflammation and remodeling after TAC in MRCdh5Cre mice was paralleled by preserved diastolic function (mitral valve E acceleration time, TAC 11.2 ± 0.6 vs. sham 12.2 ± 0.9 ms, n.s.) vs. MRwildtype mice (TAC 15.7 ± 0.5 vs. sham 12.8 ± 0.4 ms, $P < 0.05$).
Conclusion: MR deletion from endothelial cells alters cardiac leukocyte subtype composition and macrophage gene expression after pressure overload. This is paralleled by improved left ventricular diastolic function and remodeling. Our findings suggest that MR modulates endothelial-macrophage interaction.

P2320

Novel insights into regulation of proarrhythmic persistent Na current by Ca2+/Calmodulin-dependent protein kinase II

P Tirilomis[1]; S Ahmad[2]; N Dybkova[1]; S Pabel[1]; P Bengel[1]; T Fischer[1]; L Maier[2]; G Hasenfuss[1]; S Sossalla[2]
[1]University Medical Center Gottingen (UMG), Department of Cardiology and Pneumology, Gottingen, Germany; *[2]University Hospital Regensburg, 2nd Department of Medicine, Regensburg, Germany*

In human heart failure (HF) and cardiac hypertrophy (Hy), persistent Na current (INaL) is enhanced leading to arrhythmias via action potential duration (APD) prolongation and increased diastolic sarcoplasmic reticulum (SR)-Ca leak. Cardiac Hy is mostly caused by chronic pressure overload and may lead to HF. In HF, Ca/Calmodulin-dependent protein kinase IId (CaMKIId) and INaL are increased in parallel. CaMKIId has been reported to enhance INaL thereby contributing substantially to arrhythmias through early- and delayed-afterdepolarizations (EADs and DADs). Increased INaL may also activate CaMKIId promoting INaL leading to a vicious cycle.
We investigated whether the neuronal Na channel isoform NaV1.8 contributes to the regulation of INaL and SR-Ca leak in a CaMKIId transgenic mouse model (CaMKIId TG), in human Hy and in HF cardiomyocytes.
We have shown that CaMKIId, which is known to regulate cardiac isoform NaV1.5, also associates with the NaV1.8 isoform. In co-immunoprecipitation experiments, we detected an increased co-expression of NaV1.8 and CaMKIId while interaction of NaV1.5 and CaMKIId was decreased in HF. To measure the contribution of NaV1.8 to INaL generation and APD, we performed whole-cell patch clamp experiments in isolated murine and human ventricular cardiomyocytes (HF & Hy). We observed a significant reduction in INaL after addition of the novel specific NaV1.8 blocker PF-01247324 (orally bioavailable; 1 μmol/L) or a CaMKIId inhibitor, autocamtide inhibitory peptide (AIP, 1 μmol/L) in human ventricular HF cardiomyocytes. Additionally, we recorded that APD was significantly abbreviated after inhibition of NaV1.8 in hypertrophied human cardiomyocytes. Inhibition of NaV1.8 lead to a decrease of 40% in SR-Ca spark frequency (CaSpF) in hypertrophied and failing human cardiomyocytes measured by confocal microscopy (Fluo-4 AM). Increased Ca-leak can be induced by INaL via Na-dependent Ca overload which may result in DADs. To further elucidate the role of CaMKIId in NaV1.8 regulation we measured INaL and CaSpF in the presence of the novel NaV1.8 blocker in CaMKIId TG mouse myocytes. The already enhanced INaL and CaSpF were significantly decreased after exposure to NaV1.8 blocker.
Furthermore, we also generated a new mouse model by crossbreeding CaMKIId TG and NaV1.8 KO (SCN10A-/-) mice hypothesizing a rescue of the arrhythmogenic phenotype. In this new mouse model (CaMKIId TG/SCN10A-/-) measurements show a 53% reduction in INaL. A survival curve is currently under investigation to test the hypothesis whether CaMKIId TG/ SCN10A-/- mice are protected against arrhythmias compared to CaMKIId TG.
Our results demonstrate the significance of both CaMKIId and NaV1.8 in INaL generation and suggest that increased CaMKIId activity plays a substantial role in the activation of NaV1.8. Therefore, NaV1.8 seems to be a promising therapeutic antiarrhythmic target and its regulation merits further investigation.

P2321

Differential sodium channel regulation as a novel proarrhythmic mechanism in the human failing heart

P Philipp Richard Felix Bengel[1]; N Dybkova[1]; S Ahmad[1]; S Pabel[1]; P Tirilomis[1]; N Hartmann[1]; LS Maier[2]; K Streckfuss-Boemeke[1]; G Hasenfuss[1]; S Sossalla[2]
[1]University Medical Center Gottingen (UMG), Department for Cardiology and Pneumology, Gottingen, Germany; *[2]University Hospital Regensburg, Clinic and Polyclinic for internal medicine II, Regensburg, Germany*

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Heart failure (HF) is known to be associated with pathological electrical remodeling involving prolongation of the action potential (AP) and occurrence of early- (EADs) and delayed afterdepolarizations (DADs). An important role in these proarrhythmogenic changes is attributed to a pathological enhancement of the late sodium current (INaL). However, the underlying mechanisms are not entirely understood. It is suspected that other sodium channel isoforms than the cardiac isoform NaV1.5 could contribute to INaL. Therefore, we investigated the role of sodium channel isoform NaV1.8 in the human failing heart.
Using Co-immunocytochemistry, we could detect expression of NaV1.8 in t-tubules and at intercalated discs. Western Blots interestingly revealed NaV1.8 to be significantly upregulated in tissue homogenates from patients with end-stage HF compared to non-failing (NF), while expression of the NaV1.5 was decreased. We further measured INaL and action potential duration (ADP) in isolated cardiomyocytes from failing hearts in absence or presence of the selective NaV1.8-blockers either A-803467 (30nmol/L) or PF-01247324 (1 μmol/L). Both reduced INaL and APD significantly. Additionally, we measured proarrhythmic Ca2+-spark-frequency (CaSpF) using confocal microscopy (Fluo4-AM). Both, A-803467 and PF-01247324 reduced CaSpF significantly (˜58%). Moreover, the occurrence of DADs and spontaneous action potentials (sp. APs) as a parameter for cellular proarrhythmic events in the presence of low dose isoproterenol (ISO, 30 nmol/L) were potently suppressed by addition of PF-01247324.
To confirm our inhibitor-derived findings, we measured INaL, APD and CaSpF in isolated cardiomyocytes from NaV1.8-knock-out (SCN10A-/-) and wild-type (WT) mice. Application of ISO significantly increased INaL and CaSpF in both SCN10A-/- and WT myocytes, but significantly less in SCN10A-/- compared to WT. Pre-treatment with A-803467 and PF-01247324 also resulted in a small, but significant reduction of INaL and CaSpF in ISO treated myocytes. Since NaV1.8-channels are resistant to low concentrations of tetrodotoxin (TTX), we measured INaL in presence of 2 μmol/L TTX to inhibit NaV1.5-mediated INaL. ISO-induced INaL in SCN10A-/- and WT myocytes was clearly reduced by TTX, but significantly more in SCN10A-/-.
Additionally, APD was significantly shorter in ISO-treated cardiomyocytes from SCN10A-/–mice compared to WT. Also, frequency of DADs and sp.APs were lower in SCN10A-/- cardiomyocytes.
In summary, our results provide first evidence of an upregulation of NaV1.8 in human heart failure, that contributes to arrhythmogenesis by enhancing INaL. Major issues of electrical remodeling in HF like AP-prolongation, occurrence of EADs and DADs and increased CaSpF as triggers for cellular proarrhythmogenic events could be ameliorated by inhibiting NaV1.8. Therefore, inhibiton of NaV1.8 constitutes a novel specific antiarrhythmic approach in HF that needs further investigation.

P2322

C5L2 receptor, a new player in a genetic model of cardiomyopathy

M Mavroidis[1]; I Sfyroera[1]; A Varela[1]; I Kostavasili[1]; I Karakitsios[1]; C Davos[1]; Y Capetanaki[1]; C Anagnostopoulos[1]
[1]Biomedical Research Foundation Academy of Athens, Greece, Athens, Greece

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Introduction: Inflammatory activation and metabolic impairment are becoming the focus of research as novel therapeutic targets in heart failure. We recently demonstrated in a genetic model of arrhythmogenic cardiomyopathy (desmin-deficient mice, Des-/-) that modulation of innate immunity through elimination of complement C5a receptor (C5aR) resulted in impressive improvement of cardiac function.
Aim: To analyze the role of the second C5a receptor (C5L2) that has been linked to energy metabolism and inflammation as a novel therapeutic target in desmin deficient cardiomyopathy.
Materials/Methods: We generated C5L2-/-Des+/- mice by crossing C5L2-/- with Des-/- mice. Histology, electron microscopy, echocardiography, RNAseq and 18F-FDG microPET/CT were performed in 12 months old animals (n = 10) and parameters related to cardiac structure, function and myocardial glucose consumption were compared with those of wild type (WT) controls of similar age.
Results: C5L2-/-Des+/- mice developed severe cardiac dysfunction compared to WT controls (Fractional shortening 22.89 ± 2.52 vs. 46.94 ± 0.67, $p < 0.0001$). Histology revealed increased fibrosis in C5L2-/-Des+/- compared to WT (Fibrosis index, 1.5 ± 0.21, vs. 0.4 ± 0.34, $p < 0.01$). Electron microscopy showed severe mitochondrial and T-tubules abnormalities in C5L2-/-Des+/- compared to WT. Additionally, cardiac tissue RNAseq analysis demonstrated altered expression of several genes involved in metabolic pathways, indicating a "metabolic switch" in C5L2-/-Des+/- from fatty acid to glucose oxidation compared to WT. This was also confirmed by the higher myocardial metabolic rate of glucose values in C5L2-/-Des+/- compared to WT animals (168.6 ± 55.2 vs. 39.8 ± 3.3μmol/min/100g, $p < 0.05$).
Conclusions: Our results highlight the detrimental consequences on cardiac structure and function of C5L2 receptor elimination in arrhythmogenic cardiomyopathy and support the hypothesis of its implication in the metabolic impairment, which occurs in this pathological entity.

P2323

Pretreatment with propargylglycine and L-cysteine improves diastolic heart function and decreases arterial stiffness in aging

N A Natali Dorofeyeva[1]; KO Drachuk[1]; VF Sagach[1]
[1]Bogomoletz Institute of Physiology, Kiev, Ukraine

Background and aims: Aging is accompanied by diastolic dysfunction and increased arterial stiffness. Hydrogen sulfide (H2S) is a gas transmitter that has an important role in the regulation of cardiovascular function. We have recently

shown that exogenous H2S (NaHS) improves diastolic heart function in hypertension and aging. The aim of work is to investigate the effect of combination DL-propargylglycine (PAG) and L-cysteine on heart function in old rats.
Materials and Methods: The study was conducted on adult (6 months old) and old (24 months old) male Wistar rats. The functional cardiohemodynamic indicators registered via microcatheter and Pressure-Volume System. The DL-propargylglycine (11,31 mg/kg) and L-cysteine (121 mg/kg) were administered intraperitoneally with 30 min intervals between injections.
Results: We demonstrate that combination PAG+ L-cysteine c improves diastolic heart function in old rats. We found, that End-diastolic pressure decreases by 22,6% ($P < 0,05$), the end-diastolic myocardial stiffness decreases by 27,7% ($P < 0,05$) in old rats. The arterial stiffness decreased by 25,4%, that indicates an improvement the ventriculoarterial coupling. Also, we found that the parameters of pumping function increase after injections. Stroke volume increases by 12,3% ($p < 0,05$), cardiac output increases by 12 % ($p < 0,05$). We demonstrate that pretreatment with PAG and L-cysteine increases H2S levels and decreases the markers of oxidative and nitrosative stress that accompanied by increases coupling ?NOS.
Conclusion: Pretreatment with PAG and L-cysteine improved diastolic heart function and decreased arterial stiffness that may be the result of alternative ways of increasing the synthesis of hydrogen sulfide and recovery coupling of cNOS in old rats.

P2324

Times are changing: differential regulation of clock genes in mice and zebrafish with heart failure.

S Crnko[1]; DA Feyen[1]; L Peters[1]; AI Lumley[2]; JP Sluijter[1]; Y Devaux[2]; LW Van Laake[1]; I Ernens[2]
[1]University Medical Center Utrecht, Division Heart and Lungs, Utrecht, Netherlands; *[2]Luxembourg Institute of Health, Cardiovascular Research Unit, Luxembourg, Luxembourg*

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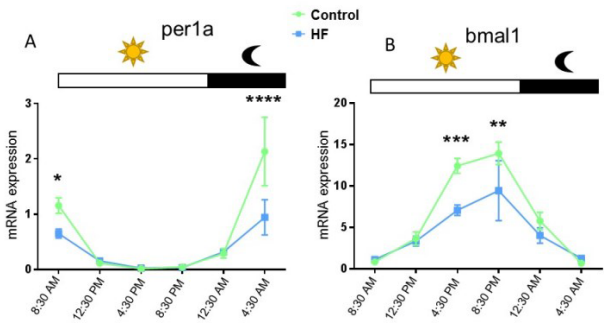
Funding Acknowledgements: NHS (Dekker 2013T056) and The Society for Research on Cardiovascular Diseases and the Ministry of Culture, Higher Education and Research Luxembourg

Background: Circadian rhythms are biological oscillations regulated by molecular clocks. Whether they are affected by heart failure (HF) remains poorly characterized. Also, the pathophysiological mechanisms remain unidentified.
Purpose: We aimed to assess whether zebrafish and mouse hearts display circadian gene expression patterns, so that they can serve as models for mechanistic studies into the circadian clock in HF. We hypothesized that circadian gene expression may be altered in the failing heart, and that nocturnal (mice) and diurnal (zebrafish) animals have different expression patterns.
Methods: Zebrafish and mice were housed on 14/10 and 12/12 light/dark schedules, respectively. HF was induced in adult zebrafish by phenylhydrazine hydrochloride (n = 108). After 5 weeks of treatment, 9 hearts from control and HF groups were isolated every 4 hours in a 24-hour period and pooled by 3. In mice, myocardial infarction followed by HF was induced by permanent ligation of the left anterior descending coronary artery or sham operation (n = 56). After 4 weeks, 4 hearts per group were isolated every 3.5 hours in a 24-hour period. Expression of core clock genes was analysed using qPCR and oscillations confirmed with cosinar analysis in R statistics. Differences between groups were assessed with 2-way analysis of variance (ANOVA) with Sidak post hoc test or with Mann-Whitney U test, as appropriate.



Clock gene expression in zebrafish heart

Results: Gene expression of core clock genes, namely per1a/2/3, bmal1, clock and cry1ba for zebrafish, and Per1 and Bmal1 for mice, showed clear circadian rhythmicity in both control and HF groups. In zebrafish, per1a of the control group raised during the rest phase (lights off) and reached a maximum at 04:30 AM before the start of the animal's active phase (lights on) (Figure A). Expression of per3 reached a maximum when the light comes on (08:30 AM), followed by per2 peak a couple of hours later (12:30 PM). However, in HF, per1a (Figure A) and per3 were significantly lower expressed during these peak phases ($p < 0.00001$) while per2 was significantly higher expressed in the control group ($p < 0.01$). Clock, bmal1 (Figure B) and cry1ba reached their maximum just before the onset of the dark phase (08:30 PM) for the control group, whereas in HF their expression was significantly down-regulated. Clock, bmal1 and cry1ba mRNA levels were in counter phase with members of Per gene family. Similarly, in mice, Per1 peak times were shifted (01:30 PM for HF and 05:00 PM for sham) and peak time of Cry2 (08:30 PM) was higher in sham animals compared to HF animals at the same time point ($p = 0.016$).
Conclusions: Failing hearts of zebrafish and mice display circadian expression patterns of clock genes. While peak and trough times of the clock genes are largely unchanged, the amplitude of the oscillations differ between healthy and failing hearts. We conclude that both zebrafish and mice represent appropriate models for future mechanistic studies into the circadian clock in HF.

P2325

Acute administration of high levels of spermidine and spermine impair ryanodine receptor type 2-dependent contractility in human atrial tissue

E Ewald Kolesnik[1]; S Kapeller[2]; M Wallner[3]; PP Rainer[1]; M Abdellatif[1]; H Maechler[4]; S Sedej[1]; D Von Lewinski[1]
[1]Medical University of Graz, Cardiology, Graz, Austria; *[2]Medical University of Graz, Graz, Austria*; *[3]Temple University School of Medicine, Philadelphia, United States of America*; *[4]Medical University of Graz, Cardiac surgery, Graz, Austria*

Funding Acknowledgements: No funding

Background: The polyamines spermidine, spermine and putrescine affect membrane excitability and cell contractility in experimental animal models. Binding of polyamines to several types of membrane ion channels alters ion homeostasis and may cause arrhythmias. Yet, the effect of polyamines on force development and arrhythmias in intact human cardiac tissue remain unknown.
Purpose: To assess acute functional effects and underlying mechanisms of the polyamines spermidine, spermine, and putrescine on human atrial tissue.
Methods: We used isolated muscle strips (trabeculae) of human atrial tissue from 35 patients undergoing cardiac surgery (coronary artery bypass graft and/or aortic valve replacement). Trabeculae were electrically stimulated at 1 Hz and perfused with modified Tyrode's solution supplemented with increasing concentrations of spermidine, spermine, or putrescine (100 nM, 1 mM, 10 mM, 100 mM and 1 mM; 20 min each concentration at 37°C). Developed force of trabeculae was measured using a force transducer. Untreated muscle strips served as controls. To elucidate underlying mechanisms of spermidine-induced changes in the force development (1 mM), trabeculae were pre-incubated with ryanodine (1 μM) and phosphoinositol 3-kinase (PI3K) inhibitors LY 294002 (5 μM) and A-66 (1 μM). Mixed ANOVA was used to test for differences within groups (time/concentration) and between groups (treatment). Data are shown as mean ± SEM. Values of $P < 0.05$ were considered statistically significant.
Results: Low concentrations (100 nM - 100 μM) of spermidine (n= 14 trabeculae), spermine (n= 10 trabeculae), and putrescine (n= 7 trabeculae) did not reduce force development (control n= 9 trabeculae). However, supraphysiological level of spermidine or spermine (1 mM) exerted significant negative inotropic effects (A). In addition, high concentrations (1 mM) of spermidine and spermine evoked arrhythmic events (spermidine: 25% of trabeculae, spermine: 50% of trabeculae, control: 0% of trabeculae) that were accompanied by impaired force development (B). Two spermidine-treated trabeculae developed sustained arrhythmias. In contrast, putrescine-treated trabeculae did not show any arrhythmic events and force development was comparable to control. The negative inotropic effect of spermidine was significantly blunted by ryanodine (n = 7 trabeculae) but not by the PI3K inhibitors LY 294002 (n = 10 trabeculae) and A-66 (n = 9 trabeculae; C).
Conclusions: Pharmacological inhibition of cardiac ryanodine receptor attenuated spermidine-induced negative inotropic effect and may be due to decreased myocardial calcium transients. Our results suggest that ryanodine receptor - dependent mechanisms are responsible for the acute negative inotropic effects of high-dose polyamines in human cardiac tissue.

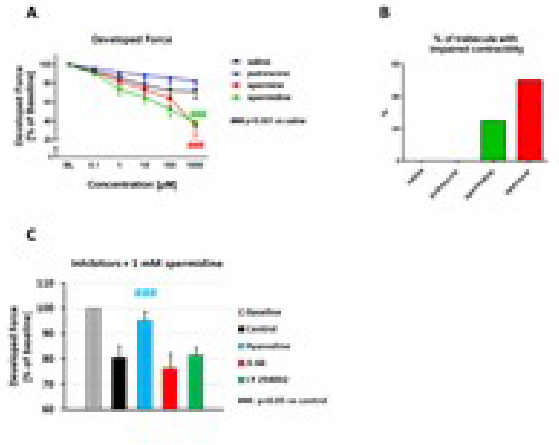


Figure A, B and C

P2326

Protective effects of exercise training against left ventricular dysfunction and remodeling in experimental pulmonary arterial hypertension

C Cristine Schmidt[1]; JA Bovolini[1]; N Goncalves[2]; F Vasques-Novoa[2]; M Santos[2]; A Leite-Moreira[2]; T Henriques-Coelho[2]; JA Duarte[1]; D Moreira-Goncalves[1]
[1]Faculty of Sport University of Porto , CIAFEL, Porto, Portugal; *[2]Faculty of Medicine University of Porto, Surgery and Physiology Department, Porto, Portugal*

Funding Acknowledgements: FCT, European Union, QREN, FEDER and COMPETE (UID/DTP/00617/2013 and UID/IC/00051/2013). C.S recived individual grant (PES/BEX 0554/14-6)

Introduction: Pulmonary arterial hypertension (PAH) directly affects the right ventricle but left ventricle dysfunction (LVD) can also be present, which is associated with left ventricle (LV) atrophy and/or neurohumoral activation.

Purpose: Analyse the hypothetical cardioprotective effects of exercise preconditioning on LV in a rat model of PAH induced by monocrotaline (MCT).

Methods: Male Wistar rats were randomly separated in sedentary (SED; 4 weeks sedentary) and trained groups (EX; running sessions of 60 mim/day, 5 days/week, at 25 m/min, during 4 weeks). After 4 weeks, animals were injected with MCT (60mg/kg; SED+MCT, n = 15 and EX+MCT, n = 15) or the same volume of vehicle (SED+V, n = 10). Afterwards, all animals remained sedentary for additional 4 weeks. Next, animals were submitted to LV hemodynamic evaluation in baseline and isovolumic conditions, and LV samples were prepared for light microscopy analysis (cardiomyocyte cross sectional area and collagen deposition) and endothelin (ET-1) mRNA analysis.

Results: in baseline conditions, systolic (peak systolic pressure, dP/dtmax, cardiac output and stroke volume) and diastolic function (dP/dtmin, Tau and end-diastolic volume) were compromised in SED+MCT but not in EX+MCT ($P < 0.05$ vs. SED+MCT). Under isovolumic conditions, SED+MCT showed additional deterioration in diastolic function (dP/dtmin and end-diastolic pressure) and prevented in EX+MCT ($P < 0.05$ vs. SED-MCT). This improved hemodynamic profile was paralleled with prevention of cardiomyocytes atrophy and fibrosis, and with normalization of ET-1 mRNA levels ($P < 0.05$ vs. SED.MCT). Exercise preconditioning also enhanced exercise tolerance and positively impacted survival. Of note, these improvements were observed 4 weeks after the cessation of exercise training, highlighting that the protective phenotype promoted by exercise training is maintained for several days.

Conclusion: Our findings suggest that exercise preconditioning can prevent LV dysfunction secondary to MCT-induced PAH, a protective effect that was observed several weeks after the end of the last training session. Mechanisms underlying exercise-induced protection can be related to the prevention of LV atrophy, fibrosis and neurohumoral activation.

Poster Session 4 - Clinical Cases

Chronic Heart Failure - Pathophysiology and Mechanisms

P2327
Severe myocardial dysfunction: a rare side effect of bevacizumab and 5 fluorouracil

PM Paula Maria Mendoza Cuartero[1]; A Elorriaga Madariaga[1]; M Codina Prat[1]; A Arregui Lopez[1]; A Andres Morist[1]; C Asla Ormaza[1]; I Bravo Martinez[1]; G Aurrekoetxea Bajeneta[1]; L Ruiz Gomez[1]; R Saez Moreno[1]
[1]Hospital de Basurto, Bilbao, Spain

We present the case of a 60 year old male, active smoker with known arterial hypertension (HTN) without medical treatment. He was diagnosed of an irresecable rectosigmoid advance staged adenocarcinoma in May 2017 and underwent 6 cycles of FOLFOX (oxaliplatin + 5-fluorouracil bolus + 5FU by continous infusion) + Bevacizumab (BVZ). Due to inadequate blood pressure controls, antihypertensive treatment with manidipine was started. Following chemotherapy, he underwent external radiation therapy and surgical resection in september 2017. Adjuvant therapy with FOLFOX-BVZ in the 6th week after the procedure was planned.
October 2017, he is derived to the emergency room because of severe diarrhoea. Blood tests showed slightly elevated troponine T levels (seriated 19-20 ng/L; normal < 14) and hemoglobin 9,3g/dL as the only abnormal findings. On the 12 lead EKG negative, symmetric T waves in precordial leads with a long corrected QT Interval were registered. Cardiological evaluation was asked for. The patient was sweaty, slightly hypotensive (100/60 mmHg) and tachyicardic with no congestive signs. Echocardiography revealed a dilated left ventricle (LV) with severe impairment of left ventricular ejection fraction (LVEF) due to diffuse hypokinesia, moderate mitral regurgitation and minimal pericardial effusion.
The patient was admitted to the cardiology station and monitored. Medical treatment of heart failure with reduced ejection fraction according to current guidelines was started. A coronariography excluded arterial coronary disease. The cardiac MRI showed a mild to severe dilated LV with a moderate to severe impaired LVEF (29%). Right ventricle was normal. No early nor late enhancements were observed. The potential cardiovascular (CV) side effects of 5FU and BVZ were assumed to be responsible for the LV dysfunction. After hospital discharge he is being followed up by the cardiooncologist. The echocardiogram performed two months later showed a non dilated LV with partial recovery of the LVEF (42%). The adjuvant therapy is on stand by waiting for the cardiovascular evolution.
LV dysfunction is not known to be a frequent side effect of BVZ nor 5FU. 5FU‘s most common CV side effects are angina, arrhytmias or EKG changes. In rare cases heart faliure (HF) has been reported. BVZ has been associated with many CV events mainly high grade HTN, arterial and venous thromboembolic events. In contrast, LV dysfunction and HF have rarely been reported. Rather than direct cardiotoxicity, the main mechanism responsible for BVZ-associated HF is suggested to be uncontrolled HTN, which could have been the mechanism responsible for LV dysfunction in our patient. This case highlights the importance of an adequate screening and baseline assesment of patients prior to initiating chemotherapy and an adequate control of CV risk factors. Periodic controls with EKG, cardiac biomarkers and echocardiogram are necessary in order to detect CV complications.

P2328
First case of successful treatment with an interatrial shunt device after market authorisation

FX Kleber[1]; PJ Koeln[1]
[1]Charité - Universitätsmedizin Berlin, Berlin, Germany

Aim: Heart Failure with preserved ejection fraction (HFpEF) has been a therapeutic dilemma for many years. Recently reports emphasise the importance of a sharp rise in left ventricular filling pressures under exercise. A device has been developed to induce a right to left shunt at the atrial level and favourable results on its efficacy in improving hemodynamics and exercise capacity as well as reducing hospital readmissions have been reported in two small clinical trials. One device has gained CE mark. We report the first patient who has been treated using this interatrial shunt device after market authorisation.
Methods and Results: This 74 years old female patient has had aortic valve replacement for severe aortic stenosis 5 years ago but has not had any relieve of symptoms thereafter. Her NYHA class was III. Systolic left ventricular function was normal. She presented with severe diastolic dysfunction: Her echocardiographic E/e' was 24, her mean resting pulmonary capillary wedge pressure (PCWP) was 20 mmHg and her right atrial (RA) pressure was 6 mmHg under optimal medical treatment with Valsartan, Torasemid and Digitoxin for rate control of atrial fibrillation. Her heart rate was optimally controlled and a further increase of diuretics seemed to be impossible. She had only mild pulmonary hypertension at rest with a mean pulmonary artery pressure of 23 mmHg. Her 6 min walk test distance was 240 m.
An interatrial shunt device was inserted in July 2017. After six months her symptomatology was greatly improved. She was able to go shopping again and to climb up one floor of stairs. Her 6 min walk test distance was 360 m. The shunt was open and the calculated orifice area using the PISA formula from an echocardiographic subxiphoid view did not reveal any narrowing of the 8 mm diameter shunt within the device.
Conclusion: This patients shows exemplarily which patients might benefit most from such a therapy: Patients with severe HFpEF and high gradient between PCWP and RA pressure, whose filling pressure cannot be further reduced by medical therapy without decreasing forward right ventricular output.

P2329
Effect of ivabradine on heart rate reduction, change of QRS width and change of LV EF and NT-proBNP in patients with non-ischemic cardiomyopathy and LBBB pattern at baseline

F Malek[1]; L Dujka[1]; A Kucerova[1]; V Lekesova[1]; P Volf[1]; K Koscova[1]; P Neuzil[1]
[1]Na Homolce Hospital, Department of Cardiology, Prague, Czech Republic

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Background: the SHIFT study showed that LBBB increased risk in the patients with chronic heart rate and heart rates = 70 bpm in sinus rhythm. Ivabradine was safe in LBBB and its effect was similar to that in patients without LBBB. We report four clinical cases of patients with non-ischemic cardiomyopathy, sinus rhythm and LBBB at baseline when adding ivabradine to optimal medical therapy was associated with heart rate reduction, narrowing of QRS complex duration and loss of LBBB pattern on ECG.
Patients: Four patients, one male and three females, with age range 28-76 years, were followed at a tertiary care heart failure clinic after diagnosis of heart failure with reduced EF caused by non-ischemic cardiomyopathy, three with idiopatic CMP and one patient post myocarditis. Patients were on optimal medical therapy including BB, ACEI/ARB and MRA.
Ivabradin was started in all subjects at dose from 5 mg to 7.5 mg twice daily when heart reates remained > 75 bpm despite maximal tolerated betablocker dose.
Observation: After mean 866 days (538-1211) days of follow-up, heart rate reduction after ivabradine was associated with clinical improvement, increase of LV EF and decrease of LV enddiastolic diameter (EDD) and reduction of NT-proBNP level. We observed reduction of QRS duration with loss of LBBB pattern on ECG too. The change of parameters after ivabradine is shown in the table.
Conclusion: Heart rated redution after ivabradine was associated with decrease of duration and change of morphology of QRS complex in patients with CHF and non-ischemic cardiomyopathy. This phenomenon might be explained by effect of ivabradine on reverse remodelling of left ventricle with improvement of intraventricular conduction.

Change of parameters after ivabradine

Case number Gender, age	Follow-up days	HR bpm	QRS width ms	LV EF %	LV EDD mm	NT-proBNP pmol/l
M 76 y	924	-28	-30	+ 20	-11	-203
F 45 y	1211	-17	-48	+18	-12	-415
F 28 y	791	-14	-54	+19	-6	-92
F 44 y	538	-17	-36	+12	-8	-65

M-male, F - female, y - years, HR - heart rate, bpm - beats per minute, LV EF, left ventricle ejection fraction, EDD - enddiastolic diameter, NT-proBNP - N-terminal B-natriuretic peptide

P2330

The Marfan syndrome case as a successful treatment of severe heart failure.

YULIYA Yuliya Martyanova[1]; DA Kondratev[1]; AV Kadykova[1]; DG Tarasov[1]; YV Frolova[1]; SL Dzemeshcevich[1]
[1]*Federal Center of Cardiovascular Surgery, Astrakhan, Russian Federation*

Patient - 29 - year man.
Symptoms: dyspnea, weakness, palpitation.
Dissecting aneurysm of ascending aorta diagnosed on TTE, CT scan.
He had high growth (1.90 m), the total length of his hands was 1.10 m.
Hypermobility and deformation of joints, chest deformation. Rude diastolic aortic murmur. BP - 110/30 mmHg.
Life history: Marfan Syndrome confirmed by genetic and dilatation of ascending aorta (44 mm) identified when the patient was 16 years old.
Also he had kidney malformation (dystopia of right kidney, dysfunctional left kidney).
In 2013 he was hospitalized with respiratory insufficiency because of Bullous lung disease. He was operated - right lobectomy. Dyspnea and weakness appeared in 2014. TTE (2014): aneurysm of ascending aorta 55 mm and AR 2. He had family history of aortic dissection (his mother was successfully operated on aorta at age of 50). He had a normal pressure, his brother was healthy.
TTE in this hospitalization (2015): aortic diameters: aortic annulus 40 mm, valsalva sinuses 100 mm, tubular ascending aorta 63 mm, aortic arch 46 mm. Dissecting aneurysm of ascending aorta from aortic valve to brachiocephalic trunk. Mean aortic gradient 17 mm Hg, total aortic regurgitation, non-calcified tricuspid aortic valve. Left ventricle volume (LVV) 176/99 ml, EF 52%.
CT scan (2015): ascending aorta (aortic annulus - 40 mm, valsalva sinuses - 94 mm, sino-tubular junction - 94 mm, tubular ascending aorta - 75 mm), aortic arch (proximal diameter - 27 mm, isthmus - 20 mm), thoracic descending aorta (maximum diameter - 19 mm), abdominal aorta (infra-renal segment - 18 mm). Detachment intimal flap - a projection ascending aorta, aortic arch and brachiocephalic trunk had not dissection.
Serum creatinine – 118 mmol/l. PRO BNP - 12000. Multidisciplinary decision and the
patient was operated - Total aortic root replacement with reimplantation of coronary arteries and prosthetic valve replacement '??? ??? 29'(Bental operation). Post Operative Outcome - uneventful postoperative course, no neurological symptoms, no simptoms of heart failure, no severe renal and respiratory failure and good surgical correction. PRO BNP - 425. Two years later: good quality of life, LVV - 115/40 ml, mean prosthetic valve gradient - 12 mm Hg, INR - 2,5.
Results: only surgery in such case of aorta pathology is effective method of treatment severe heart failure.

P2331

An unexpected cause of acute kidney injury in a patient with ischemic cardiomyopathy treated with sacubitril/valsartan

R Abete[1]; S Mazzetti[1]; J Rossi[1]; P Delfino[1]; M Chioffi[1]; A Andrea Mortara[1]
[1]*Dipartment of Cardiology Policlinico di Monza, Monza, Italy*

We report a clinical case of a 70-year-old man evaluated in May 2017 for chronic heart failure (NYHA class III) and LV ejection fraction of 20%. In 2001, the patient underwent coronary artery bypass grafting and implantation of a bicameral ICD for primary prevention. Co-morbidities included type 2 diabetes, peripheral vascular disease, chronic kidney disease G3 and systemic arterial hypertension treated with multiple antihypertensive drugs. In 2015, a CT angiography of the renal arteries showed no critical stenosis. In last May, sacubitril/valsartan (ARNI) was started at dosage of 49/51 mg BID, and titrated to 97/103 mg BID after one month of therapy. In July, an increase in serum creatinine from 1.9 to 3.7 mg/dL was documented. Diuretics were reduced and appropriate volume of liquids restored. In August, creatinine was still 3.5 mg/dL, therefore ARNI was replaced with captopril 75 mg/die (previous therapy). A week later, the patient reported oliguria associated with acute onset of dyspnea at rest and weight gain and was admitted to our ICU. Physical examination showed bilateral peripheral edema and pulmonary rales, with right pleural effusion on the chest X-ray. Blood pressure was 120/80 mmHg, body temperature 36°C and oxygen saturation 95% at room air. Serum creatinine was 4.4 mg/dL, NT-pro-BNP 34100 ng/L. ECG and echocardiogram were unchanged compared to previous exams, except for an increase in pulmonary artery pressure (80 mmHg) and IVC diameter (20 mm). Urine cultures and urinary tract echography were negative. High-dose intravenous furosemide (40mg/hr) failed to reduce the pulmonary congestion. Diuresis increased to >200/hour and clinical conditions improved after association of metolazone 10mg and canrenone 200mg to furosemide; nevertheless, creatinine remained high (3.7 mg/dL). Nephrologists were consulted and, despite the high risk of contrast-induced nephropathy, a renal angiogram was performed. It showed a marked progression of atherosclerosis with a thrombotic occlusion of the right renal artery and a 60% ostial stenosis of the left renal artery. The stenoses were not susceptible to angioplasty, because of thrombus anatomic features and a high risk of embolization. In the next days, renal function was stable with a satisfactory diuresis on oral furosemide 500mg/die. The patient was discharged on oral anticoagulant therapy with warfarin and a program of short-term evaluation of the clinical status and renal function. In conclusion, worsening of renal function may, in some patients, be interpreted as the consequence of the unfavorable effects of pharmacologic therapy, including, as in this case, a shift from ACE-I to ARNI. However, all possible causes of renal dysfunction must firstly be ruled out, including a rapid progression of renovascular disease. If, in this patient, anticoagulant treatment will improve renal perfusion, ARNI could be gradually restarted with a potentially important impact on the subsequent clinical course.

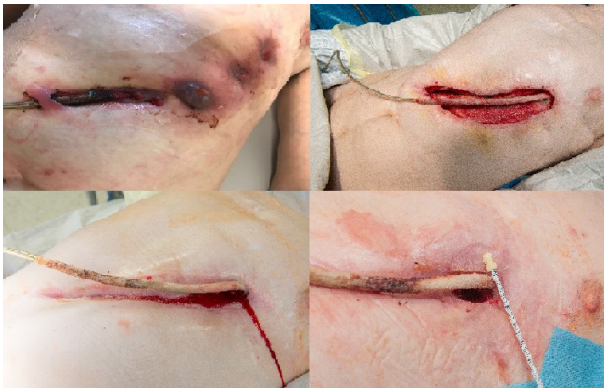
Chronic Heart Failure - Treatment

P2332

Successful wound management with vacuum-assisted-therapy

J Jamila Kremer[1]; M Farag[1]; R Arif[1]; B Schmack[1]; A Heininger[2]; A Ruhparwar[1]
[1]*University Hospital of Heidelberg, Cardiac Surgery, Heidelberg, Germany*;
[2]*University Hospital of Heidelberg, Department of Infectious Diseases, Medical Microbiology and Hospital Hygiene, Heidelberg, Germany*

Introduction:
Wound infections in patients on left assist device (LVAD) support are an imminent threat to survival and outcome after orthotopic heart transplantation (OHT). Hospitalization is prolonged and mortality rates are increased with wound infections prior to OHT. Here we present a rare case of hazardous wound infection on LVAD support with major skin lesions and vacuum-assisted-therapy.
Case Report:
A 47-year-old male patient suffering dilated cardiomyopathy after chronic myocarditis underwent LVAD implantation as bridge to transplantation in 2014 in an external hospital. Further diagnoses were severe mitral regurgitation, partial lung resection due to aspergilloma and combined restrictive and obstructive ventilation disorder. He initially developed deep wound healing disorder around the LVAD driveline in 2016. Colleagues in the referring transplantation centre treated the wound with vacuum-assisted therapy and intravenous antibiotics. However, the wound situation aggravated and the patient was removed from the transplantation waiting list due to multiresistant Pseudomonas aeruginosa infection in 2017. Upon admission at our centre the patient presented multiple wound blisters and open skin lesions along the driveline course. We did an extensive wound debridement and started another cycle of vacuum-assisted-therapy. The patient received dressing changes in the operating theatre every 48-76 hours until the wound site showed improvement.
During the last 6 months, after 47 surgical dressing changes, we observed immense amelioration under vacuum-assisted-therapy and could stop the vacuum-assisted treatment. Nonetheless, the wound is still infected by a multiresistant Pseudomonas aeruginosa, which will not be eradicated by intravenous antibiotic treatment. The patient was placed on high urgency transplantation waiting list due to LVAD-related wound infection.
Antibiotic treatment will be continued for at least 6 weeks after successful transplantation and regular blood cultures and wound swabs will monitor the actual infective status of the patient.
Summary:
With sufficient care and dedication, severe multiresistant Pseudomonas aeruginosa infection of biomaterial surfaces could be sustained by high frequent dressing changes. Wound infection in patients with a ventricular assist device, whether univentricular or biventricular, still represent the major criteria for emergent OHT. Wound care of driveline infections can be guaranteed with vacuum-assisted therapy.



Progression of the wound

P2333

Treating diuretic resistance in non-adherent 'Big Baby'

VKP Putri[1]; IW Anwar[2]; DA Sinaga[1]; A Arles[2]
[1]*Awal Bros Hospital Pekanbaru, Department of Cardiology, Pekanbaru, Indonesia*; [2]*Awal Bros Hospital Pekanbaru, Department of Internal Medicine, Pekanbaru, Indonesia*

The 57-year-old man came to the emergency department with progressive breathlessness and edema of the limbs since 10 days before admission. He also complained of an abdominal discomfort and a swollen scrotum. The patient seemed congested. There is edema in both limbs, scrotum, and abdominal ascites are also present. The patient's weight was 105 kg. On chest auscultation found crackles at the base of the lung during inspiration. Electrocardiogram results show atrial fibrillation with normal ventricular response. In laboratory tests, the serum creatinine values were increased (1.72 mg/dL), hyponatremia (128 mmol/L), and mild hyperkalemia (5.4 mmol/L). Echocardiography showed dilatation of the entire heart chambers, left ventricular ejection fraction 20%, decreased right ventricular function.
The patient with a history of CABG in 2014, after surgery he did not take regular medication. Within one year the patient is hospitalized 6 times due to heart failure. He also had a history of diabetes melitus with poor blood sugar control.
Management of heart failure was done by giving intravenous bolus Furosemide as much as 120 mg followed by intermittent bolus 100 mg 4 times per day. We also give him Ramipril 5 mg o.d and fluid restriction. On the first day of treatment, urine output is only 1000 cc per 24 hours. Edema and ascites have not diminished, the body weight is 102 kg. An additional Tolvaptan therapy is given 15 mg o.d. Tolvaptan is given within two days, without increasing urine production per day. Renal and electrolyte function evaluations were performed, no significant differences were found. Tolvaptan was discontinued, replaced with hydrochlorthiazide 50 mg o.d. Frequency of Furosemide is increased to 100 mg five times per day. After administration of HCT, urine production increased slightly to 1500 cc per 24 hours, but the edema persisted. An abdominal ultrasound examination was performed with dilated findings in the intrabdominal vein and ascites. It was decided to perform ascites puncture which drains serous fluid as much as 650 cc. Immediately after ascites puncture, urine production increased to 4000 cc per 24 hours without increased diuretic dose. Within two days, the patient's weight to 90 kg with improvement on the examination of kidney and electrolyte function. He was discharged with Furosemide 80 mg t.i.d, Ramipril 5 mg o.d, Spirolactone 50 mg o.d, Bisoprolol 1.25 mg o.d, and diabetes medication.
Diuretic resistance is common in patients with advanced heart failure, the handling becomes very difficult in patients who are not adherent to treatment. All efforts should be attempted to achieve decongestion and should be done in a short time. In this case, if no increase in urine production after ascites puncture, we have been considered for hemodialysis. A good and clear education to the patient should be done repeatedly to improve medication adherence, in order to avoid re-hospitalization due to heart failure in the future.

P2334

A young patient with heart failure and malnutrition - a holistic approach. which is the chicken and which is the egg?

E Edit Floderer[1]; R Luostarinen[1]
[1]*Karlstad Hospital, Department of Heart- and Acute Medicine, Karlstad, Sweden*

Introduction: Malnutrition and anxiety are seen in heart failure at the end stage disease. However, malnutrition as a possible underlying cause of heart failure is rarely seen in developed countries and therefore both evidence and recommendations are lacking.
Case presentation:
A 42 year old man, smoker, admitted to hospital with a feeling of malaise, chest pain, fatigue, dyspnea, dysphagia. Historically HLA-B27 positivity and idiopathic, recurrent hydrothorax were known. Also suffered from gastroesophageal reflux disease, certain grade of anxiety. No hypertension or diabetes were found. The physical examination showed tachypnea, cachexia with BMI 18 kg/m2, poor physical condition and severe panic attacks. Investigations revealed a severely dilated cardiomyopathy (with ejection fraction 10-15 %) without presentation of coronary artery disease, myocarditis, arrhythmias or myocardial infiltrative disease. Standard medical therapy failed to improve physical performance and ejection fraction. Transplantation was denied because of the poor performance status (NYHA IV) and mental health issues (severe anxiety and panic syndrome). Complementary therapy with enteral nutrition (tube feeding), treatment of anxiety and the addition of angiotensin receptor blocking neprilysin inhibitor (ARNI) improved the patient's overall health, functional capacity and fully reversed the heart failure.
Conclusions: Conventional treatment of heart failure often leads to improved cardiac status in most cases. However, it is important to recognize complicating conditions like malnutrition and severe anxiety (reason for the dysphagia) which may impede recovery. By complementing traditional heart failure treatment with additional therapies (as above) and by using a new medical therapy (ARNI) the patient's severe heart failure was fully reversed in this case and heart transplantation was no longer needed.

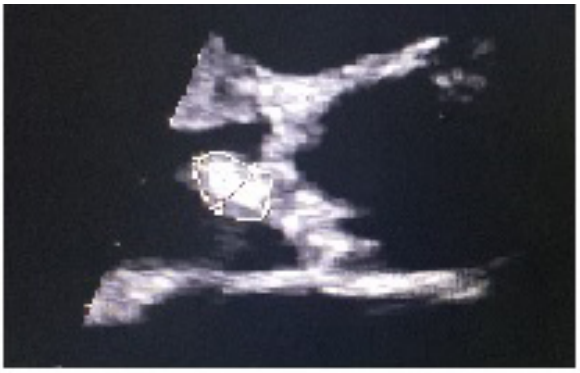
Acute Heart Failure - Pathophysiology and Mechanisms

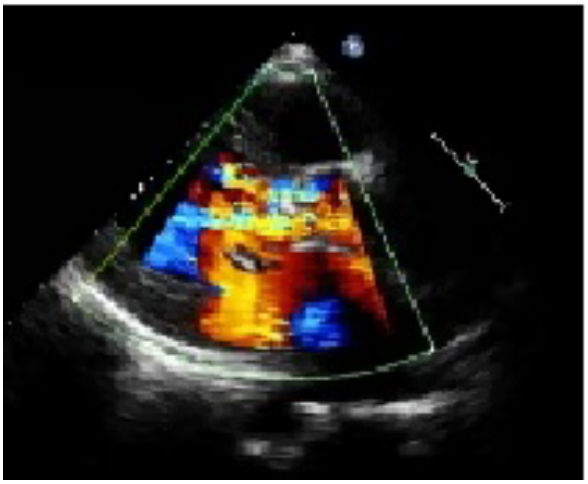
P2335

Acute heart failure in a preterm pregnant with infective endocarditis

M J Jhessica Pecson[1]; JR Bacani[1]
[1]*Philippine Heart Center, Adult Cardiology, Quezon City, Philippines*

Infective endocarditis during pregnancy is a rare but serious condition with significant fetal and maternal morbidity and mortality.
We report a 39 year old female, Filipino, known Rheumatic Heart Disease, G8P7 on her 29 weeks AOG who was admitted for worsening heart failure symptoms with history of chronic fever. She arrived at the emergency room awake in respiratory distress hence immediately intubated. Cardiovascular examination revealed dynamic precordium, displaced PMI, (+) diastolic murmur at the 2nd right intercostal space and (+) systolic murmur at the apex. Abdominal examination revealed positive for fetal heart tone. Diuretics and vasodilator given. Complete left bundle branch block seen in ECG and pulmonary edema in chest X-ray. Empiric antibiotic therapy was initiated. Transthoracic echocardiography revealed infective endocarditis of the aortic valve – a vegetation on the right coronary cusp with severe aortic regurgitation. She was referred then to surgery, infectious disease and Obstetric services. OB started patient on Dexamethasone for lung maturity. Patient was stabilized hence medical therapy continued to optimize fetal viability. However, on the 12th hospital day, Biophysical score revealed fetal distress hence patient underwent emergency cesarean section followed by valve surgery. Intraoperatively, there was perforation at right and left coronary cusps with vegetations. On the 3rd post-operative day, she was extubated, transferred to the ward and discharged on the 25th hospital day. Repeat transthoracic echocardiography 6 months post-operatively showed normally functioning metallic aortic and mitral valve with no paravalvular leak.





Aortic valve vegetation with severe AR

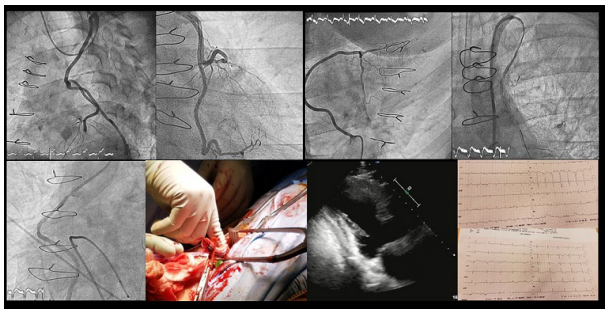
Acute Heart Failure - Treatment

P2336

Unusual vascular access for ECMO implantation after a complication during PCI.

MG Ascencio Lemus[1]; P Maiorano[2]; C Minguito Carazo[1]; L Castillo Pardo[2]; S Prieto Gonzalez[1]; C Palacios Echavarren[1]; S Del Castillo Garcia[1]; JC Morales Echarte[1]; P Menendez Suarez[1]; J Borrego Rodriguez[1]; A Perez De Prado[1]; M Castano Ruiz[2]; F Fernandez Vazquez[1]
[1]Hospital of Leon, Cardiology department, Leon, Spain; *[2]Hospital of Leon, Cardiac surgery department, Leon, Spain*

A 60 year-old man was admitted due to recurrent syncope. Medical background includes cerebrovascular disease: right internal carotid endarterectomy,1998. Severe left internal carotid stenosis. Peripheral vascular disease (aortic bifemoral bypass, 2010) and coronary artery disease (CABG in 2006: LIMA to LAD. RIMA to OM [T-graft to LIMA]. RA to PDA). 3 months prior to admission he began to experience syncopes, non-related to efforts and no chest pain.
No relevant data at physical examination. ECG at admission was a sinus rhythm with T wave inversion in leads I, AVL, V1-V2. No evidence of arrhythmias. An angio-CT was requested, reporting a moderate stenosis in right carotid territory, occlusion of left internal carotid artery and moderate stenosis in both subclavian arteries. Basal echocardiogram reported a LVEF of 55%, and apical hipokinesis. ECG exhibited new T-wave inversion in leads V2-V6. A stress echocardiography confirmed ischemia in the LAD territory; therefore he underwent an angiography that evidenced severe stenosis in the LAD, distal to the anastomosis of the LIMA graft, being permeable all of the grafts and no new stenosis in the other native coronary arteries. It was decided to perform a PCI on the LAD through the LIMA graft. After guidewire introduction to distal LAD, the patient experienced hemodynamic instability with severe hypotension and bradycardia and then cardiac arrest.
Advanced life support was initiated (orotracheal intubation, transfemoral pacemaker and intra-aortic ballon pump implantation) obtaining a pulse recovery in less than 10 minutes, high doses of amines were required. The angiogram exhibited severe spasm of the RA graft and loss of caliber in the proximal segment of LIMA, hence it was performed a DES implantation 3/48 mm into the LIMA graft; a flow recovery was proved. An echocardiogram at the bedside of the patient revealed a LVEF of 10%, no pericardial effusion, and due to the refractory cardiogenic shock, the patient was intended for ECMO placing, as a bridge to recovery.
Given the severe atherosclerotic disease the artery cannulation was a total challenge. It was planned an approach through the previous aortofemoral graft: by placing an end-to-side Dacron graft sewn into the right branch of the previous Dacron graft to insert the arterial cannula. Femoral venous cannulation was carried out by dissection and the implantation guided by TOE was successfully achieved.
Sufficient flow, adequate gas exchange and ventricular unloading were confirmed. A remarkable improvement on clinical, hemodynamics and echocardiographic findings were proved (LVEF 35 %, Simpson biplane). And thus, ECMO weaning was accomplished being possible its removal on the 6th postoperative day.
This case illustrates how this unusual approach by might be a safe and feasibly procedure for those patients with severe generalized atherosclerosis requiring mechanical support with no other alternative options for arterial cannulation.



Complicated PCI resulting in ECMO.

Coronary Artery Disease - Treatment

P2337

A case report of ischemic cardiomyopathy and purulent pericarditis

Y Niu[1]; CC Pai[2]
[1]Chang Bing Show Chwan Memorial Hospital, Cardiology, Chang Hwa, Taiwan ROC; *[2]Show Chwan Memorial Hospital, Surgery, Chang Hwa, Taiwan ROC*

Introduction: We report a case of a drug abuser with purulent pericarditis, accidentally found at bypass surgery for his severe ischemic cardiomyopathy.
Case Report: A 57-year-old male patient had presented with exacerbated dyspnea and intolerable chest pain since one week before admission. He has type II diabetes mellitus, hypertension, hepatitis B and hepatitis C, and a history of heroin dependence under methadone treatment. The patient also has peripheral artery occlusive disease with chronic ulcer over bilateral lower legs. Wound culture of the ulcer lesions was Klebsiella Pneumonia. When he visited emergency room, physical examination revealed blood pressure of 137/94 mmHg, heart rate of 82 beats/min., respiratory rate of 17/min and body temperature of 37°C. Laboratory data showed leukocytosis, significant elevated C reactive protein (CRP): 23.07 mg/dL, and mild elevated troponin I: 0.87 ng/mL. EKG showed abnormal Q wave over inferior and anterior leads, showing non-ST-elevation myocardial infarction. A chest X-ray demonstrated cardiomegaly. Coronary angiogram revealed 3-vessel-disease with left main lesion. His right coronary artery (RCA) showed chronic totally occluded (CTO, Figure 1, Panel A). The left main showed 50% stenosis, left anterior descending artery (LAD) showed CTO, and the proximal segment of left circumflex artery (LCX) showed 70% stenosis (Figure 1, Panel B). Echocardiogram revealed mild pericardial effusion (PE) and inferior-lateral wall hypokinesia (Figure 1, Panel C). Bypass surgery was performed. However, severe adhesion over mediastinum, thickened pericardium, moderate amount of yellowish fluid in the pericardium was noted during operation. There was fibrin peeling over pericardium and abscess rupture over posterior wall of pericardium (Figure 1, Panel D). Left internal mammary artery (LIMA) was connected to LAD, and left radial artery was used to connect aorta and LCX. The symptom of chest pain subsided and his infectious signs were improved soon after surgery.

Conclusion: We report a drug abuser of severe ischemic cardiomyopathy with purulent pericarditis. The implication of the case is to notify the possible existence of multiple etiologies of acute chest pain. Acute chest pain should be differentiated from aortic dissection, myocardial infarction, myocarditis, pneumonia / pleuritis, pulmonary embolism, pneumothorax and pericarditis. The preliminary diagnosis of myocardial infarction was not complete until the abscess was found during surgery.

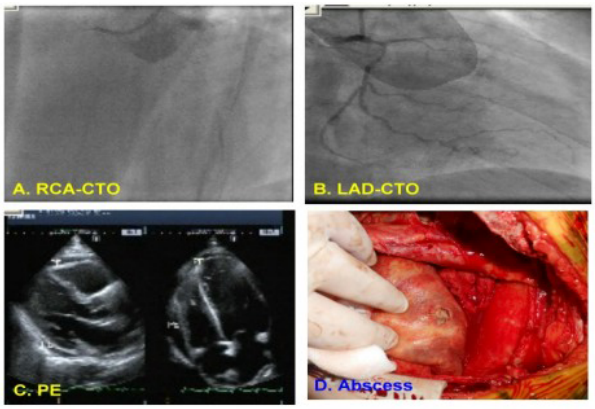


Figure 1 Diagnosis

Myocardial Disease - Clinical

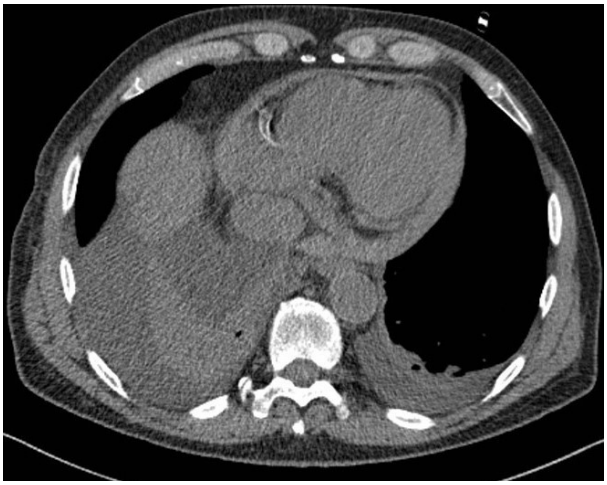
P2338

Autoimmune pericarditis after device implantation and atrial lead reposition

S Garkina[1]; S Nemtzov[1]; V Lebedeva[1]; R Konoshkova[1]; S Gureev[1]; R Tatarsky[1]; D Lebedev[1]; G Nikolaev[1]
[1]*Almazov National Medical Research Centre, Saint-Petersburg, Russian Federation*

We present case report of a 71-year-old male who underwent uncomplicated dual chamber pacemaker implantation due to binodal disease (transient 2 degree SA block, transient 2 degree AV block). His clinical status was stable, except moderate thrombocytopenia (platelets count was 93*10 9/l. During in-hospital follow up high atrial lead threshold was registered (up to transient loss of capture). Despite chest X-ray results without lead dislocating the revision of pacemaker system revision was performed. During the procedure massive subcutaneous hematoma near subclavian vein punction points was noted. Atrial lead was repositioned in right atrial appendage with acceptable parameters (2 mV endocardiogram amplitude, pacing threshold of 0.8 mA/0.4 ms , impedance of 700 Oms). During postoperative period patient was stable. In a week after implantation the patient developed retrosternal chest pain, hypotension (systolic BP was 60/40 mm Hg), severe hiccough and pain in the back during deep breath, low grade fever (37,5 - 38 C). X-ray showed right-sided hydrothorax. Blood test showed hemoglobin level lowering to 92 g/l, erythrocytes - 3,06*1012 /l, C-reactive protein level was 12,5 g/l. Chest CT-scan demonstrated the liquid content of the layer thickness in the posterior sections up to 6-7 cm (figure 1), hemorrhagic pericardial effusion (up to 14 mm). The patient received symptomatic therapy and hemotransfusion of 2 doses of red blood cells. Right pleural cavity drainage was performed with evacuation of 1000 ml of slightly turbid liquid. The pleural fluid analysis revealed lymphocytosis (no erythrocytes), single mesothelium cells with reactive changes, indicating reactive emptying with a lymphoid response involving an autoimmune response. Drainage of the pericardial cavity was not recommended. Further therapy with NSAIDs promoted regression of symptoms. Control chest X-ray showed no air or fluid in pleural cavities.

This case illustrates typical signs of post-pericardiotomy syndrome including fever, pleuritis and pericardial effusion with underlying autoimmune mechanism. It is observed rather rarely after interventional procedures and device implantation but should be always considered by clinicians especially in early post-operative period.



Chest CT scan

Pulmonary Circulation, Pulmonary Embolism, Right Heart Failure - Clinical

P2339

The difficult diagnosis of dyspnoea - PH due to HFpEF

M Magdalena Dudek[1]; M Kaluzna-Oleksy[1]; J Migaj[1]; M Lesiak[1]; E Straburzynska-Migaj[1]
[1]*Poznan University of Medical Sciences, 1st Cardiology Department, Poznan, Poland*

70-year-old male presented to our hospital because of progressive dyspnoea and massive oedema of lower limbs. His medical history was significant for hypertension, diabetes mellitus type 2, persistent atrial fibrillation, chronic renal failure - stable for many years (CKD G3a), and obesity (BMI 35,3 kg/m2). On admission, physical examination revealed, legs oedemas, unregularly heart rhythm with HR about 120 bpm, BP 140/80 mmHg, no abnormalities in pulmonary auscultation. Laboratory tests showed elevated levels of NT-proBNP (2552 pg/ml). Transthoracic echocardiography showed enlarged right ventricle (RV 36 mm - parasternal long axis view; 52 mm 4-chamber-view (4CHV)) with normal size of the rest chambers of the heart - left ventricle (LV 44 mm, 4CHV 25mm), posterior wall of the left ventricle (11 mm), interventricular septum (12 mm), left atrium (LA 35 mm) and preserved ejection fraction (LVEF 50%), as well as shortness of pulmonary artery acceleration time (ACT 59 ms), elevated right ventricular systolic pressure (RVSP 70 mmHg), s' wave 5 cm/s and paradoxical movement of interventricular septum. Coronary angiography revealed with severe stenosis of distal left main (LM)-70% and left circumflex artery (LCx) - 50% proximally and 90% distally. Percutaneous coronary intervention (PCI) of LM with DES implantation was successfully performed. Despite successful coronary angioplasty, dyspnoea was increasing, so computed tomography angiography (CTA) of the chest was performed. It revealed no features of pulmonary embolism and significant amount of fluid in right pleural cavity. Lung scintigraphy showed low probability of pulmonary embolism. Due to suspicion of pulmonary hypertension (PH) based on clinical symptoms and echocardiography the right heart catheterization was performed. Results of catheterization showed mean pulmonary artery pressure (PAP) 42mmHg, pulmonary capillary wedge pressure (PCWP) 24 mmHg, pulmonary vascular resistance (PVR) 3 Wood Unit, diastolic pulmonary gradient (DPG) 3 mmHg. Based on the carried out diagnostics isolated post-capillary pulmonary hypertension was diagnosed. The patient was treated with optimal pharmacotherapy in accordance to guidelines. Currently, the patient is treated optimally, in a stable clinical condition (NYHA II), and is under constant medical supervision.

Hypertension - Other

P2340

Assessment of the polymorphic genes variants of the lipid and carbohydrate metabolism, vascular inflammation and neurotransmitter system in the first ischemic stroke

V Veronika Shishkova[1]
[1]*Moscow Medical Centre Neurorehabilitation , Moscow, Russian Federation*

Aim: To study the relations of polymorphic variants of the genes: ????, MTHFR, IL8, IL6, TNF-?, VEGFA, ADIPOQ, ADIROR, APOB, APO?-V,
APOC-IV, LPL, LP(a), BDNF, GRM1, GRM3 and development of the first ischemic stroke (IS).

Material and methods: The alleles frequencies and genotypes assessed for 20 mono-nucleotide polymorphic gene variants in 435 patients, who had first IS, and 229 persons with no stroke, comparable with age, gender, place of living and ethnicity. Genotyping of polymorphisms was done with the prepared TaqMan probes.
Results: For polymorphisms ???? (rs676210) and IL8 (rs1803205) there was significant difference between groups in the variety of minor alleles and genotypes.
Conclusion: There is significant relation of mononucleotide polymorphisms of the genes ???? (rs676210) and IL8 (rs1803205) with the development of first IS in the studied groups.

Chronic Heart Failure - Other

P2341
A fatal case of the Barth Syndrome in 1-year-old boy

TS Loevets[1]; NM Boldina[1]; EV Yakovleva[1]; TL Vershinina[1]; AA Kostareva[2]; ES Vasichkina[1]
[1]National Almazov Medical Research Centre, Pediatric Cardiovascular Diseases Research Department, Saint Petersburg, Russian Federation; *[2]National Almazov Medical Research Centre, Institute of Molecular Biology and Genetics, Saint Petersburg, Russian Federation*

Barth syndrome is a rare condition characterized by cardiomyopathy, skeletal myopathy, neutropenia, growth delay, exercise intolerance, distinctive facial features and 3-methylglutaconic aciduria. Barth syndrome occurs almost exclusively in males. Mutations in the tafazzin gene (TAZ) which is located at the long arm of the X chromosome are associated with Barth syndrome.
Objective: To present a rare clinical case.
Methods: Complex inpatient examination.
History of the disease: At the age of 3 months patient was hospitalized to intensive care unit with severe heart failure (HF) and high temperature. After the first examination enlarged LVEDD (45 mm), decreased EF (25%), hypertrophy of interventricular septum (IVS, 10 mm), mitral insufficiency 2-3 were diagnosed by echocardiography (ECHO), bilateral pneumonia and right-sided hydrothorax was established by chest X-ray. The disease was regarded as acute myocarditis. The early management included mechanical ventilation, tube feeding, intravenous inotropes, loop diuretics and immunoglobulin G. After the stabilization ACEi, diuretics and Digoxin per os were prescribed with positive result by ECHO (LVEDD 38,5 mm. EF 40-45%).
Results: Patient was admitted in our clinic at the age of 8 months with such complaints as excessive sweating, dyspnea, poor growth, poor weight gain, delay of motor skills. He had no syncope. No family history of cardiac disease.
Laboratory findings: intermittent neutropenia (2,53-0.85x109/L), high level of NT-proBNP (11927.00 pg/ml), Troponin I (0.0655 ng/ml). No data for infection agents by PCR and bacteriological methods and lysosomal storage diseases.
ECG and Holter ECG monitoring were demonstrated characteristic "sagging" ST segments and T waves, short QT interval without heart rhythm disturbances.
ECHO: enlarged LV (LVED 32-35 mm), low EF 37%, hypertrophy of IVS 9 mm.
Anomalies of the coronary arteries were excluded.
Neurological examination with conducting of electroneuromyography and skeletal muscle biopsy showed nonspecific signs of myopathy.
Research of 108 genes associating with different variants of cardiomyopathy using Illumina MiSeq system and Sanger's method sequencing was conducted. The pathogenic mutation in TAZ chr X153648583 which associated with Barth Syndrome was found.
Therapy of chronic HF was corrected: dose of digoxin was reduced, furosemide - increased, ß-blocker (Carvedilol) - added.
At the age of 12 months child fell ill with acute urinary tract infection, which led to cardiac decompensation, and eventually to a fatal outcome.
Conclusions: The highlights of the reported case that it is difficult to differentiate the etiology of cardiomyopathies in infants because of its similar clinical course in the debut. Combination of cardiac pathology with involvement of other systems occurs, complete clinical examination including genetic testing is necessary. It could be useful for determining the tactics of further management and prognosis for patient and his family.

P2342
Heart failure in patient with hypothyroidism

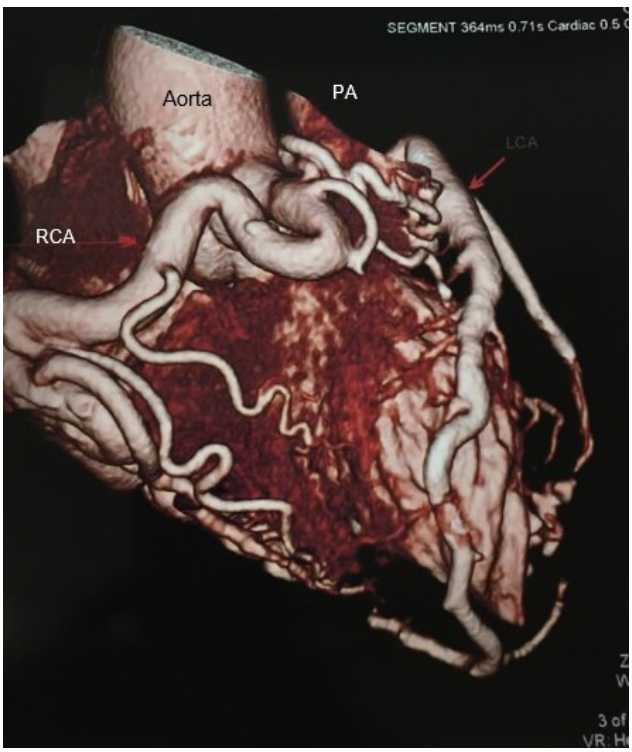
L Levan Gugushvili[1]
[1]LTD MKL, ER, Batumi, Georgia Republic of

The cardiovascular system is the main target organ of thyroid hormone. Overt hypothyroidism decreases myocardial contractility, and diminished myocardial contractility reduces thyroid hormone metabolism. 32 years old woman comes for consultation to cardiologist with complaints: swelling mainly of the face and upper extremity, difficulty breathing and dysritmia, dry skin. These changes started about 2 weeks ago. By anamnesis shown that about 2 years ago conducted a tonsillectomy, preoperative examinations with any pathological changes. Is not married, never been pregnant and does not take any contraceptives. Cardiologist did the ECG and echocardiography, they were found impaired left ventricular ejection fraction, the negative T wave in I, II, aVF, V4-6. A small amount of free fluid in the both pleural, C-reactive protein in normal, by blood chemistry hypo chromic anemia, blood plasma BNP(B-type natriuretic peptide) - 225pg/ml (N - <130ng/ml), Troponin I <0.1ng/dl (N- <0.1ng/dl).
Suspected that patient has hypothyroidism, by ultrasound research main volume - 39.9 ml, thyrotrophic hormone (TSH) - 63.3 (N-0.27-4.2mIU/L) and FT4 - 0.1 (N-1.0 - 1.6 ng/dl) they was diagnosed primary hypothyroidism. We start replacement therapy with increasing doses of levothyroxine to 100mkg. After compensation of hypothyroidism left ventricular ejection fraction returned to normal levels, ECG changes are corrected, free fluid in the pleural not observed all complaints disappeared. Patient continues treatment with levothyroxine. We will look after in dynamic. In conclusion, as seen cardiovascular changes are reversible when the underlying thyroid disorder is recognized and treated.

P2343
A rare case of Bland-White-Garland syndrome in a 60-year-old woman

H Thai Hao Phan[1]
[1]Pham Ngoc Thach University of Medicine, Cardiology, Ho Chi Minh, Vietnam

Background: Bland-White-Garland syndrome or Anomalous origin of the left coronary artery from the pulmonary artery (ALCAPA) is a rare congenital anomaly. The usual clinical course is severe left sided heart failure and mitral valve insufficiency presenting during the first months of life. However, in some cases collateral blood supply from the right coronary artery is sufficient and symptoms may be subtle or even absent. We report A Rare Case of Bland-White-Garland Syndrome in a 60-Year-Old Woman.
Case presentation: A 60-year-old female patient presented with a 10-day history of shortness of breath and exertional angina, with ischemic heart disease, mitral regurgitation, heart failure 5 years ago. Her physical examination revealed a grade III/VI systolic murmur over the apex. Electrocardiogram showed normal sinus rhythm with left ventricular enlargement, poor R wave progression in the precordial leads.



Cardiac MS-CT 640 Slices

The patient's echocardiographic imaging revealed dilated left-sided heart chambers, as well as reduced left ventricular ejection fraction (43%), severe mitral valve insufficiency and elevated systolic pulmonary artery pressure (60 mmHg). Multislice computed tomography with three dimensional reconstruction showed that the left main coronary artery originated from posterior side of the main pulmonary artery, confirming the diagnosis of ALCAPA (Figure). The patient was treated by ligation of the left coronary artery from the pulmonary artery combined with coronary artery bypass grafting and mitral valve repair.

Discussion: 85% of all cases of ALCAPA present within the first two months of life. However, symptoms may be misinterpreted (as in our case) or even be absent. In adult life patients with ALCAPA could present with symptoms of heart failure, mitral valve insufficiency, angina or arrhythmias. Objective findings include cardiomegaly on chest X-ray, and ECG may display an anterolateral infarct pattern. The diagnosis can often be made by two-dimensional echocardiography with direct visualization of the abnormal origin of the left coronary artery and retrograde flow into the pulmonary artery. In cases where the clinical suspicion is strong, a coronary angiography or CT-angiography should be performed.

Conclusion: the diagnosis of ALCAPA should be considered in adults without evidence of ischemic heart disease presenting with arrhythmias, left sided heart failure with or without mitral valve dysfunction, since an early diagnosis and surgical treatment generally results in an excellent prognosis.